Posters

Posters Adaptive & IGRT

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A NON-CONTACT METHOD FOR THE ACQUISITION OF BREATHING SIGNALS THAT ENABLE DISTINCTION BETWEEN ABDOMINAL AND THORACIC BREATHING

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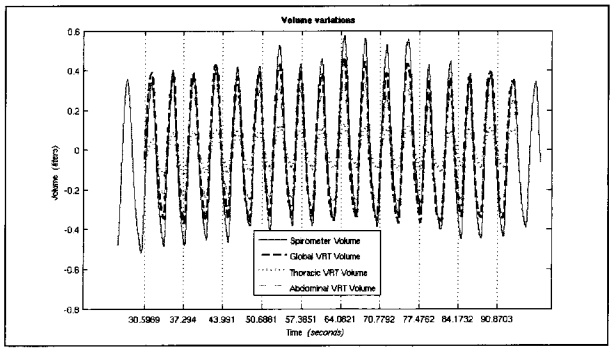
Purpose/Objectif: For adaptive radiotherapy of lung cancer, it is crucial to acquire a meaningful breathing signal in order to build 4D-CT models and to gate or track radiation delivery. Current methods are: spirometry, tracked marker on the patient's skin, or both combined. We propose an alternate method based on the acquisition of stereoscopic video images of a patient's breathing torso. This work establishes its equivalence to spirometery and demonstrates several advantages.

Materials/Methods: A stereoscopic system acquiring video images of the patient's torso (Vision RT) was used to capture dynamic surfaces of the subject's skin (reconstructed by the Vision RT system). Spirometric data was simultaneously captured (Micro Medical). 5 volunteers underwent this study each breathing: 1 minute freely; 1 minute thoracically; 1 minute abdominally. Volumetric information is derived from the surfaces by computing at each capture time the volume between the couch and the portion of the stereoscopically acquired surface included in a predefined bounding-box. A global volumetric signal is thus extracted. Flow information is then computed by differentiation of the volumetric signal. Abdominal and thoracic components are similarly obtained by splitting the bounding-box in two along the inferior part of the rib cage. Correlation between the spirometer and surface-based signals, Fourier transforms of the signals, and proportions of abdominal and thoracic breathing were investigated.

Results: A statistically significant good agreement between the simultaneous spirometric signals and the surface-based signals was observed (Kendall's τ: flow: 0.69—0.87; volume: 0.45—0.85 - outlier 0.28; max p-values: flow: 1.69E-87; volume: 7.29E-10). Furthermore, all the signals except the spirometric volume signal exhibited the same period and were synchronous; the spirometric volume usually showed a drift, which induced a longer period. Contributions of thoracic and abdominal components per breathing cycle were also quantified. The surface-based flow data was hence found to be equivalent to the spirometric flow data and exhibited the advantage over spirometry of outputting a drift-free volumetric signal. This surface-based acquisition of respiratory signals also shows advantages over the marker-based approach. It is global and bears extractable information on abdominal and thoracic components.

Conclusions: We present a non-invasive non-contact method for acquiring respiratory signals that: (1) provides information equivalent to spirometry, (2) is drift-free and (3) is decomposable in abdominal and thoracic components.Acknoldgements: Vision RT, Micro Medical.



504 poster

A NON-INVASIVE APPROACH TO TRACK INTRA-FRACTIONAL TUMOUR MOTION

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Purpose/Objectif: It is not straightforward to detect the position of a moveable tumour to determine intra-fractional motion. Existing approaches to obtain the tumour trajectory make use of markers or active sensors implanted in or near the tumour, fluoroscopic imaging or a combination of both. For simplicity the respiratory signal alone is often utilized as a surrogate for tumour motion for e.g. respiratory-gated treatments (RGRT) instead of the true tumour position. Several studies have shown that for RGRT the residual tumour motion and base line shifts can be considerable and as a consequence have suggested not to reduce treatment margins for gated treatments unless the residual tumour motion can be either detected or reduced. In this work we present an alternative approach to observe tumour motion of lung tumours during irradiation without invasive markers and without giving any additional imaging dose. The idea is to make use of two independent data sets that complement each other to have redundant information regarding the tumour position available in case one method yields doubtful information.

Materials/Methods: The primary data is based on continuous MV imaging with the therapy beam on a standard electronic portal imaging device (EPID) at a rate of 2-15 Hz. Previous investigations have shown that it is indeed possible with suitable algorithms and image processing to track lung tumours in real-time in portal images despite the limited image quality. The second data set is based on the abdominal movement due to breathing. This is acquired by placing a specially designed tool on the abdomen of the patient which is tracked at a rate of 20 Hz with an IR camera. The same tracking camera has also been installed in the CT room and it is envisaged to correlate the 3D abdominal movement with tumour motion at the time of imaging. This information can than be used as a priori information at the time of treatment.

Results: So far primary and secondary data of more than 10 patients treated for lesions in the lung have been acquired and analyzed. In most cases it was possible to track tumour motion albeit not always from all beam angles. Using mathematical models based on System Identification excellent correlation with the abdominal movement could be obtained.

Conclusions: The results are promising but need to be verified. Further work includes the verification of the approach with a phantom designed in-house with which realistic non-symmetrical tumour motion can be simulated by means of an industrial robot capable of movements in six degrees of freedom.

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A TECHNIQUE FOR MODELING LUNG TUMOR RESPONSE TO RADIATION THERAPY

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Purpose/Objectif: Volumetric imaging data acquired during CT-based Image Guided Radiation Therapy (IGRT) can be used to

measure tumor response. Predictive Adaptive Radiation Therapy is a novel treatment technique that utilizes volumetric IGRT data to actively predict the tumor response to therapy and estimate clinical outcomes during the course of treatment. The goal of this study was to develop a model for predicting tumor response during treatment using serial Megavoltage CT (MVCT) imaging.

Materials/Methods: MVCT images were acquired prior to the delivery of 660 lung treatment fractions for 20 non-small cell lung cancer patients. A Predictive Adaptive Radiation Therapy response model was developed using locally weighted polynomial regression (LWPR), which is a non-parametric, memory-based technique that predicts future tumor response by processing a memory matrix of retrospective tumor response data. When new tumor response data is entered during treatment, the algorithm locates similar tumor responses from the memory matrix and performs a weighted polynomial regression with nearby observations. Retrospective data from 20 patients was used to build the initial memory matrix of tumor responses verses elapsed days of treatment. A genetic algorithm (GA) was used to calculate the optimal days to measure the tumor volume from the IGRT images. In addition, the GA was used optimize kernel bandwidths.

Results: The LWPR predictive algorithm was used to predict the tumor response and the confidence intervals for 20 patients. The GA found that predictive accuracy was the greatest for tumor response data acquired on days 0, 3, 7, 11, 12, 15, and 18 during treatment. Figure 1 shows the MVCT images and tumor response model results for a typical patient. The predictive model was extremely accurate in predictions made near the end of a patient's treatment. The average error for the predictions of the final tumor volume was 12%, with the true volumes always bounded by the 95% confidence interval. The greatest model uncertainty occured during the middle of treatment where the tumor response relationships are more complex and the predictors are more varied.

Conclusions: A Predictive Adaptive Radiation Therapy model was developed that accurately predicted final tumor volumes for 20 lung cancer patients. These predictions were made using imaging data from 8 fractions early in the course of treatment. This allowed the final tumor volume to be predicted near the beginning of treatment without having to go through the tedious process of acquiring the MVCT and contouring the tumor many times. Since the predictions are accurate with quantified uncertainty, they could eventually be used to optimize treatment.

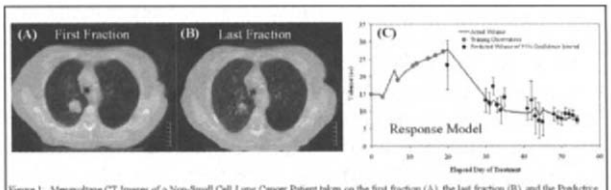

Figure 1: Megavoltage CT Images of a Non-Small Cell Lung Cancer Patient taken on the first fraction (A), the last fraction (B), and the Predictive Adaptive Therapy tumor response model (C). The measured tumor volumes from 8 imaging sessions (*highlighted by pink circles*) was used to predict the tumor response (*black circles bound with 95% confidence intervals*). Note that all 8 observation points indicated that the tumor was increasing in volume. The Predictive Adaptive Therapy tumor response model correctly identified that the tumor would begin regressing after 20 elapsed days of treatment.

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ACCELERATED DEFORMABLE REGISTRATION OF REPETITIVE MRI DURING RADIOTHERAPY IN CERVICAL CANCER

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Purpose/Objectif: Tumour regression and organ deformations during radiotherapy (RT) of cervical cancer represent major challenges regarding accurate conformation and calculation of dose when using image-guided adaptive radiotherapy. Deformable registration algorithms are able to handle organ deformations, which can be useful with advanced tools such as auto segmentation of organs and dynamic adaptation of radiotherapy. The aim of this study was to accelerate and validate deformable registration in MRI-based image-guided radiotherapy of cervical cancer.

Materials/Methods: Three MRI scans (0.2 T, Philips Panorama) were obtained for each of two patients with locally advanced cervical cancer: first scan before and two scans during external beam RT. Bladder and rectum were manually contoured on all MRI scans and used as a reference. The deformable registration algorithm was based on a viscous fluid model using image intensities to guide the fully automatic registration process. A graphical processing unit (GPU) found on modern graphics hardware was utilised to accelerate the registration process. The deformable registration was validated by comparing manually delineated contours during RT to auto segmented contours predicted by applying the deformable registration on the organ contours delineated on the initial MRI scan. The overlap of contours was quantified by the co-incidence index (CI) defined as the ratio between the union and the intersection of the contours. In case of a perfect overlap of contours CI would be 100% and no overlap would result in CI of 0%. Conventional rigid registrations were additionally performed, and corresponding CI's were calculated.

Results: The deformable registration was accelerated by a factor of up to 25 compared to a version not using a GPU. A registration time in the order of 5-10 minutes was achieved. The volume of bladder and rectum varied due to difference in filling with a mean standard deviation of 30% and 45%, respectively. For the rigid registration, soft tissue deformations caused by movement and organ filling resulted in low co-incidence indices of 49% ± 15% and 19% ± 7% for bladder and rectum, respectively. The benefit of the deformable registration as compared to rigid registration was demonstrated by a significant increase in co-incidence index: from 49% to 83% ± 7% (bladder) and from 19% to 86% ± 4% (rectum).

Conclusions: The registration time was accelerated significantly by using a GPU based algorithm compared to a conventional implementation. Bladder and rectum was auto segmented with high degree of reliability, and deformable registration was far superior to rigid registration for these organs in cervical cancer patients. The perspective of the method is that viscous fluid deformable registration can be performed on a time scale relevant for adaptive dose planning.

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ACCEPTANCE TEST OF AN IMAGING SYSTEM FOR IGRT

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Purpose/Objectif: IMRT technique is a good solution to shape dose distribution round the target volume and it allows to deliver a high dose to the tumor. However target can move both during treatment session and from one session to another as a result of organ motion and different settings of patient. IMRT alone cannot reduce margins around CTV and OAR: for this purpose new image-guided techniques of tumor localization and tracking are necessary.

The aim of this study is to assess the performance of an imaging device for IGRT and the method to commission it for clinical use.

Materials/Methods: We use a Varian Clinac 21EX accelerator equipped with On Board Imager (OBI), an X-ray imaging system with an aSi flat panel mounted on the gantry of the machine via robotic controlled arms which operate along three axes of motion.

Following the description of the acceptance test: first of all we verify the alignment of the imager panel to the beam isocenter and the co-

incidence of the arm rotational axes of the detector and the source to the gantry rotational axis throughout the entire 360° of gantry rotation. Tests can be divided in safety, mechanical, radiological and connectivity proofs. Safety tests are those typical of radiological devices together with the check of collision detection switches. Mechanical tests concern movement accuracy of both, X-ray source and detector. As for radiological proofs, we execute accuracy tests of radiological parameters for both digital fluoroscopy and digital radiography, and measure the image quality parameters: high contrast resolution, gray scale linearity, automatic brightness control, low contrast sensitivity. Since OBI can acquire CBCT the main CT image quality parameters are measured using Catphan phantom: density resolution, spatial linearity, image uniformity, slice distance, high and low contrast resolution. Connectivity of imaging device to VARiS Vision (R&V system and TPS) is tested to guarantee the availability of images for both patient positioning, comparing them to reference images, and eventually for planning on the new CT data set.

Results: All tests and measurements are in agreement with factory specifications. Values of high and low contrast resolution of CT images are quite good: for head scan 10 lp/cm and 1% (5 mm detail diameter) respectively, while ring artifacts in the central area, frequent in CBCT images, are negligible. We also verify CT image quality using Alderson Rando.

Conclusions: One of the main interest is CT image quality, above all in the perspective of using CT data sets for planning during treatment course whenever patient anatomy significantly changes. Acceptance test proposed by factory does not include dosimetric measurements while it should be advisable to quantify dose contribution to OAR. Integration and optimization of preexistent acquisition protocols for different anatomical zone is desirable too.

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ACCURACY OF TARGET LOCALIZATION AND HOUNSFIELD-UNIT RECONSTRUCTION OF CONE-BEAM CT ACQUISITION WITH VARIAN`S ON-BOARD IMAGER

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Purpose/Objectif: Improved target localization using Cone-Beam CT (CBCT) acquisition with the Varian On-Board Imager (OBI) offers the possibility of reduced margins and dose escalation. In addition, CBCT imaging simplifies replanning of patients with significant tumor shrinkage as a result of convenient 3D imaging of the patient at the treatment session. These applications impose strict requirements to the geometrical accuracy and the Hounsfield unit reconstruction of the CBCT images. Therefore, the geometry and the Hounsfield unit reconstruction of the CBCT images are thoroughly investigated.

Materials/Methods: After online correction of the patient position using CBCT imaging, the main contributions to the uncertainty of the target localization arises from geometrical errors of the CBCT image, misalignment between the center of the CBCT image and the radiological isocenter of the accelerator, matching errors, and errors of the couch translation. Each of these errors are examined separately. Special attention is given to the geometry of the CBCT image for different anatomic sites, scan parameters and couch configurations. These tests are performed using a Perspex phantom with regularly-spaced holes with a distance of 25 mm. The phantom is modular, making it possible to simulate CBCT scans of head and neck, pelvis and extremities. In addition, the combined geometrical error is investigated with Varian's marker seed phantom. The Perspex phantom is also used to investigate the Hounsfield unit reconstruction for different anatomical sites, scan parameters and couch configurations.

Results:

A detailed understanding of the accuracy of the target localization and Hounsfield-unit reconstruction of CBCT acquisition with the Varian OBI is obtained. Based on the results, a complete quality assurance program for CBCT acquisition is developed.

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ADAPTIVE EXTRACRANIAL STEREOTACTIC RADIOTHERAPY: A FEASIBILITY STUDY

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Purpose/Objectif: Extracranial Stereotactic Radiotherapy (ESRT) represents an interesting modality of cure for small neoplasms based on the use of ablative doses. Small CTV to PTV margins are required to limit the amount of irradiated tissues, based on sophisticated immobilization systems. The aim of this analysis is to present a method developed in our institution to individualize the set-up and internal margins.

Materials/Methods: ESRT was implemented by the Precise-Plan treatment planning system (Elekta, UK). Patients were immobilized using the Elekta Stereotactic Body-Frame. Five consecutive fractions were delivered; dose/fraction and total dose were defined based on a dose-escalation institutional protocol. A class solution with 4 non-coplanar fixed beams (plus 1-2 beams for isocenter verification) based on the tetrad configuration was used in all patients. Before treatment, patients underwent 3 CT studies in the treatment position. Additional CT simulations were planned in patients in whom major deviations were recorded. Reference points were tattooed at the first CT. CT-images of the sequential studies were superimposed using the image fusion utility of the Oncentra system (Nucletron, The Netherlands). Isocenter displacements were measured in the three axes. In order to define individual organ motion, in patients with neoplasm located in the thorax or abdomen, 30 consecutive scans were obtained with the patient freely breathing, without moving the CT couch. Portal images were obtained daily, at 0° and 90°, before any delivered fraction. Corrections were made until less than 3 mm deviation (between isocenter and bony references) was obtained in all directions. The CTV to PTV margin was defined as maximum tumor displacement (recorded at sequential CT-scan studies) in every axis, plus almost 5 mm, in 5 mm steps (example: 3mm in AP-PA direction à 10 mm margin; 8 mm in CC direction à 15 mm margin).

Results: 20 patients (M/F: 14/6; median age: 67, range: 55-85) were included in the analysis. Mean (±SD) isocenter displacements in the x, y, and z axis were (mm) 1.7 ± 2.0, 1.5 ± 0.9, 2.5 ± 2.6, respectively. CTV to PTV margin ranged between 5 mm and 10 mm in AP-PA direction, between 5 mm and 10 mm in LL direction, and between 5 mm and 15 mm in cranio-caudal direction.

Conclusions: The use of an adaptive planning procedure, for patients enrolled in an ESRT protocol, allowed to individualize anisotropic treatment margin and therefore to optimize the conformity of irradiation in the single patient. Furthermore, repeated treatment simulations of the CT couch improved patients confidence with the immobilization system, before treatment.

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ANALYSIS OF INTRA-FRACTION PROSTATE MOVEMENT USING IMPLANTED GOLD MARKERS

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Purpose/Objectif: We have treated 453 prostate patients utilizing implanted gold markers for off-line position verification. With off-line correction protocols we can reduce the systematic positioning errors. On-line correction protocols aim at reducing the random errors as well, but the results are influenced by the intra-fraction movement. Therefore we assess the intra-fraction prostate movement in this group of patients.

Materials/Methods: 453 prostate patients were implanted with two or three gold markers inside the prostate. We used an equidistant five beam step-and-shoot IMRT technique. The first segments of all five gantry angles were imaged using the iView GT portal imaging facilities on our Elekta accelerators. The markers can be reconstructed from a combination of two sequential images. This results in four prostate positions per fraction. Taking the first position as the reference position of a fraction, the other three show the intra-fraction prostate movement. The time between the first (reference) and the last position is approximately 5~minutes.

Results: On average, the displacement increases during a single fraction as is shown in Figure 1. This figure also shows that for the last time point, in 17% of the fractions we find a total displacement of less than 1mm. 63% stay within 2mm.

Conclusions: The displacements found in this study show that intra-fraction movement in the range of 1-3 mm, occurs in a significant part of the fractions. For our off-line correction strategy this has no impact. However for on-line position verification this implies that determination of the prostate position at the start of a fraction is not sufficient to characterize the prostate position with a millimeter accuracy.

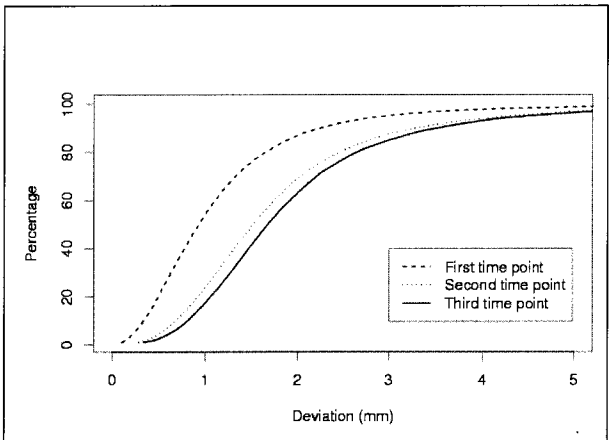

Figure 1: Cumulative deviation histogram for the three (intra-fraction) time points relative to the reference prostate position. The curve shows the percentage of fractions where the deviation from the reference position is smaller than the indicated value.

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ANATOMICAL VARIABILITY OF HEAD AND NECK CANCER PATIENTS

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Purpose/Objectif: Head and neck cancer patients in our clinic receive radiotherapy while immobilized by a 5 point mask. A rigid body approach for setup verification and correction is used. In this study geometrical uncertainties of local anatomical regions were quantified and compared with global patient setup errors.

Materials/Methods: Cone beam CT (CBCT) scans of 15 patients (on average 7 scans per patient) were routinely acquired for setup verification. Local rigid body registration (chamfer matching) was used as a tool to measure 3D displacements of bony anatomy from CBCT to planning CT. For this study the following regions of interest (ROI) were specified: the vertebrae C1 to C3, C3 to C5, C5 to C7, the mandibula, the jugulum, the os occipitale, the bony anatomy in the proximity of the PTV and the remaining bony anatomy anterior and caudal of the PTV (indicated by remainder). Positional changes of a ROI contain a rigid part (global patient setup errors, common to all ROI) and a non-rigid part (local deformations). To make this distinction, the displacements were taken relative to a common reference: C3-C5 (retrospectively simulating an online correction protocol based on vertebrae C3-C5 including corrections for rotations). Results were analyzed in terms of group mean error M, systematic error Σ and random error Σ.

Results: Table 1 shows local variability of bony anatomy relative to ROI C3-C5. In general deformations tend to become larger with the distance from the reference. In magnitude they become comparable to or even larger than global setup errors. The data on global setup of the ROI C3-C5 results from an offline shrinking action level protocol. Considerable group means after corrections to the reference were found for the jugulum (AP direction 1.3 mm), the os occipitale (LR direction 0.9 mm) and the mandibula (CC direction 0.8 mm). Correcting for rotations of the reference did not always yield improvement of systematic and random errors due to low correlations. Instability of the mandibula was observed mostly with patients using a biteblock.

Table1. Local setup errors, with C3-C5 as reference. C3-C5 global setup results from of a shrinking action level protocol.

	Σ(mm)			Σ(mm)		
ROI	LR	CC	AP	LR	CC	AP
Mandibula	2.1	2.0	1.7	1.9	1.9	1.4
Jugulum	0.6	1.2	1.4	1.3	1.4	2.1
Os Occipitale	2.3	2.0	1.4	2.1	1.4	1.3
C1-C3	0.5	0.7	0.6	0.6	0.5	0.7
C3-C5	-	-	-	-	-	-
C5-C7	0.6	0.6	0.4	0.6	0.7	0.5
PTV	1.2	1.3	1.3	1.2	1.6	1.0
Remainder	2.0	1.2	1.6	1.9	1.4	2.0
C3-C5 Global Setup	1.6	1.3	1.2	1.5	1.6	1.9
AR						

Conclusions: Head and neck cancer patients often show interfractional anatomical variability that cannot be corrected with a simple couch shift. Local setup errors are in the same order of magnitude as global patient setup errors. Careful registration and selection of the reference point is required to avoid underdosage of the PTV and overdosage over OAR. Deformations increase further away from the reference and planning margins should be adjusted accordingly.

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CLINICAL INTRODUCTION OF RESPIRATION CORRELATED (4D) CT/PET SCANNING.

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Purpose/Objectif: Respiratory motion may reduce the accuracy in imaging lung cancer patients. Especially with a combined CT/PET

scanner differences occur since the acquisition time is different for both modalities. The purpose of this study was to commission and validate respiration correlated (RC) software for the CT/PET clinically and to test the feasibility for patients.

Materials/Methods: The Siemens Biograph16 CT/PET scanner was used for the RC scans. RCPET images were acquired with list mode PET software. RCCT images were reconstructed with in house built software. The respiration signal was recorded with a pressure sensor in a chest belt. Phantom testing was performed with a lollipop phantom, which was filled with 18F-FDG. Different movement amplitudes, frequencies and volumes were imaged to investigate the accuracy of the phase binning reconstruction. We found an interesting correlation between the optimal number of bins and the calculated volume for the reconstruction of the RCPET. The first patients underwent a normal free breathing CT/PET, a RCCT and a RCPET. In all modalities tumor volume and movement were compared to each other.

Results: The volume of a sphere with an actual volume of 16 cm^3, was measured for three different movement amplitudes on average 16.3 ± 0.3 cm^3 and 16.3 ± 0.2 cm^3 for the RCCT and the RCPET. The movement could accurately be determined with both modalities within acceptable tolerance level (3mm for cranial-caudal direction (due to slice thickness) and 1mm for the other directions). The calculated volume was overestimated by 123% for the 2 phase RCPET reconstruction and decreased down to 0.5% for 8 phases or more. With a varying frequency during scanning, differences between prospective and retrospective phase binning were determined, the volumes were 102.5% and 518.1% relative to the real volume for retrospective and prospective binning respectively. For the first patients, with both RC image modalities, binned in 8 phases, we measured comparable tumor movements in all three orthogonal directions, this movement could not be seen in the free breathing PET scan and hence the volume was overestimated.

Conclusions: The RC software was able to accurately determine the actual volume and movement of the phantom. For the RCPET, phase binning in minimum 8 phases is required to reconstruct accurate volumes. Retrospective phase binning showed significantly better volume determination than prospective binning when scanning lesions with different movement frequencies. The RC software improves movement quantification and volume determination in patients.

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COMPARING BREATHHOLD AND FREE BREATHING CT DERIVED MOTION MODELS FOR PREDICTING RESPIRATORY MOTION OF LUNG CANCER AND LYMPH NODES

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Purpose/Objectif: It has been proposed that tidal Breathhold (BH) CT scans can be used to obtain information on respiratory motion. Alternatively, 4D CT and related modelling methods can provide information on the motion that occurs while the patient is Free Breathing (FB), as they would during treatment. However, 4D CT requires an increase in radiation to the patient, more advanced planning techniques, and is not always available.

We have studied respiratory motion using both BH and FB data in order to assess how well the motion exhibited at BH represents that which occurs during FB. A motion model was used as it allows the automatic tracking of points of interest over the respiratory cycle, and averages out some of the inter-cycle variation that can occur.

Materials/Methods: BH: Two high quality BH CT scans were acquired at tidal inhale and exhale. A non-rigid registration, based on B-splines, was then performed to recover the motion due to respiration.

FB: Motion models were constructed from 'unsorted' 4D CT data using a technique previously developed by our group.

FB CT data was acquired in cine mode, at 3-4 couch positions. For each, 20-30 FB volumes were acquired over ~20 seconds.

The BH exhale scan was non-rigidly registered to each of the FB volumes. The motion model was then constructed by fitting a periodic function to each of the registration parameters over the respiratory cycle.

Data: A clinician manually identified the centre of the tumour and each nodal area on the BH exhale CT. The BH registration and the motion model were then used to calculate the location of these points at BH inhale, BH exhale, FB inhale, FB exhale, and 18 intermediate FB positions.

Data has been compared from 4 patients, with a total of 14 points.

Results: The distance between BH and FB exhale was between 0.5 and 3.9 mm (mean 2.2 mm). The distance between the BH and FB inhale was between 2.2 and 7.8 mm (mean 4.9 mm). The difference between the BH and FB magnitudes was between 0.3 and 3.4 mm (mean 1.6 mm), with neither BH nor FB being consistently larger. The angle between BH and FB motion was over 45° for 7 points, and over 90° in one case.

To assess how much the FB motion differed from a straight line, the distance between the 18 intermediate FB locations and the corresponding points on the FB inhale-exhale line was calculated. 3 of the 4 patients had a point with a mean distance over 2mm (range 0.8 to 2.8 mm), suggesting the straight line was not a good approximation of the FB motion.

Conclusions: These results suggest that although BH and FB respiratory motion may sometimes be similar, BH data cannot be relied upon to accurately predict FB motion in all cases.

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COMPARISON OF 4D CONE BEAM CT AND 4D SPIRAL SCAN CT USING A DEDICATED CHEST PHANTOM

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Purpose/Objectif: Radiotherapy of moving objects has to regard intra- and interfraction variation of the target position. One possible solution is the acquisition of helical 4D CT for treatment planning. Under the assumption of a reproducible breathing pattern, the treatment plan can be based on multiple reconstructions of different respiration phases. Modern linear accelerators now allow to validate organ motion just prior to treatment by acquiring a 4D cone beam CT with either the MV or an additional kV source. By comparing both 4D data sets, differences in the motion patterns can be identified.

Materials/Methods: To estimate potential differences in the data sets obtained with both modalities, a porcine lung explant was prepared with artificial nodules (diameters of 10-30 mm) and inflated inside a dedicated chest phantom. The lung was then exposed to respiratory motion by inflation and deflation of a flexible diaphragm. Images were acquired at fixed inspiration levels in the 0%, 50% and 100% exhale position and during respiratory motion (7 per min) using the 3D and 4D modes of diagnostic spiral CT and the linac based cone beam CT. The corresponding images to the 3D data sets were reconstructed from the 4D-CT according to the signal of a simultaneously recorded respiratory curve (ANZAI device with respiration belt). The reconstructed images were then manually registered using the hull

of the phantom as landmark. Differences in the images from static and dynamic acquisitions were then quantitatively compared using the inhouse developed treatment planning system Virtuos.
Results: The static data sets obtained with both imaging modalities correlated well. The overlay of different static images showed position errors of less than 3mm for the diaphragm. Similarly, image reconstructions from dynamic acquisitions matched as well. However, additional artifacts were introduced by to the reduced number of projections in 4D cone beam CT. The extreme positions (in- and expiration) obtained with cone beam CT differed from the static datasets by several millimeters due to the limited number of available projections. This mismatch was not observed close to the 50% phase.
Conclusions: The 4D cone beam mode of the linear accelerator allows for repeated monitoring of breathing motion pattern prior to each fraction. However, the impact of irregular breathing patterns on image quality can not be estimated from this ex vivo study and is subject to further evaluation.
Disclaimer:
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COMPARISON OF IMPLANTED GOLD MARKERS AND CONE BEAM CT FOR HIGH PRECISION ON-LINE IMAGE-GUIDED RADIOTHERAPY OF PROSTATE

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Purpose/Objectif: The On-Board Imager, OBI (Varian medical systems, Palo Alto, CA) has been in routine clinical use at the Karolinska University Hospital since June 2004. Three alternative image-guided protocols are being evaluated in this study for their relative accuracy and precision in compensating for inter-fractions target displacements. A well-established on-line position verification of prostate implanted with fiducial gold markers based on orthogonal kilovoltage radiographic images is being compared to a volumetric kilovoltage cone beam CT, CBCT.
Materials/Methods: At our department, the radiation technicians are responsible for the daily on-line patient set-up correction using the OBI. Ten prostate patients with gold markers were chosen. Prostate patients are treated in the supine position and get three gold markers implanted under transrectal ultrasound control. The kV-kV (2D-2D) based method employs two orthogonal radiographic images from anterior and lateral directions before each treatment fraction and manual alignment with plan-based DRR for estimating the position error of the isocener. Immediately after the kilovoltage radiographic localization corrections which takes less than 1 minute a volumetric cone beam CT set with a Field of view, FOV of 20 cm of the patient acquired. A new 3D-3D manual matching applied to the planned CT and CBCT scans to insure the position of the prostate. An option in OBI called MarkerMatch allows us also comparing the 3D locations of fiducial markers in the planning CT (reference CT) with the locations of the same markers during treatment. The gold markers are identified in the same two kV radiographs and their 3D location identified by combining information from both images sets. A further comparison between the CBCT (3D-3D) and MarkerMatch (2D-3D) has been performed randomly in five treatment fractions. A protocol is in use and the patient position errors in three dimensions will be quantified and analysed.
Results: There is a large variation in set-up corrections in between different patients. For some patients the daily vertical correction was larger than 1 cm. The lateral and longitudinal corrections are usually smaller than the vertical corrections. Our work shows that the treatment set-up corrections using the CBCT has comparable precision and accuracy but significant time slot differences to kV-kV since the rotation of the table is not considered in this work. The CBCT still has the advantage to localize the soft target as prostate without using fiducial gold makers and further investigation needed to study this technique. The process using the MarkerMatch program shows similar results to the radiographic 2D-2D procedure. The kV-kV and Markermatch techniques does not require any longer daily appointment time yet the CBCT requires twice the time.
Conclusions: OBI with CBCT is an excellent tool to verify and control target misalignments and patient set-up deviations. But considering that the CBCT requires longer time and does not increase considerably the precision of the treatment set-up we prefer for this particular case to use kV-kV or Markermatch for prostate patients with gold markers. The prolonged time-slot in the CBCT method may increases the risk for inter-fraction motion of the prostate.

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CONE BEAM COMPUTED TOMOGRAPHY (CBCT) GUIDED HIGH DOSE SINGLE FRACTION INTENSITY MODULATED RADIOTHERAPY (IMRT) FOR THE MANAGEMENT OF SKELETAL OLIGOMETASTASES.

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Purpose/Objectif: Three dimensional image guided (IG) radiotherapy using real time CBCT has greatly improved the precision of treatment. IMRT provides highly conformal radiation therapy. With robust immobilization, IG IMRT has made high dose single fraction radiation possible, even when in close proximity to sensitive normal tissues. Preliminary results are presented.
Materials/Methods: Thirty eight patients with oligometastatic disease in the bone underwent IG IMRT incorporating CBCT . Twenty four percent were sites in the appendicular skeleton. A custom fit body cradle was used for immobilization. The median prescribed dose was 2400 cGy (2100-2400 cGy). An on-table CBCT was used to verify the isocenter. CBCT was obtained immediately after treatment. Infrared stereoscopic tracking was performed during treatment. The accuracy of CBCT was compared to portal images using implanted fiducial markers in paraspinal lesions. Patients were followed with cross sectional imaging every 2 months initially, then every 3-4 months thereafter. Treatment failure was defined as any evidence of disease progression at the treated site. Toxicity was graded with the NCI CTC (v2).
Results: CBCT agreed with portal imaging (with fiducials) within +/- 1mm. Patient motion with respect to the immobilization cradle between the pre and post treatment cone beam scans was found to have a mean ± standard deviation of 0.3±1.3, 0.6±0.6, and 0.4±1.3. mm in the left, anterior, and inferior directions. The median follow up was six months (2-15 months). Eighty four percent of patients complained of pain requiring the use of opioid analgesics at presentation. Ninety five percent reported improvement in pain at the time of first follow up (2 months), and 65% did not require opiates at the time of last follow up. One patient failed to respond to treatment. Actuarial local control rate was 85%. No patient has experienced higher than grade 2 acute toxicity. No late toxicity has been seen.
Conclusions: CBCT IG IMRT provides a high degree of accuracy that permits the use of highly conformal high dose single fraction radiotherapy. Although results are preliminary, single fraction treat-

ment appears to be safe and efficacious in the management of oligometastatic bone disease. Since oligometastatic patients tend to have slowly progressive disease, aggressive non-surgical treatment of macroscopic disease may be warranted in these patients.

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CONE BEAM CT ON LINEAR ACCELERATOR - EXPERIENCE IN WARSAW

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Purpose/Objectif: Cone-beam CT (CBCT) systems are useful and reliable tool to detect and correct for patient set-up errors, patient movements, organ movements and organ changes.
We will present our experience with the routine clinical use of kilovoltage volume imaging system on Elekta Synergy accelerator.
Materials/Methods: XVI was commissioned in our hospital in January 2006. Since April it is used on regular basis for selected groups of patients. These are patients with brain, head and neck, abdominal and pelvic tumors. About 20 % of them are children. The main goal of our first-stage study is to correct for systematic set-up errors and verify presently applied set-up margins. Cross-validation of set-up measurements using CBCT and EPID is applied. CBCT bony structures based decision rules are developed for off-line protocol. Cone beam CT together with EPID are taken for each patient on the 1st, 3rd, 16th and 21st fraction. If the mean translations from the two first image registrations exceed established, tumor site dependent action level, the patient position is adjusted on the 4th fraction. Than additional images are acquired and registered before irradiating the patient. Bony structures included in registration lie in close vicinity of the PTV and are of its extension, for brain tumors they can include a whole skull. In a second step of image analyses also manual matching is performed for prostate or some well distinguishable critical structures like liver and kidney in order to assess inter fraction movements and deformations.
The workload is about 5 min for single XVI acquisition and registration.
Stability of the mechanical calibration of the system is regularly checked as a part of a QA of the system.
Results: During the first four-months period of observation the XVI system was mechanically stable. The best correlation between the reference CT and verification CBCT was observed in patients with brain and orbital tumors (mainly pediatric). The results of the set-up errors measurements using XVI and EPID will be presented.
Conclusions: Our preliminary study shows that XVI has the potential to significantly improve the accuracy of radiation treatment, which is especially important in pediatric radiotherapy.

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CONVENTIONAL 3D CONFORMAL RADIOTHERAPY VS. ULTRASOUND IMAGE GUIDED RADIOTHERAPY FOR PROSTATE CANCER: PRELIMINARY RESULTS OF ALIGNMENT FINDINGS AND TOXICITY OF A PHASE III MULTICENTRE STUDY

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Purpose/Objectif: To validate ultrasound alignment as a tool for Image guided radiotherapy (US-IGRT) and to compare acute toxicity with 3D conformal radiotherapy alignment with portal imaging (PI-3D-CRT)
Materials/Methods: A phase III multicentre study was activated in June 2005, to compare treatment acute toxicity and patient outcome after 77,4 Gy in 43 fractions to the prostate and seminal vesicles using either PI-3D-CRT or US-IGRT. The dose in both groups was specified to the entire prostate and seminal vesicles. In both cases, patient alignment for each fraction was done by use of electronic portal imaging correcting setup errors relative to bony structures. In the US-IGRT group, just after alignment correction, transverse and sagital ultrasound images were obtained. The planning volumes were overlaid on the ultrasound images and adjusted until they matched. Treatment table was moved so that the treatment area was in the correct location and new ultrasound images were taken to confirm that new position agreed with anatomic images and planning contours as well as with reference isodoses. The First 127 patients (63 in the PI-3D-CRT group and 64 in the US-IGRT group) are the subject of this preliminary analysis. Side effects were graded on a 1-4 scale, using the SOMA-LENT criteria with self-administered validated questionnaires.
Results: Prostate (and average) displacements in the US-IGRT group in the superior to inferior, anterior-posterior and left to right were 0-2.3 (0.98) ; 0-2.1 (0.53) and 0-1.4 (0.19) cm respectively. Grade 2 or higher rectal toxicity for PI-3D-CRT and US-IGRT were 21% and 8% ($p<0.045$) respectively.
Conclusions: US-IGRT revealed as very useful in daily repositioning of patients, allowing a reduction of margins around prostate and seminal vesicles. The use of tighter margins supposed a reduction of the relative risk of having grade 2 or more acute rectitis in a factor of 2.4.

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CT BASED IMAGE GUIDANCE FOR EVALUATING HEAD AND NECK INTER-FRACTION MOTION

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Purpose/Objectif: CT-based Image-Guided Radiation Therapy (IGRT) can be used to measure, evaluate, and correct for patient positional error immediately prior to treatment delivery. For head & neck patients (H&N), positional error can originate from 1.) Changes in how the patient is positioned on the headrest, 2.) Changes in how the aquaplastic mask is positioned on the patient, 3.) Changes in the size and shape of the mask; and 4.) Changes in the size and shape of the patient. The purpose of this retrospective study was to use imaging from CT-based IGRT to evaluate the immobilization of H&N patients for each fraction throughout the course of therapy.
Materials/Methods: Ten H&N patients were positioned for treatment using megavoltage CT (MVCT) images acquired before each treatment fraction. An automatic MVCT-to-kVCT mutual information based fusion algorithm was used in combination with visual alignments by the investigators to measure the offsets from the laser alignment marks to the optimized treatment position prior to each treatment fraction. The volumetric imaging data was extracted from the database and the investigators visually evaluated the images for 1.) Patient position on the headrest, 2.) Patient position inside the aquaplastic mask, 3.) Changes in the mask shape, 4.) Patient weight loss, and 5.) Tumor response. The measured offsets from the laser alignment marks were then correlated with the underlying cause of the setup error.
Results: The total anterior/posterior, superior/inferior, and right/left lateral shifts from the external marks were measured for 335 fractions. The random error (1Σ) for the population as a whole was ±3.1 mm in the anterior/posterior (AP) direction, ±3.3 mm in the lateral direction (LAT), and ±4.9 mm in the superior/inferior (SI) direction.

All ten patients had a decrease in the cross-sectional volume due to a combination of weight loss and/or tissue response to radiation. Four out of the ten patients had inconsistent placement of the head on the headrest, which resulted in setup errors that ranged from 3.1 to 10.3-mm. One patient had substantial tumor regression (>25%) which allowed the patient to move 2.4 to 7.8-mm inside the mask. The use of a simple bite-block greatly reduced the random setup error to 1.6-mm AP, 1.6-mm LAT, and 1.5-mm SI.

Conclusions: All H&N patients immobilized with aquaplastic masks will have residual motion inside the mask due to weight loss, incorrect positioning, and/or response to treatment. The amount of residual motion can be greatly improved by using a simple bite block.

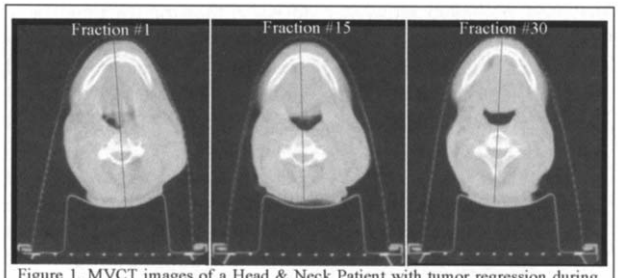

Figure 1. MVCT images of a Head & Neck Patient with tumor regression during therapy. As the tumor regressed in volume, the mask became loose and the patient rotated on the headrest.

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DAILY ON-LINE PATIENT SETUP IN CLINICAL ROUTINE

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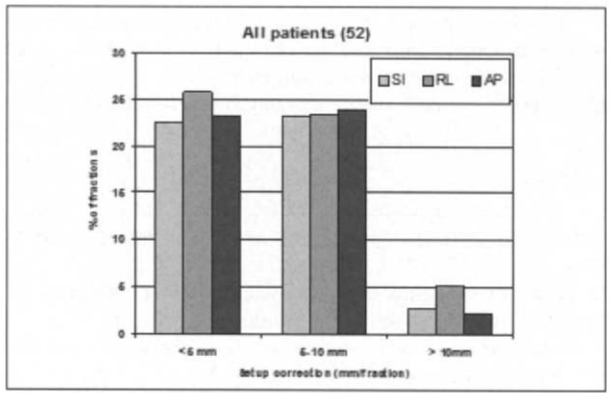
Purpose/Objectif

To present the patient setup strategy at the new radio-oncology centre in Biel .

Materials/Methods: For initial positioning the isocentre is marked on the patient'skin with a Dorado CT-1-4 laser system. Before daily treatment orthogonal localization images are acquired with the aS500 portal imager. The IAS3 acquisition system allows taking MV-images with the new Radshot Mode (1MU/image). The DRRs generated for the setup beams serve as reference for the setup portals. The radiation therapists compare the positions of bony landmarks and correct the patient position by moving the treatment couch to the new coordinates calculated by the software, when a setup error >2mm in any direction is detected. Both, the treatment couch and the exact arm holding the aS500 can be repositioned conveniently by remote controls in the control room allowing to perform setup verification and correction within a common time slot of 15min. Setup correction data of patients treated for breast (28), prostate (15), and other carcinomas (9) were collected.

Results: In only 16% of 1311 fractions applied no setup corrections in any-one direction were necessary, i.e. for >80% of all fractions a setup accuracy of better than 2mm could be reestablished with our daily online setup procedure. The mean (0.1cm, SD +/-0.3) of all applied corrections (range, -1.2 to 1.6cm) sampled over all patients is close to zero and no significant difference between treatment sites was seen. The Figure shows the frequency of setup corrections of different magnitude.

Conclusions: Daily on-line setup verification and correction by the aid of setup fields is feasible and improves treatment accuracy considerably.



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EARLY EXPERIENCE OF REIRRADIATION WITH HELICAL TOMOTHERAPY FOR LOCALLY RECURRENT RECTAL CANCER

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Purpose/Objectif: The objective of this study was to present the cases of reirradiation with helical tomotherapy for locally recurrent rectal cancer patients after radiation to pelvis.

Materials/Methods: Helical tomotherapy was applied for the two patients who had been previously irradiated and then subsequently showed in-field tumor recurrence. Case 1(65-year-old male) received concurrent chemoradiation on pelvis with a total dose of 54 Gy after low anterior resection. He had recurrence on the anastomotic site after 30 months of follow-up. He underwent salvage abdominopelvic resection after neoadjuvant radiotherapy a total dose of 30 Gy. However, local recurrence was noted on tumor bed after salvage surgery. Case 2(52-year-old male) was diagnosed of rectal cancer and simultaneous iliac bone metastasis. He was treated with anterior resection and staged as T2N0M1. He received systemic chemotherapy and radiotherapy on the iliac bone metastatic lesion with a total dose of 50 Gy. With continuous follow up, he experienced local recurrence on the same site. Subsequently radiotherapy of 40 Gy was given and then followed by another 60 Gy to the adjacent site of tumor regrowth. Due to patients' reluctance to chemotherapy, radiotherapy using helical tomotherapy has been considered as only salvage treatment.

Results: In case 1, PTV(Planning target volume) was prescribed to 41.8 Gy (19 fractions of 2.2 Gy each). Mean dose to small bowel and bladder was 6.33 and 8.35 Gy, respectively. In Case 2, the prescribed dose was 60 Gy (24 fractions of 2.5 Gy each) to the GTV(gross tumor volume) and 48 Gy to the CTV(clinical target volume). Mean dose of case 2 to small bowel was 15.8 Gy. Dose volume histograms of both the tumor and the critical structure were obtained in each case. In case 1, V40 for small bowel and bladder was 2.5, and 0%. In case 2, V_{40} for small bowel was 0%. All patients showed symptom palliation and mass reduction. The delivered radiation dose to critical structure was within the acceptable range. No significant bowel and bladder toxicity occurred during the treatment.

Conclusions: Reirradiation using tomotherapy may provide a good chance of symptom palliation and mass reduction for patients with locally recurrent rectal cancer. Longer follow-up is needed to evaluate late complications.

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EFFECT OF INTER-FRACTION BREAST POSITION AND SHAPE CHANGES ON BREAST IMRT DOSE DISTRIBUTION

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Purpose/Objectif: Breast radiotherapy is planned on image data acquired pre-treatment, however the delivered distribution of radiation may vary from the plan due to changes in position and shape of the breast at the different fractions of treatment. This study uses anatomical information from repeated cone beam CT (CBCT) imaging at the point of treatment to assess the delivered dose distribution at different fractions of treatment.

Materials/Methods: Breast surface and lung contours were defined for CBCT images acquired immediately following treatment of 5 patients undergoing forward planned IMRT breast radiotherapy. Between 9 and 14 images were acquired per patient. The dose that was delivered on each day was re-calculated using the Pinnacle treatment planning system. Beam segments and monitor units were taken from the original treatment plan, and bulk density corrections were applied based on the CBCT contours for each day. Daily PTV outlines were also created using the breast surface and back edge of the beam as defined by skin markers visible in the CBCT image. Dose-volume histograms for the PTV on each day of treatment were calculated for the IMRT technique. Volumes of the PTV receiving greater than 105% or less than 95% of the prescribed mean PTV dose were found for each day of treatment, and compared to the planned dose distribution.

Results: For IMRT treatments, the mean percentage volume of the PTV receiving greater than 105% of the prescribed dose (V_{105}) was 0.4% for the original treatment plan, and 0.9% when the dose was recalculated using the CBCT contours. The mean percentage volume of the PTV receiving less than 95% of the prescribed dose (V_{95}) was 2.2% as planned, increasing to 8.7% when recalculated using the CBCT contours.

Conclusions: Daily variations in breast shape and position increased the volume of tissue within the PTV receiving less than 95% of the planned dose and, to a lesser extent, the volume receiving greater than 105% of the planned dose.

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ENHANCEMENT OF IMAGE QUALITY WITH A FAST ITERATIVE SCATTER CORRECTION SOLUTION FOR KV CBCT

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Purpose/Objectif: The problem of the enormous amount of scattered radiation in a kV CBCT is addressed.

Materials/Methods: Our iterative scatter correction method is based on a superposition of pre-calculated Monte Carlo generated scatter kernels and in addition on a look-up table that contains the system calibration and thus corrects for beam-hardening. Therefore the algorithm is very fast, that means 1.6 seconds per projection for 4 iterations on a standard PC. In this study we compare scatter corrected CB-images of several phantoms (cylindrical water phantom, cylindrical contrast-and-resolution phantom, Alderson head-and-neck phantom) to the fan-beam ones we acquired with a reduced cone-angle (a slice-thickness of 14 mm in the isocentre) at the same system. The dose we currently apply amounts to about 2 cGy for 360 projections in the isocentre.

Results: Some representative results are shown in the figure below. The observed image quality of the scatter corrected CBCT images is quite comparable concerning contrast, resolution, cupping and attenuation coefficients to those with the fan-beam geometry. After 4 iterations (cylindrical water phantom and contrast-and-resolution phantom) and 7 iterations (Alderson phantom) the algorithm converges.

Conclusions: Besides the achieved image quality there are still some subtle points to be investigated. First the scatter kernels are generated using a cylindrical water phantom geometry positioned upright and therefore symmetrically around the isocentre. Consequently the algorithm works perfect if the reality fits this setup. But in clinical cases, the patient is positioned on a table whose thickness and form can cause further problems. The scatter contribution can be enormously increased when the detector is below the table compared to the situation when the detector is located on the opposite side. For our model the thickness the x-rays have to traverse is the same and therefore the number of scattered photons the algorithm subtracts is also the same. In addition when the patients are fixed in high attenuating fixation-systems or positioned with the aid of markers the algorithm causes a lot of artefacts. Moreover, for lateral directions the combination of table, extracranial fixation systems and voluminous patients lead to infinity values as a result of our algorithm. So, there is still work in progress. Last but not least we have to state that a lot of care and therefore time has to be spent to calibrate the system. And every time one changes a part of the system like x-ray tube or detector the calibration procedure has to be done again.

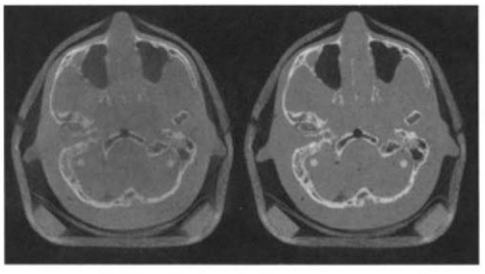

Figure: Alderson head-phantom. For each image the pre- and post-processing steps are the same, including the same greyscale-level. Left: CBCT without scatter correction. Right: CBCT with scatter correction.

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EVALUATION OF 4DIMENSIONAL-COMPUTED TOMOGRAPHY FOR DELINEATION OF THE CLINICAL TARGET VOLUME (CTV) FOR BREAST BOOST RADIOTHERAPY.

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Purpose/Objectif: A number of studies support the role of breast boost radiotherapy in reducing the risk of local recurrence in young breast cancer patients with negative surgical margins. At present, there is limited information on the effect of respiratory movement on breast and surgical tumor bed motion during radiation planning. Our objective was to evaluate the impact of respiration and motion artifacts on delineation variability of the clinical target volume of the breast boost (CTV boost) by comparing the observer variability in CTV boost delineation using helical CT vs 4D-Computed Tomography (4D-CT).

Materials/Methods: Five patients who participated in a prospective study to evaluate the use of 4D-CT for planning breast radiotherapy were included in this sub-study. Five radiation oncologists delineated the CTV boost for each case. The Contouring was based on a non-contrast standard helical CT and on 4D-CT image datasets at the inspiration phase (IP) and the expiration phase (EP). To evaluate the intraobserver variability, two observers repeated the contouring for the same cases after an interval of least 7 days. The variability in the delineated CTV boost was expressed as the ratio of the common volume to the maximum volume encompassing all contours

(Vcom/Vmax).
Results: The interobserver variability of CTV boost delineation based on helical and 4D-CT datasets was not significantly different (P=0.85), with mean Vcom/Vmax of 0.33 vs 0.31 vs 0.32 for helical, IP- and EP- 4D CT datasets, respectively. The mean Vcom/Vmax ratio for intraobserver variability was also not significantly different (P=0.84) with values of: 0.77 (helical CT), 0.74 (4D-CT IP) and 0.75 (4D-CT EP).
Conclusions: There is substantially less intraobserver variability than interobserver variability in CTV boost delineation for both helical and 4D-CT. The use of 4D-CT image datasets for delineation of breast CTV boost does not significantly reduce the inter-and intraobserver variability compared to standard helical CT delineation.

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EVALUATION OF ON- AND OFFLINE STRATEGIES IN ADAPTIVE RADIATION THERAPY USING NUMERICAL SIMULATION OF ORGAN MOTION AND DEFORMATION.

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Purpose/Objectif: To evaluate mixed on- and off-line adaptive correction strategies for IMRT-treatments of patients with prostate cancer. To study the effect of organ deformation on the choice of correction strategy.
Materials/Methods: Research software for IMRT planning and numerical simulation of adaptive treatments with functionality for dose tracking and accumulation was used. This software was extended with functionality for numerical simulation of changing patient geometries where organs may change position, orientation, scale and shape. IMRT treatments were planned based on the RTOG protocol, but with stricter objectives for organs at risk. Different sizes of PTV margins were used in the numerical investigation of the following two adaptive correction strategies. OnlineCouch (OC): Onboard CT images are acquired for every fraction and the target centre of mass is localized. The treatment couch is shifted to eliminate the detected target shift. Couch/Replan (CR): The same procedure as in OC, but the first 4 images are contoured and dose is accumulated by deformable dose registration. The treatment is replanned offline before delivery of fraction 5 taking accumulated dose and systematic errors into account. The image acquisition and contouring steps were not actually performed, but the effect of these steps was simulated numerically. The strategies were evaluated for the following organ motion models. Rigid: Prostate moved as a rigid body with systematic and random motion components. Deformed: Bladder and rectum moved as rigid bodies with systematic and random motion components. The prostate was deformed as a consequence of this. Two different deformations were considered, one where the prostate is compressed and one where it is stretched out. These two deformations were simulated for 3 different patients.
Results: Rigid: OC and CR gave similar CTV coverage and organ at risk protection when no PTV was used for planning. A small deviation from the required target coverage was observed but considered clinically acceptable. Deformed: Results are reported för OC (6mm PTV margin) and CR (4mm PTV margin). Over simulations, CTV dose (D99.5, D98) difference between CR and OC was -1.5 to 2.5 Gy and for OARs, dose (D15, D25, Dmean) difference was -12 to 2 Gy for bladder and -16 to 5 Gy for rectum. For each simulation, the dose difference levels above were averaged for CTV and OARs respectively. For 1 out of 6 simulations, the difference between these two averages was 1 Gy in favour of OC over CR, and for 5 out of 6 simulations, 2 to 10 Gy in favour of CR over OC.
Conclusions: Prostate deformation plays an important role when assessing the need for adaptive replanning. Online correction of patient position enhances treatment quality. Results suggest that in the presence of prostate shape change, organ at risk protection can be further enhanced by adaptive replanning after a few fractions.

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EVALUATION OF POSITION REPRODUCIBILITY IN BRAIN TUMOURS.

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Purpose/Objectif: Reproducibility of correct treatment position is essential for all advanced radiotherapy techniques. In spite of introducing and development of IGRT megavoltage portal imaging remains a reality for good clinical practice in many departments.
Materials/Methods: Evaluation of treatment positions using EPID (electronic portal imaging device) were done in 20 brain cancer pts, in 45 different treatment fields and 119 images (2004 - July 2005). 2 physicians and 2 physicists performed the evaluation independently. Heads of all pts were fixed by individual thermoplastic masks. Megavoltage images were compared to simulation images off line.
Results: Average absolute deviation in craniocaudal direction were 1.59mm with S 0.44mm, average absolute deviation in laterolateral direction were 1.53m with S 0.50mm and in anterioposterior direction were 1.25mm with S 0.39mm. Calculated 2D vector deviation were 2.31mms with S 0.41mm and calculated 3D vector deviation were 2.56mms with S 0.46mm. No statistically significant discrepancies were observed between physicists' and physicians' measurements.
Conclusions: Head fixation by individual fixation masks with regular evaluation of treatment position is adequate technique by EPID is considered to be a standard for 3D conformal radiotherapy of brain tumours, with achievable tolerances +-2mms in any direction. Choice of suitable images with bony structures to compare can improve the results of this method.

527 poster

EVALUATION OF TRANSABDOMINAL ULTRASONOGRAPHY PROSTATE LOCALIZATION FOR 3-DIMENSIONAL CONFORMAL RADIOTHERAPY

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Purpose/Objectif: To evaluate the feasibility and accuracy of daily ultrasound based target localization and to compare it with daily computer tomography (CT) and electronic portal imaging (EPI) in 3-dimensional conformal radiotherapy (3D-CRT) for prostate cancer.
Materials/Methods: Ten prostate cancer patients were treated 3D-CRT with use of 2 dynamic lateral 100°-wide arcs (40°-140°, 220°;-320°). Daily B-mode Acquisition and Targeting ultrasound system (BAT™, Nomos) was used for target localization. For the first 5 fractions, set-up errors were evaluated with EPI and then subtracted from couch shifts suggested by BAT, in order to quantify the organ motion.
For the same first 5 fractions, daily CT images were fused according to pelvic bone structure and target volume was contoured by the same radiation oncologist in order to evaluate the organ motion. Isocenter placement relative to initial planning CT images were recorded and compared with the organ motion obtained from the BAT.
Results: Two hundred eighty six BAT alignments, 50 CT alignments and 50 EPI verifications were performed. The average BAT total misalignments (organ motions and setup errors) in latero-lateral (LL), antero-posterior (AP) and cranio-caudal (CC) directions were -0.9 ± 3.3 mm, 1.0 ± 4.0 mm and -0.9 ± 3.9 mm, respectively. The average

BAT organ motions (total misalignments - setup errors suggested by EPI system) in LL, AP and CC directions were -0.4 ± 2.0 mm, 1.9 ± 3.4 mm and -1.1 ± 3 mm, respectively. The average CT organ motions in LL, AP and CC directions were -0.1 ± 0.7 mm, 0.7 ± 3.3 mm and -0.6 ± 2.3 mm, respectively. The difference between BAT and CT organ motion in LL, AP and CC directions were 2.6 ± 1.7 mm, 3.9 ± 2.7 mm and 3.4 ± 2.9 mm, respectively. Weak correlation was found between BAT- and CT-organ motion in AP direction was observed (R=0.29, p=0.04), while no correlation was found in LL and CC directions.
Conclusions: Daily BAT ultrasound positional verification of the prostate can be performed through the acquisition of high-quality images in most patients with only a modest increase in treatment setup time. Our initial evaluation revealed ultrasound targeting of prostate to be functionally equivalent to CT and prostate organ motion appears to predominate over setup error as the major component of variation in target localization.
Further study is warranted in order to establish the clinical value of BAT in prostate cancer.

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FEASIBILITY OF ADAPTIVE IMAGE-GUIDED IMRT FOR HEAD AND NECK CANCER USING CONE-BEAM CT OBTAINED AT THE TREATMENT COUCH

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Purpose/Objectif: During the course of fractionated RT many head and neck cancer patients develop significant anatomical changes mainly due to tumor shrinkage and/or weight loss. The dosimetric effect of these changes can be severe, potentially leading to both over dosage of critical normal tissues and under dosage of target volumes. The aim of this study was to test the feasibility of adaptive image-guided IMRT using cone-beam CT (CBCT) for periodic adjustment of conformal treatment plans in head and neck cancer.
Materials/Methods: Consecutive head and neck cancer patients treated with inverse planned IMRT underwent a weekly CBCT scan during the course of treatment. The CBCT scans were conducted on the treatment couch with Varian's On-Board Imager (OBI) system. Volumetric and geometrical changes of the patient anatomy were evaluated by registration of each CBCT scan with the pre-treatment planning CT scan. The original IMRT treatment plan was recalculated on each CBCT scan to monitor possible dosimetric changes. Plan adjustments were performed when necessary to maintain the prescribed target dose or an acceptable dose to organs at risk. The dosimetric consequences of tumor shrinkage, patient weight loss and other factors during the treatment course were recorded. In addition to the CBCT scans, regular conventional CT scans were performed for comparative studies between the two CT modalities. This feasibility study will evaluate the first 15 patients entered in the IMRT-CBCT protocol from February-September 2006.
Results: The preliminary data analysis from the first three patients treated with IMRT showed that in two out of three cases, there were very little changes in anatomy and therefore insignificant dosimetric effects. For the third patient, a potential increase in the maximum dose for the spinal cord of 5.2 Gy was observed whereas the mean dose to 95% of the planning target volume was reduced by 2.5 Gy due to tumor shrinkage. The preliminary comparison of the dose distributions obtained from CBCT and conventional CT showed a difference of 2-3 percent in absolute dose. The image quality of the CBCT scans was governed by more artifacts than in conventional CT.
Conclusions: Cone-beam CT obtained with the patient at the treatment couch provided a strong and versatile tool in adaptive image-guided IMRT for head and neck cancer. The benefit is more frequent, fast and convenient imaging than with conventional CT, and it allows monitoring of both the patient positioning uncertainty and the anatomic changes occurring gradually over time.

529 poster

FEASIBILITY OF FREE-BREATHING RESPIRATORY GATED LIVER RADIOTHERAPY WITH MRI-DERIVED MOTION MODELS.

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Purpose/Objectif: To assess the feasibility of guiding free-breathing respiratory gated radiotherapy of the liver with MRI derived models of hepatic motion.
Materials/Methods: Prediction of liver position via skin markers for gated radiotherapy is investigated for reproducibility using 4D MRI. Initial work assesses different scanning protocols (based on 3D multi-shot echo planar imaging (EPI) with parallel imaging techniques to achieve and image of the liver with temporal resolution of 1-2 s). Volunteers were imaged during breath-hold (for high resolution registration quality) and in free-breathing with MR-visible skin markers in place; models describing the resulting liver motion and relating it to position of the skin markers were built using two non-rigid registration methods (one based on B-spline interpolation and the other on a fluid flow model). The MR-visible markers are used to synthesize a gating signal such as that obtained during Radiotherapy from e.g. a Varian reflective RPM marker. The second stage verifies the accuracy of predicted motion via repeat MRI scans and fluoroscopic imaging (patients only).
Results: The chosen MR imaging protocol consisted of a 15-sec breath-hold (BH) high resolution scan followed by a lower resolution 1.5 s dynamic free-breathing scan, with roughly 3mm isotropic resolution acquired for a total of 1-2 minutes. Using B-spline registration on volunteer, average modulus error between predicted and realized deformations were 1.3 mm model and test data acquired during the same visit). Fluid registration has produced a more accurate registration in another two volunteers (<1mm). Fluoroscopic verification results of predicted motion will be presented for 15 liver patients.
Conclusions: Results for healthy volunteers suggest that liver deformations may be predicted using a simple skin marker system combined with a previously-acquired MRI model. This may allow a more controlled delivery of gated radiotherapy of the liver based on external surface marker only. In addition, due to superior soft-tissue contrast the 4D MR data itself allows better motion visualization for liver target definition compared to 4D CT.

530 poster

FEASIBILITY OF USING NONRIGID REGISTRATION FOR PLANNING ADAPTATION IN RECTAL CANCER RADIOTHERAPY

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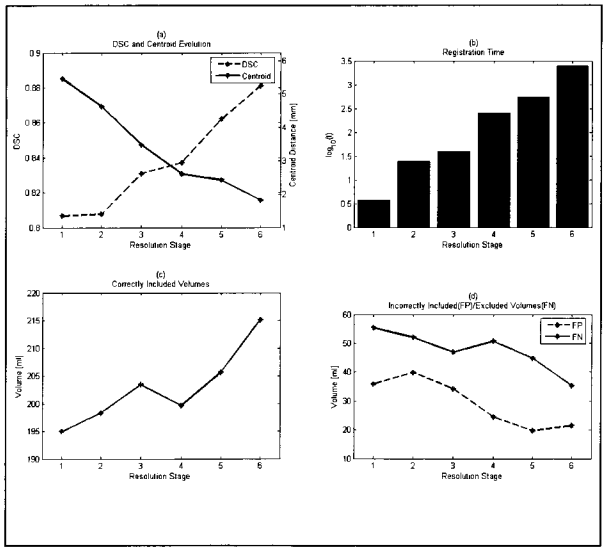
Purpose/Objectif: In this work we investigate the possibility of using a nonrigid image registration algorithm to improve the accuracy of target localisation in radiotherapy for rectal cancer patients.

Materials/Methods: Nonrigid registration is performed using a B-spline transformation model. Mutual information (MI) constrains the registration and no regularisation penalties are used. Optimization is carried out using a multiresolution approach. Five patients received three CT scans (512x512x94); one before (planning CT), one during (week 3) and one after treatment (5 weeks after completion of radiotherapy). The mesorectum, the major part of the target volume, was manually delineated on each scan by a trained expert. Volume overlap, measured with the Dice similarity coefficient (DSC) defined as $2U/(V_1+V_2)$ with V_1 and V_2 the volumes and U the union of the volumes, and centroid distance (CD) were evaluated for the mesorectum at each resolution step of our registration. In addition, the correct volume overlap (true positives, TP) and the incorrect volume differences (false positives, FP and false negatives, FN) were calculated in millilitres (ml). Registration time was assessed at each stage.

Results: For all registrations a strong increase in DSC and a decrease in CD were observed from rigid to nonrigid registration (a) with the mean DSC increasing from 0.81 to 0.88 and the mean CD decreasing from 5.5 to 1.8 mm. The TP (c) increased with 20ml (10.3%), whereas the FN and the FP (d) decreased with 20 and 15 ml (36.4% and 40.4%), respectively. The time needed for each stage increased almost exponentially (b). The first 5 stages took about 8 minutes while the last stage took about 30 minutes (on an AMD Opteron250 with 2 GB memory). To minimize the influence of bowel gas, threshold based segmentation excludes low intensity voxels from the calculation of the mutual information in the final stage (at the finest resolution).

Conclusions: Our results indicate that nonrigid registration allows a strong increase in the accuracy of target localisation. This method could be used to register daily cone-beam CT images taken in treatment position in order to adapt the treatment plan online according to the changes in target location. For this, our registration needs to be sufficiently fast. We can reduce calculation time by omitting the last steps of our registration since in the first 4 steps, which only take about 2 minutes, a significant improvement in DSC and CD is already seen. By incorporating our registration results in an updated treatment plan we could achieve more accurate irradiation of the target volume.



531 poster

IMAGE GUIDED INTENSITY MODULATED RADIOTHERAPY FOR BLADDER CANCER: ISOCENTRE SHIFTS, MARGINS AND THE IMPACT ON TARGET DOSE COVERAGE AND HOMOGENEITY

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Purpose/Objectif: Image-guided radiotherapy (IGRT) has great potential to improve the treatment of tumour sites that exhibit large geometrical uncertainties. The treatment of bladder cancer is a prime example and this study quantifies the size and direction of the daily 3D isocentre shift resulting from the use of IGRT, its impact on reducing the margins required and changes to target dose coverage, prescribed dose and dose homogeneity.

Materials/Methods: The study is performed using a series of 19 patients presenting with bladder cancer that underwent weekly repeat conventional CT scanning during their treatment course of 6-7 weeks. The isotropic margin required to cover various percentages of the volumes of the CTV positions from the repeat scans is found by growing the PTV from the planning scan by incrementing the margin in steps of 1mm until full coverage is obtained. The optimum daily isocentre shift is determined by moving the CTV from the repeat scan in 3D so that its volume that lies outside the planning CTV is minimised. Reduction in the isotropic margin by applying the optimum isocentre shift is found by repeating the above procedure and the individual optimum sizes of the 6 margins required in the sup/inf/ant/post/right/left directions are determined using a recently published empirical margin determination method. Finally, 5-field IMRT plans are set up (that minimise the dose deviation throughout the target) using different CTV margin alternatives, the optimal isocentre shifts are applied and the target dose distributions are assessed after recalculation without changing any of the beam parameters.

Results: Without use of IGRT (i.e without shifting to the optimal isocentre), an isotropic margin of 30mm is required to cover fully all the CTV positions from the repeat scans. The margin reduces to 20mm for 95% coverage. The direction of the isocentre shift required is random with an average directional shift less than 1mm and is unlikely to exceed an absolute value of 15mm (average of 7mm). Applying the optimum isocentre shift reduces the isotropic margin to 16mm for full coverage and to 12mm for 95% coverage. Determining the optimum margin individually in each of 6 orthogonal directions reduces the irradiated volume by approximately 30% but requires complex planning on a daily basis. Applying the optimum isocentre shift to IMRT plans shows little change to the mean target dose of 100% (an average increase of 1%), but produces a spread in the mean dose ranging from 96% to 106%. The 3D dose variation over the target is within a -5% to +7% acceptable range in approximately 90% of cases. The minimum and maximum doses within the target can show significant changes.

Conclusions: The use of IGRT in the treatment of bladder cancer is shown to reduce markedly the treatment margins required. When used in conjunction with IMRT, the plan calculated prior to treatment is shown to be acceptable for daily treatment in terms of the changes resulting to the dose distribution in around 90% of cases.

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IMAGE GUIDED RADIATION THERAPY (IGRT) NEEDS A CLARIFICATION IN BREATH CONTROL : A SITE DECISION.

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Purpose/Objectif: Breathing control is almost always implemented on the basis of equipment choices and not on studies of expected benefit in radiotherapy. The equipments of IGRT are currently in phase of generalization but few teams have already a sufficient knowledge of what is advisable to do with the respiratory movements.

Materials/Methods: We have treated 82 lung cancers, 48 liver cancers and 5 breast cancers using a Deep Inspiration Breath Hold method (DIBH). We used a dedicated spirometer SDX/DYN' R especially developed to implement a voluntary breathing control

assisted by a video-feedback. Compliance, additional time, set-up error and dosimetric benefits were evaluated. We currently use an IGRT OBI/Varian equipment which must enable us to still improve the daily precision.

Results: Lung: Many publications describe the use of a free breathing (FB) control concerning small tumours isolated in the parenchyma. However, the PTV of lung tumours are often of important size. Their treatment requires to protect the healthy lung by the use of a deep inspiration method very well followed by 95% of the patients. The mean lung dose is always decreased thus creating better treatment conditions. However, precision based on bony landmarks needs IGRT to be based on tumor localization. Liver:It is necessary to reach approximately 60Gy to deliver a curative treatment to an intra hepatic tumour. The external movements are not correctly correlated with displacements of the liver, so we apply a DIBH method. However, the reproducibility remains with a 1 cm error which often brings closer to complications. IGRT will be essential to still get improvements helping maybe to implement the FB method. Breast: The main goal of breathing control in the breast radiotherapy is to spare the heart from the tangential beams. It only relates to the left breast irradiation and only the DIBH method can bring an adapted solution. This irradiation improvement can be done jointly with a mono-isocentrique technique and a dosimetric compensation. IGRT would, under these sophisticated conditions, help to reach an adequate daily precision.

Conclusions: Each anatomy site drives towards very different objectives which build all current decisions and all future IGRT protocols. Every one should consider, even if it seems to be emotional, that the breath hold is the best way to cover all the precisions needed. IGRT will help in new improvements but will be so, implemented on a good bases. The incorporation of the movements in the planning and the gating of IMRT treatments appear unrealistic. Conclusions: IGRT is quickly coming so, it's time to definitively implement a breathing control. Our opinion from our experience is that Breath hold seems to be the best way to cover all situations. A desired dosimetric benefit should drive the equipment choices and not the reverse to, once again, optimize the PTV covering and the protection of surrounding tissues.

533 poster

IMAGE-GUIDED RADIOTHERAPY WITH CONE-BEAM CT AFTER PROSTATECTOMY: EVALUATING THE IMPACT ON PTV MARGIN

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Purpose/Objectif: Radiation-induced toxicity after radical prostatectomy correlates with the dose delivered to normal tissues. In order to reduce the planning target volume (PTV) margin, uncertainties such as daily positioning and setup errors, inter- and intrafraction organ motion, and organ deformation must be addressed. To implement image-guided radiotherapy (IGRT) with on-line cone-beam CT (CBCT), we conducted a study to quantify inter- and intrafraction motion of the clinical target volume ($CTV_{prostate\ bed}$), and to evaluate the quality and potential impact of daily CBCT image guidance on the PTV margin.

Materials/Methods: CBCT images were acquired every other day for twelve patients undergoing radiotherapy after radical prostatectomy. Patients were immobilized supine with a custom-fitted VacLoc device, and planned with a standard 4-field box technique to receive a total dose of 66Gy in 33 fractions. Interfraction motion was analyzed for the superior right and left lateral, and the most inferior surgical clips visualized within the prostate bed CTV. Motion of these surgical clips was measured on the CBCTs relative to the planning CT. MRI (1.5T GE) was performed with VacLoc immobilization at the time of simulation in 17 patients. Intrafraction motion was analyzed using sagittal cinematic MRI (2D FIESTA, TR:6.6ms, TE:1.1ms, ST:6mm, FA:60, FOV:28x28cm, Matrix:256x192, 150 images, scan time 2min) acquired at two separate time points over a mean interval of 26 min (15-40 min). Motion was quantified by placing a 16x16 pixel template over the bladder/rectal interface at the level of the bladder neck. This template was automatically tracked across images using a cross-correlation algorithm developed in our institution. The PTV was derived by separating uncertainties for delineation, CT-MRI registration, inter- and intrafractional uncertainty into random and systematic components. These were used in a margin calculation to determine the appropriate PTV margins.

Results: CBCT image quality permitted good visualization of bones, soft tissues, and surgical clips. The mean (SD) interfraction motion for the right lateral, left lateral and inferior surgical clips was, in millimeters, [AP 5 (4), RL 4 (3), SI 4 (6)], [AP 4 (3), RL 3 (2), SI 3 (6)] and [AP 4 (3), RL 3 (2), SI 3 (6)], respectively. The mean (SD) intrafraction motion (AP and SI) was, in millimeters, 1.4 (3.4) and 0.4 (4.9) over a 15-40 minute interval. Derived PTV margins (AP, RL, SI) for the superior and inferior aspects of the $CTV_{prostate\ bed}$ were (15mm, 12mm, 14mm) and (11mm, 8mm, 11mm) without CBCT guidance, respectively. With daily CBCT guidance, derived PTV margins (AP, RL, SI) for the entire $CTV_{prostate\ bed}$ were 7mm, 5mm, and 8mm.

Conclusions: Our results indicate that interfraction motion is more pronounced at the superior aspect of the $CTV_{prostate\ bed}$. In the absence of image-guidance, a PTV margin of 15mm is appropriate. The addition of daily on-line correction with CBCT may permit up to a 50% reduction in the PTV margin. This data supports further evaluation of IGRT in patients receiving radiotherapy after prostatectomy.

534 poster

IMPACT OF DEFORMATION IN IMRT TREATMENT PLANNING BASED ON REPEATED MRI OBSERVATION OF THE PROSTATE: RATIONALE FOR THE MRI ACCELERATOR

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Purpose/Objectif: Interfractional movement and deformation of the prostate lead to uncertainties in the definition of the target volume. These uncertainties are conventionally countered by applying margins. In this study we compared MRI based repeated planning, accounting for translation, rotation, and deformation, with the best fiducial marker based method, accounting for translation and rotation.

Materials/Methods: Until now we acquired five 3T MRI scans of three healthy volunteers on different days. The repeated images were rigidly registered to the first image with respect to the prostate, accounting for translation and rotation. Seven-beam IMRT plans were created on all geometries with our treatment planning system (PLATO, Nucletron) for irradiating the prostate to 84 Gy. IMRT optimization was done using constraints on the 2cc dose of rectum and bladder. PTV was defined as CTV (prostate plus seminal vesicles) plus 4 mm. To investigate the marker based method we projected the dose distribution of the day with maximum rectum filling and the day with minimum rectum filling on the other four geometries. We compared the daily optimized treatment plans with the marker based method in terms of dose to the prostate (99% dose) and the rectum (2cc dose).

Results: Taking the treatment plan with maximum rectum filling as reference, we found for the marker based method a dose decrease

to the prostate (1.0-4.0 Gy) and the rectum (0.5-2.2 Gy). In case of repeated planning we found a dose increase to the prostate of 0.4-1.3 Gy while not exceeding the rectum constraints. Taking the treatment plan with minimum rectum filling as reference, we found for the marker based method a dose decrease to the prostate (0.0-1.4 Gy) and a dose increase to the rectum (0.1-5.2 Gy). In case of repeated planning we found a dose decrease to the prostate of 0.0-2.4 Gy due to rectum constraints.
Conclusions: Patients with variation in rectum filling can benefit from repeated planning in terms of tumor coverage and rectum sparing. When the entire treatment is based on a single observation, dose decrease to the prostate can occur due to variation in rectum filling during the treatment. In case of repeated planning this dose reduction can be compensated. In addition, repeated planning can exploit favorable geometries of rectum and prostate. Evaluation of more volunteers is required to improve statistics and to assess the impact on a treatment of 35 fractions.

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IMPLEMENTING IMAGE-GUIDED RADIATION THERAPY USING HELICAL TOMOTHERAPY

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Purpose/Objectif: The introduction of new technologies such as IGRT and IMRT into a busy clinical environment requires resource analysis and optimisation. In Ottawa, we installed a helical tomotherapy unit (TomoTherapy Hi-Art, Madison, Wisconsin) in a pre-existing bunker too small for a modern linac. The aim of this work was to measure operational impact of IGRT and tomotherapy.
Materials/Methods: We report parameters from the first 8 months clinical operation where a three-dimensional image was obtained prior to each treatment. Throughput was measured by recording the time spent at each stage of the preparation and delivery processes. A record of machine interrupts was maintained. At least one patient treatment plan per day is delivered to a phantom to check all integrated tomotherapy subsystems (i.e. gantry rotation speed, couch speed, dose rate, MLC, jaw calibration and calculated dose). At our centre, three radiation therapists are responsible for all aspects of tomotherapy treatment planning and delivery. Patients were selected according to pre-arranged protocols designed to evaluate image-guidance for patient positioning. Sites treated to date include high-risk prostate, bladder, spine, hemithorax, brain, head and neck. All dose distributions were verified by measurement prior to treatment.
Results: Tomotherapy implementation was faster than a single energy linac photon beam (23 vs.31 days) but 5 days of operational training reduced the difference. Mean time for treatment preparation per patient was 8.9 hours (median 6.6); mean overall time for patient setup, daily imaging, registration and treatment was 26.5 minutes (median 25.0). Eliminating imaging and registration reduces the mean to 18 minutes. For an 8-hour shift, a 3-therapist team is able to maintain a patient load of at least 16 patients with daily imaging: 24 patients with weekly imaging. Over the first 130 treatment days the mean output was 0.5% above reference and varied about the mean with a SD of 0.32%. Approximately 1.5% (2 of 132) of output measurements exceeded 2% from reference and 5 days have been lost to machine failure. Single point doses were normally distributed (SD 2.4%), 92% and 97% of all points were within 3% and 5% respectively of expected dose. All coronal plane film measurements had a distance to agreement of less than 3 mm.
Conclusions: In summary, our experience using tomotherapy to introduce IMRT and IGRT has been successful and has generated excitement within all professional groups.

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IMPROVED PATIENT POSITIONING USING A CONE BEAM CT IN COMBINATION WITH A ROBOTIC TABLE TOP

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Purpose/Objectif: In image guided radiotherapy (IGRT) the precision and exact positioning of the patient is of fundamental importance. Using a linac with on board cone beam CT (CB-CT) it is possible to detect translational and rotational errors in positioning of the patient by using image registration methods. Both errors can be compensated by using the HexaPOD table top (medical intelligence). This paper describes the resulting accuracy of the combination of a Synergy S linac (Elekta) with a robotic HexaPOD couch.
Materials/Methods: For analyzing the reproducibility and accuracy an Alderson head phantom was fixed on the table top. First the spatial resolution of the CB-CT registration software was tested by using a series of dose plans and a CT-scan of the head phantom in the reference position. The displacements of the shifted plans were calculated and compared to the numerical values to evaluate the accuracy of the CB-CT. The stability of the X-ray volume imaging (XVI) system was tested in terms of reproducibility and with a focus on the moveable parts, i.e. the influence of kV panel and the source arm on the reproducibility and accuracy of both bone and grey value registration. In consecutive measurements the positioning accuracy of various translational, rotational and a combination of translational and rotational corrections were investigated.
Results: The spatial resolution of the system is in the range of tenth of a millimeter in all directions though the reference CT (5mm) and the CB-CT (1mm) have minor resolution. The system performance of the XVI system alone was very stable with mean translational and rotational errors of below 0.2 mm and below 0.2°, respectively. The mean positioning accuracy of the HexaPOD table in combination with the XVI system summarized over all measurements was below 0.3 mm and below 0.3° for translational and rotational corrections, respectively. The grey value match was found to be slightly more accurate than the bone match.
Conclusions: With the cone-beam system displacements in positioning of tenth of a millimeter can be detected with high accuracy. The XVI image acquisition and registration procedure were very reproducible within only marginal bounds. Both translational and rotational positioning errors can be corrected very precisely with the HexaPOD. The HexaPOD table is therefore well suited to complement cone-beam CT to take full advantage of position correction in six degrees of freedom for IGRT.

537 poster

INCLUDING MOTION IN IMRT PLANNING: SIMULTANEOUS OPTIMISATION ON A SET OF BREATHING PHASES

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Purpose/Objectif: Recently 4D CT data sets of patients with lung tumours have become readily available, showing the deforming patient anatomy in several different breathing phases. Instead of only using this information to delineate an enlarged target volume - covering the tumour position in all breathing phases - it would be

desirable to spare as much healthy tissue as possible by gating or tracking and therefore to include the knowledge about voxel movements in IMRT treatment plan optimisation.

Materials/Methods: The required voxel tracking between the different breathing phases was done by image registration with the method of fluid deformation. The existing treatment planning system (research version of KonRad) was extended by an option to include those deformation fields in the optimisation, allowing different fluence matrices for the different phases. As first test cases simple phantoms with only two 'breathing phases' were used, with a 'tumour' motion of 4cm and a stationary 'organ at risk' (OAR). The resulting plans for different phantoms and beam geometries were compared to the plans obtained by just using a single phase (which corresponds to gating) with respect to their fluence matrices, dose distributions and dose volume histograms.

Results: '4D optimisation' on phantom data showed plausible results, where the option to vary the fluences from phase to phase could be used to achieve better target coverage with less dose to the OAR depending on the choice of beam directions. For beams irradiating the OAR in one phase but not the other, the 'bad' phase was suppressed, reproducing a gated treatment. For beams being equivalent in both phases the delivered dose was distributed equally between them, which corresponds to tumour tracking.

Conclusions: The presented method performed well in choosing 'good' phases for the dose delivery, so as a first application it could be used to select a specific breathing phase for gating. Currently the optimisation is tested on 4D CT data of patients with lung tumours. As a next step a modification to steer the trade-off between dose delivery efficiency (tracking) and simplicity (gating) is to be implemented.

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INFLUENCE OF DAILY SETUP MEASUREMENTS AND CORRECTIONS ON THE ACTUALLY DELIVERED DOSE FOR 222 IMRT TREATMENTS OF PROSTATES WITH IMPLANTED MARKERS

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Purpose/Objectif: In this study the impact of marker-based position verification, using daily imaging and an off-line correction protocol, was evaluated by calculating the actually given dose to prostate, rectum and bladder.

Materials/Methods: Patients were treated for prostate cancer in the period 2001-2006. All patients were planned with IMRT using Plato (Nucletron, Veenendaal, The Netherlands) and received 35 fractions. Plans with 5 beams were optimized taking target coverage (prostate) and organs at risk (rectum, bladder) into account. At least 99% of the CTV should receive 95% or more of the prescribed dose of 70 Gy ($D_{99\%}$ 66.5 Gy). A boost volume was defined with a prescribed dose of 76 Gy. Margins around the boost volume were 8 mm, excluding overlap with rectum and bladder. The volumes of rectum and bladder receiving a high dose of 72 Gy (V_{72}Gy) should be smaller than 5% and 10%, respectively. The prostate position was verified daily using implanted fiducial gold markers. For these measurements the first segment of all five beam portals was imaged on an EPI (iView, Elekta Ltd., Crawley). Markers were detected with in-house developed software and their position was reconstructed in 3D. Decisions on setup corrections were taken off-line using an adapted shrinking action level protocol. Calculation of the actually delivered dose, including organ movements during each fraction, was done using a version of Plato's dose engine, enabling batch processing of large numbers of patients. The dose was calculated with and without inclusion of setup corrections, and evaluated with respect to the original static plan. Movements as measured with the markers were considered representative for all organs.

Results: Table 1 (results are mean ± SD (range)) shows that daily organ movements would result in a significant underdosage of both CTV and boost volume relative to the original plan. This underdosage was prevented by the daily setup corrections. The dose to rectum and bladder was on average unchanged, but there was a large spread introduced by the organ movements, which was reduced by including setup corrections.

Table 1	No corrections vs. Static	Corrections vs. Static
Boost: $D_{99\%}$	-2.2 ± 3.2 Gy (-15.7 - +1.5 Gy)	-0.3 ± 0.4 Gy (-2.5 - +0.4 Gy)
CTV: $D_{99\%}$	-2.1 ± 3.7 Gy (-35.1 - +1.4 Gy)	-0.2 ± 0.4 Gy (-3.6 - +0.5 Gy)
Rectum: V_{72Gy}	-1 ± 5 % (-15 - +28 %)	-1 ± 1 % (-5 - +2 %)
Bladder: V_{72Gy}	+1 ± 8 % (-19 - +28 %)	-2 ± 2 % (-12 - +6 %)

Conclusions: Calculation of the actually delivered dose shows that, in the absence of position verification and setup corrections, margins of 8 mm are insufficient to account for position uncertainties in the treatment of prostate cancer. With our daily off-line correction protocol the remaining random variations are accommodated adequately by the margins.

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INTRA- AND INTERFRACTIONAL MOVEMENTS OF THE BEAMCATH URETHRAL CATHETER FOR IMAGE-GUIDED RADIOTHERAPY OF PROSTATE CANCER

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Purpose/Objectif: Radiation treatment of prostate cancer is characterized by the necessity of a very high dose to the PTV region and a narrow margin to one of the risk organs, the rectum. A high geometrical precision is therefore needed. It can be achieved by daily patient positioning based on the location of the prostate itself. Image-guided prostate localization can be obtained by the BeamCath urethral catheter, which contains radiopaque fiducials for prostate visualization. The catheter is held in place by a balloon inflated with air in the bladder and a weight pulling in the caudal direction [1].

[1] P. Bergström, P.-O. Löfroth, and A. Widmark, Int J Radiat Oncol Biol Phys 1998; 42, 305.

Materials/Methods: The BeamCath technique was investigated for 52 prostate cancer patients with a catheter inserted at the planning CT scan and at four treatment fractions in supine position. The planned isocenter coincided with a catheter fiducial lying in the prostate. At treatment, a left-lateral setup film was used for alignment of the isocenter catheter fiducial with the central axis of the accelerator. After couch adjustments, portal films of the left-lateral and right-lateral treatment fields were acquired for setup verification. The planning DRRs, the initial setup films and the portal films were analyzed for intra- and interfractional catheter movements.

Results: The intrafractional cranio-caudal (CC) catheter movement was asymmetric with a tendency of a gradual caudal motion (mean 1.0 mm). The anterior-posterior (AP) motion showed no asymmetry. The interfractional catheter movement within the pelvis was characterized by a systematic displacement with standard deviations (SD) S of 2.4 mm (CC) and 2.6 mm (AP). SD of the random displacement s was 2.0 mm (CC) and 1.7 mm (AP).

In 5% of the setup films, large caudal catheter displacements of 7-30 mm along the urethra were observed. This was most often associated with a reduced volume of the air-filled balloon. Recatherisation often led to a catheter position close to that of the planning DRR.
Conclusions: In the AP direction, which is most critical with regard to rectum sparing, the BeamCath technique allows a narrowing of the CTV to PTV margin. However, the technique seems to suffer from instabilities in the direction of the urethra. Further insight can be obtained from an analysis of repeated CT scans where prostate and catheter movement can be separated (to be published).

540 poster

INTRA-PATIENT VARIABILITY OF TUMOR VOLUME AND TUMOR MOTION DURING RADIOTHERAPY FOR NON-SMALL CELL LUNG CANCER

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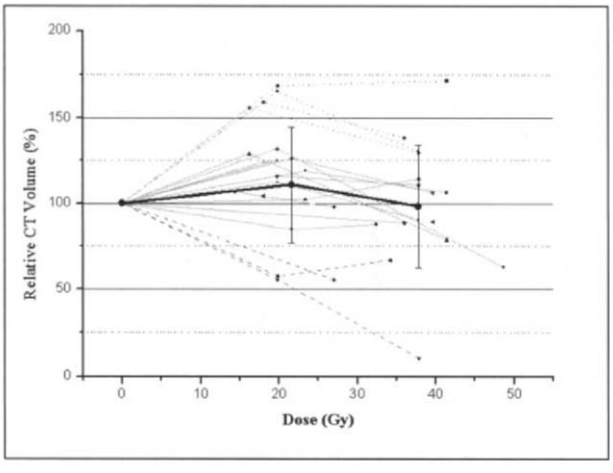
Purpose/Objectif: To investigate the change in tumor volume, motion and breathing frequency during a course of radiotherapy, for locally advanced non-small cell lung cancer.
Materials/Methods: Twenty-three patients underwent CT-PET and Respiration Correlated CT scans prior to treatment, which was repeated in the first and second week following the start of radiotherapy. Patients were treated with an accelerated fractionation schedule, 1.8 Gy BID, with a total tumor dose depending on pre-set dose constraints for the lungs and the spinal cord.
Results: A striking heterogeneity of tumor volume changes was observed at all time points. In some patients the volume decreased > 30% (3/23) in others the volume increased > 30% (4/24) but for the majority of patients (16/23) the tumor volume only changed slightly (< 30%). No significant changes in average tumor motion or breathing frequencies were seen during treatment. Although quite some changes in individual tumor motion were seen, only in one patient would this have led to an increase of the internal margin > 1 mm in one direction, one week after the start of treatment, and in 3 patients, 2 weeks after the start of the treatment.
Conclusions: A large variability of changes in tumor volume between the patients was observed. This underscores the need for repeated imaging during the course of radiotherapy. However, the changes in tumor motion are small, which indicates that repeated respiration correlated CT does not appear to be necessary.



541 poster

KVCT-MVCT MATCHING ON A HELICAL TOMOTHERAPY UNIT (HT): VALIDATION OF AN AUTOMATIC REGISTRATION TECHNIQUE AND ESTIMATION OF THE CAPABILITY TO POINT OUT SET-UP ERRORS.

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Purpose/Objectif: To investigate the accuracy of an automatic registration technique implemented in the HT unit to match KV- and MVCT images to correct any set-up errors and to define the minimum shift detected by the registration procedure.
Materials/Methods: KVCT scans of the pelvic region of a Rando phantom with several internal markers (1mm size) were performed with different slice thicknesses from 2 to 6mm (2_KVCT-6_KVCT); 3 and 5mm represent the slice thicknesses used in clinical practice, whereas 2, 4 and 6mm are those of the allowed MVCT acquisition modality (Fine-Normal-Coarse). Several MVCT were acquired for each KVCT scan: for 3_ and 5_KVCT scans the corresponding MVCT images with all three modality acquisition were taken, whereas for 2, 4 and 6 mm only the same slice thickness MVCT scan was acquired. All MVCT scans were repeated both for the whole and for a limited (~ 6cm) pelvic region. For each scan KVCT and MVCT images were matched with the automatic bone registration technique and misalignment between correspondent markers was evaluated along 3 main axes and in 3D space. To estimate the minimum recognizable shift, fixed translation movements were applied (10mm , 5-1mm) and after automatic matching the estimated couch shifts and the distance between the markers were evaluated. Independent lateral, longitudinal and vertical shifts and global translations were applied.
Results: Globally, 201 points were considered with only 11 markers not visible on MVCT. For the complete phantom scan (159 points) an average position difference equal to 0.1mm (1SD=1.8mm) and an average point distance equal to 1.7mm (1SD=2.6mm) were estimated; the same parameters were equal, respectively, to 0.03mm (1SD=1.0mm) and 1.4mm (1SD=1.0mm) for the partial phantom scan (42 points). The automatic registration technique seems to be more accurate for similar slice thickness of KVCT and MVCT scans. Average markers distances were estimated equal to 2.7mm (1.6-2_KVCT- 4.6-5_KVCT), 1.8mm (1.4-3_KVCT-2.3-5_KVCT) and to 1.3mm (1.1-6_KVCT-1.5-5_KVCT) respectively for Fine, Normal and Course MVCT scan. For fixed translations, the average estimated couch movements were always within 1 mm (0.07-1.21mm) with respect the applied shifts and the mean 3D distance £2mm.
Conclusions: The automatic bone registration technique implemented in the HT unit shows very good accuracy both in the matching KVCT-MVCT images and in the capability to point out even small shift errors.

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LINAC CONE-BEAM-CT OPTION FOR TREATMENT PLANNING: A POSSIBLE APPROACH FOR DART (DYNAMIC ADAPTIVE RADIOTHERAPY)?

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Purpose/Objectif: For image-guided radiotherapy (IGRT) the different vendors of linear accelerators offer new kV imaging tools. These systems include - besides a radiographic and fluoroscopic mode - CT functionality. The aim of this study was to evaluate the future poten-

tial of such a cone beam CT option for therapy planning purposes allowing dynamic adaptation for target volume changes.

Materials/Methods: The Varian On-Board Imager® (OBI) Cone Beam CT (CBCT) option consists of a kV-source and kV-Imager mounted on robotic arms perpendicular to the MV therapy beam. In a single 360° rotation a volumetric CT data set can be acquired with 14 cm scan length and - depending on the geometrical setup - a 25 or 45 cm field-of-view. In order to calibrate the system with regard to HU a special phantom has been designed to include the whole imager area. Removable inserts allow a 3D calibration as well as measurements of central axis doses. A planning study has been carried out to determine the usability of CBCT data and compare these to with diagnostic CT data.

Results: Comparisons of data between a diagnostic CT scanner and the 3D-calibrated Cone Beam CT with regard to image quality and Hounsfield units representation for an humanoid phantom (RSD Alderson) indicate good accordance. Central axis doses applied during the acquisition of one volumetric data set are between 1.5 and 4 cGy depending on the geometry. Results with real patient data show excellent image quality. Low contrast resolution in CBCT slices turns out to be even better than for diagnostic CT scans, whereas the spatial resolution of CBCT data is inferior. Relative dose distributions in CBCT-based plans show minor differences to plans calculated using a diagnostic CT image dataset ($p=0.002$) and absolute dosage deviations are within 1 % ($p=0.001$).

Conclusions: This work illustrates that a properly calibrated Cone Beam CT option allows offline treatment planning. Furthermore the image quality is sufficient for contouring of target outlines. CBCT can serve as control CT in order to adapt the target volume and resize the treatment fields and/or optimize the treatment plan. For this purpose CBCT data were matched with the reference CT data using automatic matching followed by manual fine adjustments. As the acquisition time for the scan is around 1 minute, blurring due to organ movements is a limitation when scanning in the thoracic region. Future potential is online re-planning, but such an approach will have the need for automatic segmentation.

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METHODOLOGY OF IMPLANTED FIDUCIAL MARKERS FOR IMAGE-GUIDED RADIOTHERAPY (IGRT) IN THE TREATMENT OF SPINAL LESIONS

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Purpose/Objectif: To examine the methodology of insertion of fiducial markers for precise set-up and real-time positioning in patients with spinal/paraespinal lesions treated with intensity modulated radiotherapy (IMRT).

Materials/Methods: Three gold markers (1 x 3 mm) were implanted into deep muscle, near the tumor, using a transcutaneous approach under CT guidance.

CT planning was done with the patient in supine position, with arm fixation and a vacuum system for the extremities. Routine CT scan with intravenous contrast and Magnetic Resonance Imaging were used to identify the target volume. Inverse planing was done using the Eclipse (Helios) planning system (the especific method of treatment delivery was the sliding window) The coordinates of the three markers were manually transferred from the RT planning system to the Clinac workstation. Before each session the patient was positioned on the treatment couch and 2 orthogonal portal images were adquiered using an amorphous silicon panel (aS 500, Varian). To localizate of the 3 gold seeds and the target position a commercialized computer program (ISOLOC® software, MED-TEC) was used. This program provides the couch movements required to move the target to the CLINAC isocentre and the distance between each marker. Radiation was delivered by a Varian 2100CD 6 MV photon beam using the 120 leaf dynamic multileaf collimator (DMLC) for IMRT. A weekly CT scan was done to verify the relative position between markers and isocenter.

Results: Three gold markers were implanted in 3 patients (median age: 43 years, range 25-63) with paraspinal metastases in two cases: 1 non small cell lung cancer and 1 endometrial carcinoma, and 1 recurrence after surgery and radiotherapy in an adult patient with a Wilms' tumor. In this case salvage surgery was able to be performed. The treatment was deliverated with a 5-7 coplanar beam arrangement and hypofractionation: 2.5Gy/d x 15 days in one, 3 Gy/d x 15 days in other and 3,75 Gy/d x 10 in the last one. Doses to the GTV was: median 41.8 Gy (range 36.1-45.1 Gy). Doses to the spinal cord: median 17.9 Gy (range 6.2-23.5 Gy).No serious complications related to the gold markers insertion were noted. Acute tolerance to the treatment was remarkable with excellent palliation. The 3 patients are alive and free local disease at 7, 9 and 12 months after the treatment.

Conclusions: The use of implanted fiducial markers is an optimal technique for precise set-up in paraspinal lesions. This technique is a suitable method for delivering high dose of radiation to the target while maintaining a low doses to adjacent normal structures.

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ON-LINE CORRECTION IN PROSTATE RADIOTHERAPY USING THE ACCULOC™ FIDUCIAL LOCALIZATION SYSTEM-IS THIS THE GOLD STANDARD IN IMAGE GUIDANCE TECHNOLOGY?

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Purpose/Objectif: To assess the feasibility and accuracy of using the Acculoc™ fiducial localization system to facilitate an on-line correction protocol during conformal radiotherapy of prostate carcinoma.

Materials/Methods: The image guided radiotherapy (IGRT) technology available is vast, and much is limited by the expense of installation, commissioning and quality assurance. We have assessed whether a simple IGRT system using implanted fiducial markers in combination with software to detect errors could be clinically implemented within a busy department.

In this feasibility study, six patients with localised prostate cancer had 3 small non-migratory gold seed markers implanted transrectally into the prostate gland. Two portal images separated by at least 30° were taken immediately prior to each fraction of radiotherapy. The operator manually clicks on any part of the seed, and an automated on-line analysis calculates the registration of the planned and treated volumes with 6 degrees of freedom (3 translational and 3 rotational). Couch movements to correct the isocentre position are given. Standard deviations (SD) of systematic and random errors were calculated in 3 directions, left-right (LR), superior-inferior (SI) and anterior-posterior (AP). The duration of treatments were timed and compared to standard radiotherapy on the same unit with matched patient related parameters. Interuser variability and phantom transfer errors were calculated to determine the accuracy of the system.

Results: Seed implantation was well tolerated and no complications reported. 120 interfractional displacements were analysed.

Mean total treatment times using daily imaging with implanted markers was 12.1 minutes compared with 9.7 minutes for treatment

including standard imaging. Interuser variability was a small component of the total errors. Phantom study analysis shows a translational shift accuracy of 0.4mm (1SD) and rotations of 0.4°(1SD).
Conclusions: The Acculoc™ localization system is accurate and feasible to use within a busy department. This time efficient software requires a short training session and has minimal interuser variability. Clinical implementation of IGRT with this system has now commenced within the department. This study highlighted the rotational component of errors and a strategy for responding to this is currently being pursued.

	Translational (mm)		Rotational (mm)	
Axes	Systematic SD	Random SD	Systematic SD	Random SD
LR	3.4	2.6	9.3	6.1
SI	3.6	2.9	6.1	5.5
AP	4.3	3.5	4.5	3.8

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ON-LINE CORRECTIONS USING A CONE-BEAM CT FOR EXTRACRANIAL STEREOTACTIC TREATMENTS

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Purpose/Objectif: The use of image guidance is strongly indicated in stereotactic radiotherapy, where the high doses, conformed to small targets, demand high geometric precision. From January 2006 in our Institution for these treatments, beside the use of a Body-frame, we start to acquire a pretreatment KV cone beam CT (Elekta Synergy-XVI) to perform on-line positioning corrections. In this work we analyze the displacements along the 3 axes obtained by the XVI system, respect to the isocenter position generated by the Body Frame; we also focus on the problem of a correct imaging and positioning of the target volume for the different treatment sites.
Materials/Methods: 33 Patients (18 lung, 7 abdomen, 4 vertebral body, 4 other) have been treated with a stereotactic radiotherapy. Patients were immobilized using a body cast or a vacuum pillow; isocenter coordinates were generated by a Body frame and used for patient set-up at each fraction. Before the treatment delivery, a kV Cone beam CT was acquired (a total of 65 acquisitions), and on-line corrections for set-up and target position were performed. N.14 patients were transported from the CT room after the acquisition of the CT data set used for planning, directly to the linac room on a rigid table, remaining immobilized inside the body frame (A group). N.19 Patients (B group) were completely re-positioned at the Linac.
Results: The 3D displacements predicted by the system on a QA phantom and the statistic of displacements along the 3 axes obtained by XVI acquisitions for each groups are reported in table 1. The distributions of displacements respect to the Body-frame isocenter position result narrower for group A than for group B along the lateral and longitudinal axes, due to an incorrect re-positioning of the patient inside the body frame for the B group. This effect is not observed for displacements along the vertical axis, that are almost the same for both groups. For lung nodules treatments, it is generally possible to check visually the tumor match between cone beam and reference CT and a good agreement (within 3 mm for 10 patients) is observed comparing automatic grey-value registration and tumor manual matching. Target positioning in the abdomen is more difficult and probably needs the use of internal markers (or post-surgical clips).

		Lateral X (cm)	Longitudinal Y (cm)	Vertical Z (cm)
Phantom	mean	0.10	-0.04	0.07
	standard deviation	0.06	0.05	0.04
Patients Group A	mean	0.07	-0.02	-0.3
	standard deviation	0.29	0.44	0.25
Patients Group B	mean	-0.09	0.18	-0.26
	standard deviation	0.60	0.78	0.27

Conclusions: In our clinical experience, the implementation of Cone-beam-CT image guidance for extracranial stereotactic radiotherapy is a safe and effective way for performing high precision Patients set-up and isocenter localization overcoming some errors that can occur using Body-Frame alone.

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PATIENT SETUP VERIFICATION: ERRORS ESTIMATED BY CONE BEAM CT AND ELECTRONIC PORTAL IMAGING DEVICE

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Purpose/Objectif: For many years we used 2-dimensional (2D) localization images of the electronic portal imaging device (EPID) for setup verification. Recently 3D imaging became available with the introduction of Cone Beam CT (CBCT) integrated with the treatment machine. We compared setup errors of prostate cancer patients monitored with CBCT or EPID.
Materials/Methods: We selected patients from 2004/2005 (N=103) treated at similar accelerators for whom setup was monitored within an off-line shrinking-action-level protocol. In case of 2D verification (n=50), 2 digitally reconstructed radiographs from the planning CT were registered with two EPID's taken just prior to treatment with an amorphous silicon detector (1 anterior-posterior (AP), 1 lateral). The AP image provided information about the left-right (LR) and cranial-caudal (CC) position, the lateral image about the CC and AP position (the CC position was averaged, rotations were ignored). For 3D verification (n=53), the planning CT was registered with a 3D CBCT scan acquired just prior to treatment (impact of rotations were minimized). Both methods used automated registration of the bony anatomy based on chamfer matching.
Results: The systematic setup errors Σ for the LR, CC and AP direction (corrections included) were similar for the 3D and 2D evaluation due to the corrections (Table). The mean 3D vector length of the setup error (Σ) was 1.9 mm for both groups with a maximum of 3.4 mm. Estimated random errors Σ were largest for the AP and LR direction for both groups. For 3D evaluation, the estimated Σ was significantly larger for the AP direction ($p=0.04$) and LR direction ($p<0.001$) compared to 2D evaluation. The group mean in the AP direction significantly deviated from zero for both 2D and 3D evaluation ($p\leq0.01$). Seventy percent of the patients with 3D evaluation were shifted against 46% with 2D evaluation ($p=0.01$); for the three directions the number of shifts was 23% vs. 18% (CC, $p=0.6$), 49% vs. 26% (LR, $p=0.02$), 49% vs. 26% (AP, $p=0.02$). Shifts in the AP and LR direction were correlated for both groups ($p\leq0.02$).
Conclusions: With 3D setup evaluation larger deviations were detected, and therefore they were shifted significantly more often than patients with 2D evaluation. Given the high geometrical accuracy of

CBCT registration assessed with phantom studies, it is most likely that the true 3D setup variation is larger than estimated in the past by 2D verification, especially for the AP and LR direction.

Errors 1SD (mm) including corrections

Device	Direction	Σ	σ	mean
2D EPID N=50	LR	1.2	1.9	-0.1
	CC	1.1	1.1	0.3
	AP	1.0	1.5	0.7
3D CBCT N=53	LR	1.2	2.2	0.0
	CC	1.3	1.3	-0.1
	AP	1.0	2.2	0.4

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PHANTOM DOSE MEASUREMENTS FOR THE EXACTRAC X-RAY 6D POSITIONING SYSTEM

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Purpose/Objectif: ExacTrac x-ray 6D (BrainLAB, Heimstetten) is a system used for positioning of patients before radiation treatment. The ExacTrac positioning system consists of a stereo IR-camera and two x-ray imaging devices. The initial set-up is guided by the IR camera and the final target localization is done with the x-ray device. The images are matched with DRRs obtained from the CT scan. Ideally two (one pair) x-ray images are taken before set-up and two after for verification per fraction. In total 100 x-ray images are acquired for a 5 fractions / week and 5 weeks treatment. The purpose of this study was to determine the skin dose and estimate the potential additional risks, both deterministic and stochastic.

Materials/Methods: A PTW M31002 ionization chamber (no build-up) was attached to the BrainLAB pelvis phantom and in a solid water phantom at depths 3 and 5 mm, FSD = 150 cm. X-ray images were acquired with the BrainLAB ExacTrac x-ray 6D positioning system with different kV and mAs with beam filtration of 2 mm Al equivalent. The PTW 11051 electrometer was used and the measurements were correlated according to IAEA TRS-398.

Results: The additional entrance dose, using 120 kV, 160 mA, and 130 ms was determined to be 0.58 ± 0.02 mGy per exposure (95% CI). To reach the threshold of 1 Gy, which is the limit for acute skin erythema, up to 1724 exposures or 4 minutes of fluoroscopy, with 7 frames per second could be aquired. The dose at depths 3 and 5 mm were determined to be 0.84 ± 0.04 and 0.81 ± 0.06 mGy per exposure, respectively. In a worst case scenario, an average of 5 image pairs per day are acquired during 5 weeks treatment and the skin dose will be 72.5 mGy, which is much lower than the threshold dose. With the weighting factor of 0.01, the effective dose HE is determined to be 1.45 mSv per treatment, which should be compared to the effective dose of 10 mSv obtained from a pelvis CT scan.

Conclusions: Patients positioned using ExacTrac will not suffer from any acute skin erythema even though a large amount of images are acquired for the set-up. For future real-time tumor tracking solutions based on fluoroscopy, the skin-dose may become a limiting factor.

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PHANTOM VERIFICATION OF A RESPIRATORY GATING SYSTEM FOR LUNG AND LIVER

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Purpose/Objectif: A commercially available, infrared / x-ray based image guidance system (Novalis Body / ExacTrac X-Ray 6D, BrainLAB) has been modified to allow respiration triggered treatments. Methods to verify the system performance have been developed and tested.

Materials/Methods: The system features real-time tracking of the patients' external breathing signal via an infrared tracking device. Additionally, stereoscopic x-ray images are acquired at user-defined moments within the patient's breathing cycle to image the position of an implanted marker. A relation between the externally detected breathing curve and internal tumor motion is established to first set-up the moving target correctly and second define a gating window. To verify system performance and accuracy a special gating phantom, simulating a breathing pattern was developed. The computer-controlled phantom consists of a moving platform, a slab-phantom with film inserts and integrated radio-opaque markers as well as a 5mm tungsten sphere. The markers are used for positioning and tracking. The phantom was used to assess: (a) the ability and accuracy of positioning and treating a moving target to a specific point within the breathing cycle. The center of the 5mm tungsten sphere was set as treatment isocenter and positioned in gating mode. Positioning and treatment verification was undertaken via a gated Winston-Lutz test on the positioned marker with a 10mm conical collimator and a small gating window. (b) the real-time capabilities of the system. System latency was measured by comparing two fields delivered with a 4mm conical collimator, one delivered during exhale and inhale and one delivered only during exhale. The difference in the blurring of the delivered fields in the direction of motion is due to system latency and can be assessed. (c) the beam-on/off effect on the total dose. The dose delivered by an un-gated field was compared to a field with app. 50 beam-on/off cycles. (d) the verification of the prediction alg. used to predict the correct moment for x-ray imaging. A phantom motion simulating coughing was used and multiple verification x-ray images of the positioning markers were analyzed for correct marker position. (e) the effect of target motion and gating window size on dose distribution. Single static, gated and un-gated fields as well as complete treatment plans were compared.

Results: Overall accuracy in positioning and treating a moving target was within 1mm. Imaging system latency, important for the real-time capability of the system was smaller 200 msec. Overall system latency resulted in a dose shift of app. 0.3 mm for the measurement set-up. The effect of gating on the amount of dose delivered showed to be insignificant. Target motion showed to have a large effect on the dose delivered by IMRT fields and entire treatment plans. By using a gated approach the desired dose distributions were well restored with the remaining deviations depending on the gating window size.

Conclusions: The Phantom tests for breathing synchronized irradiation showed promising results. Certainty in accurately delivering radiation to the target and therefore the ability to reduce safety margins are the most important factors.

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PLANNING ORGAN AT RISK VOLUME MARGINS FOR ORGAN MOTION OF THE INTESTINE

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Purpose/Objectif: To account for internal organ motion and set up uncertainties around organs at risk (OR) in radiotherapy (RT), the ICRU report no 62 introduced the Planning organ at Risk Volume (PRV). Although the ICRU have recommend the use of PRVs, it is

at present unclear how to deal with this concept, i.e. what kind of ORs PRVs should be applied for and what degree of the geometrical uncertainties should the margins around ORs account for. In the present study we have used an empirical approach to quantify PRV margins for the intestine, an important OR in pelvic RT.

Materials/Methods: The present study was based on intestine contours outlined in a total of 149 CT scans of 20 male bladder cancer patients (20 planning scans, 129 during treatment). From these data, we created location probability maps of the intestine for each patient. The maps contained voxels with values from zero to one, corresponding to the probability of intestinal occupancy for the voxel. A commercial treatment planning system was used to add 3D isotropic intestine PRV margins (from 5-30 mm, in intervals of 5 mm) around the intestine outline as seen in the planning scan. We then derived the fraction of patients for which a given PRV encompassed various degrees of intestine motion (85, 90 and 95 % of volumes with different probabilities of intestinal occupancy). As a measure of the specificity of the PRV, we also calculated the fraction of the PRV containing volumes with zero probability of intestinal occupancy.

Results: Isotropic margins of up to 30 mm are required to account for all intestine motion in 90 % of the patients, while isotropic margins of 5-10 mm will encompass 85-95 % of the volumes having a probability of intestinal occupancy of ≥75 % in the same fraction of patients. Intestine PRVs are not specific and will also include volumes where the intestine will rarely or never be located.

Conclusions: Large intestinal motion was found, but isotropic PRV margins of 5-10 mm will include most of the volumes with a large probability of intestinal occupancy in most patients. Currently, inverse planning studies focusing on the effect of using intestine PRVs when planning intensity-modulated whole pelvic RT have been initiated, and the first results from this study will also be presented at the meeting.

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QUANTITATIVE ANALYSIS OF MEGAVOLTAGE CONE BEAM CT IMAGES ON PROSTATE PATIENT DAILY TREATMENT SETUP BY BONY ANATOMY VS. GOLD SEED MARKERS

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Purpose/Objectif: MVCBCT is a new imaging modality that provides one potential route to practical IGRT. Recent advances in this technology have made it increasingly attractive for accurate quantitative analysis for prostate localization based on either bony anatomy or implanted gold seed markers. This study analyzes MVCBCT data to ascertain (1) if bony land marks are sufficiently accurate for reproducible prostate alignment and (2) parameters to determine a valid prostate target with gold seed markers.

Materials/Methods: Both planning CT and MVCBCT images were loaded into the MVision system (Siemens Medical Solution, Concord, CA). The automatic image fusions were executed based on bony anatomy and then manual fine-tunes were applied. The MVision system calculated the patient shifts based on the fusion results. The gold seed marker coordinates from both planning CT and MVCBCT were obtained and calculated for prostate shifts. The prostate drifts after bony anatomy alignment were calculated by gold seed marker shifts and subtracting the bony anatomy shifts. To define a valid prostate target with gold seed markers, two quantitative parameters were introduced: (1) the deformation coefficient calculated by distances (a, b, c) and (2) the inner angles (α, β, γ) between seeds. The overall coefficient was the root mean square (RMS) of all the distance and angle discrepancies between the plan and the MVCBCT determinations. The second parameter was the x, y, z axis rotational differences between the plan and MVCBCT. The overall rotation angle differences were also calculated by RMS of the x, y and z angles.

Results: For the accuracy of patient alignment based on bony anatomy, the results are shown in table 1. The prostate drifts in the lateral direction were less significant; however, the drifts in the longitudinal and vertical directions can be as much as 8 to 9 mm.

Table 1: Prostate Drifts while Bony Anatomy Aligned (mm)

	Lat	Long	Vert
Min	0.0	0.1	0.0
Max	2.7	8.1	8.8
Mean	0.6	2.4	2.6
S.D.	0.5	2.2	2.2

For the second study, the results are shown in table 2 and 3. The gold seed deformation on average was observed within acceptable clinical criteria; however, there were some extreme cases requiring special attention. The gold marker rotations generally exceeded the acceptable criteria in X-axis rotation while within criteria for Y and Z axes.

Table 2: Gold Seed Marker Deformation Coefficients

	Distance	Angle	RMS
Criteria	2.6	3.5	4.3
Min	0.7	0.1	1.3
Max	4.0	5.0	5.6
Mean	2.0	2.1	3.1
S.D.	0.8	1.1	1.0

Table 3: Gold Seed Marker Rotations

	X-rot	Y-rot	Z-rot	RMS
Criteria	3.0	3.0	3.0	5.2
Min	0.4	0.2	0.3	1.5
Max	7.5	3.4	6.4	9.8
Mean	4.0	-	-	-

Conclusions: For the first study, we found that the alignment of prostate patients using bony anatomy might miss the target by as much as 8 to 9 mm. For the second study, using the prostate labeled with gold seed markers to observe the deformation and rotation of the gland, we found that the pushing did not deform the prostate beyond acceptable criteria, but it did turn the gland in X-axis more than expected.

The MVCBCT provides an acceptable level of accuracy for localization of the prostate patients in the IGRT process.

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QUANTITATIVE EVALUATION OF THE REGULATED BREATH FOR MOTION ADAPTIVE RADIOTHERAPY

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Purpose/Objectif: Targets inside lung or liver usually move significantly due to respiratory motion. A generous margin must be allowed and large volume of normal tissue is irradiated with intensive radiation. Several techniques have been suggested to minimize the PTV relating to respiratory motion. One of methods developed in our institution, adapting radiation fields continuously to a moving

target needs information on the location of internal target by detecting it directly or indirectly. In our previous study, each volunteer's representative respiration signal was generated iteratively for guiding signal, and the audio guiding and visual guiding was compared. The purpose of this study is to evaluate the guided breath quantitatively.

Materials/Methods: A system regulates patient's respiration, consists of a ReMM (Respiratory monitoring mask), a thermocouple module, a screen, a inner earphones, and a laptop. ReMM with thermocouple was developed to measure the patient's respiration. A software was written in LabView 7.0 (National Instruments, USA), which acquires respiration signal and display its pattern. Two curves are displayed on the screen: one is a curve indicating patient's current breathing pattern, the other is guiding signal, which is iterated as a real respiration signal. A cycle of representative guiding curves are acquired by monitoring each volunteer's free respiration, then it generated iteratively. Five healthy volunteers are enrolled to regulate their breaths by this system. The time domain of the guided respiratory curves was converted to frequency domain by fourier-transform. The full width half maximum (FWHM) of each respiratory curve in the frequency domain was measured and compared. The smaller FWHM is, the more regulated breath is.

Results: The FWHM of breathing curves followed by audio and video guidance were estimated as less than 0.2 /sec, and 0.3 /sec for audio guidance. The discrepancies between guiding curves and breathing curves agreed with 26% and 24% of standard deviation for audio guidance only and for audio and visual guidance, respectively.

Conclusions: It was easier for volunteers to follow the guided curves, since the system generates a representative cycle of their real respiration iteratively. As an external respiration signal can be assumed to correlate with an internal tumor motion, target can be supposed to move following guided curves, when breathing is regulated.

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RE-PLANNING OF INTENSITY MODULATED RADIOTHERAPY (IMRT) FOR HEAD AND NECK CANCER PATIENTS

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Purpose/Objectif: Majority of patients with H&N cancers develop experience significant anatomical changes during treatment which may cause significant changes in doses delivered to targets and critical structures. The purpose of this study is to investigate the magnitude of these changes in doses to the targets and critical structures via retrospective re-planning using repeat CT imaging acquired during the course of IMRT treatment.

Materials/Methods: Six patients with locally advanced H&NSCC who were treated with IMRT and had repeat CT were selected. For each patient, the target volumes consisted of GTV including primary and involved lymph nodes with a 5mm margin(PTV_1), GTV with a 1 cm margin(PTV_2) and elective nodal regions (PTV_N). The prescription doses were 68.1 - 70 to PTV_1, 60 Gy to PTV_2, and 54 Gy to PTV_N, delivered simulataneously in 30-33 fractions. The critical structures included cord, brainstem, parotids, and mandible. The initial IMRT plans for each patient were created using the simulation CT images. A repeat CT scan for each patient was acquired after approximately 20 fractions. The targets and the critical structures were re-delineated. The initial IMRT dose distributions were applied to the new anatomic structures on the repeat CT images. This dose distribution reflects the real dose to various structures at the time of repeat CT scan. In addition, a new IMRT plan was created using the repeat CT scan for the remaining treatment course to assess whether replanning could optimize dose distribution to the tumor and other critical structures. Initial IMRTplans that were applied to the repeat CT scans and new plans created using the repeat CT plans were assessed using dose-volume statistics.

Results: PTV_1 and PTV_2 volumes between the initial and repeat CT scan decreased by an average of 39%, with a range of 25-57% ($p=0.01$) and of 30%, with a range of 20-43% ($p=0.003$). Without re-planning, both D_{98} and D_{95} for PTV_1 and PTV_2 decreased 3.6%, ranging from 1.7% to 10% ($p=0.06$ and $p=0.228$, respectively). Without re-planning, the average spinal cord and brainstem D_2 increased by 14% and 9%, respectively ($p=0.02$ and $p=0.27$). The average decrease in contralateral parotid D_{50} and mean dose with re-planning was 24.4%($p=0.18$) and 5.5% ($p=0.84$) respectively. The decrease in mandible D_2 with re-planning was <2% ($p=0.4$), although there was up to an 8% decrease for some patients.

Conclusions: The doses delivered to both target structures and normal tissues can significantly change during IMRT treatment as a result of tumor shrinkage. These changes could adversely affect patient outcome. The dosimetric accuracy of H&N IMRT treatment plans would likely improve with repeat CT imaging and re-planning. Further investigations will involve more frequent imaging of H&N IMRT patients using in-room megavoltage cone beam CT and offline re-planning on repeat CT images.

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REDUCTION OF IMAGING ARTIFACTS DURING REGISTRATION OF CT AND CBCT IMAGES

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Purpose/Objectif: Accuracy of treatments in radiation therapy is limited by patient motion and large daily changes in patients. Efficient imaging is needed to improve the treatment quality. Good quality volume images of patient must be available at treatment time and imaging must be performed in the treatment position. This is possible with Cone Beam CT. To find the differences between planning and treatment conditions for plan adaptation, the treatment time and planning volume images must be matched together using deformable image registration. However, the differences between CT and CBCT images may cause misregistration. Because treatment slots are limited in time, performance of registration and reconstruction algorithms is critical for the practical applicability of adaptive radiation therapy. Higher quality reconstruction allows better registration results, but requires more computing time. More computing time spent on image reconstruction leaves less computing time for image registration, which decreases the quality of match. Purpose of this work is to enhance the quality of registration in presence of imaging artifacts with very small computational overhead.

Materials/Methods: We used Thirion's deformable image registration algorithm and a special artifact reduction algorithm developed in this work. The implementation was tested with both clinical data and mathematically distorted images.

Results: Increase in registration quality was observed for both clinical test case and mathematically distorted image. Very small computational overhead was introduced.

Conclusions: We have developed a method to improve the quality of match between CT and CBCT images by performing fast artifact reduction during the registration process. The implementation was tested with both clinical data and mathematically distorted images. Significantly improved registration accuracy was achieved with very small computational overhead.

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STABILITY OF INTRA-PULMONARY TUMOR POSITION AND TUMOR BREATHING MOTION EVALUATED IN REPETITIVE 4D-CT STUDIES

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Purpose/Objectif: To evaluate the stability of tumor breathing motion and the stability of the tumor position with repeated 4D-CTs for stereotactic treatment of intra-pulmonary tumors.
Materials/Methods: Five patients treated with hypo-fractionated stereotactic radiotherapy for pulmonary metastases were included. For treatment planning one single spiral 4D-CT study (Siemens Somatom Sensation 20) was acquired. On the first day of treatment four repetitive 4D-CT studies in 10min intervals were acquired in treatment position. A pressure sensor pocketed in an abdominal belt was used for generation of the respiratory signal. With amplitude based gating 8 CT series were reconstructed equally distributed over the total breathing cycle for each 4D-CT study. All 200 CT series were transferred into Pinnacle treatment planning system. Relative to the series reconstructed in maximum inspiration phase the position of the tumor was evaluated using automatic image registration. For comparison of planning CTs and repetitive CTs, images were registered based on the bony anatomy to rule out bias due to set-up errors.
Results: The maximum amplitude of tumor breathing motion was 9mm on average in the planning 4D-CT studies for the five patients and was not different in the 4 repetitive 4D-CTs ($p>0.05$). One patient however showed decreased maximum motion on the repetitive 4D-CTs (12mm vs. 5mm±2mm). One patient with poor pulmonary function showed increasing tumor motion range during the 4D-CTs (plan: 14mm; 0min: 17mm; 30min: 28mm). During the repetitive 4D-CTs the mean position of the tumor was within a ±2mm range for 4/5 patients, for one patient a range of 5mm was seen. The stability of the 8 reconstructed series per 4D-CT during the repetitive CTs was similar; no series reconstructed in inspiration or expiration breathing phase showed significant increased or decreased stability during this period of 30min. Differences in tumor position between the planning CT and the first repetitive 4D-CT were similar for all reconstructed series.
Conclusions: The breathing motion range and breathing pattern assessed in one single planning 4D-CT study was found to be representative and consequently reliable for treatment planning. However, for selected patients especially with poor pulmonary function repeated 4D-CTs may be necessary. 4D tumor position was different between planning and treatment indicating the need for image-guidance for correction of this error.

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TARGET COVERAGE IN IMAGE-GUIDED HYPOFRACTIONATED RADIOTHERAPY OF LIVER TUMOURS

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Purpose/Objectif: In the Erasmus MC, stereotactic radiotherapy of liver patients is performed using a Stereotactic Body Frame (SBF) with abdominal compression to restrict the respiratory tumour motion. Prior to each of the three or five treatment fractions, a contrast enhanced CT-scan is acquired for daily localisation of the tumour in the SBF. The patient is then transported to the treatment unit, while remaining positioned in the SBF. Before delivery of the high fraction dose, electronic portal images are acquired to verify the set-up of the patient in the frame. The application of abdominal compression reduces tumour motion, but does not fully prevent it (residual motion >5mm). This motion causes artefacts in the planning CT-scan, and in the scans used for daily image guidance, yielding increased uncertainty in the tumour size and position. We have analysed the tumour coverage in our patients with a focus on the CT artefacts related to residual respiratory motion, and patient mobility in the SBF in between CT-scan acquisition and dose delivery.
Materials/Methods: Tumour coverage was evaluated for 57 cases, comparing the clinical image guidance protocol with alternative set-up protocols. The ITV^+ concept was introduced as an extension of the Internal Target Volume (ITV) to explicitly include the uncertainties in tumour position and dimensions related to breathing artefacts in CT-scans. Patient stability in the SBF was evaluated by identifying changes in the position of the bony anatomy in CT-scans and electronic portal images.
Results: Our clinical protocol resulted in ^{3}99% ITV^+ coverage in 77% of cases. A procedure based on a full 3D on-line geometrical analysis, achieved this high coverage in 96% of the cases. It was demonstrated that a PTV margin of 1.5 times the full breathing excursion compensates for all uncertainties related to (residual) respiratory tumour motion. Patient motion in the frame was generally small (£2mm, 1 SD). Twice, however, a treatment fraction was cancelled, because of observed large displacements.
Conclusions: Despite residual respiratory tumour motion in the SBF, resulting in geometrical uncertainties due to CT-artefacts, excellent coverage can be obtained with daily CT-assisted tumour set-up and small PTV-margins. The ITV^+ construct is useful to evaluate tumour coverage in the presence of CT-artefacts due to respiratory tumour motion. EPIDs provide important information on the patient stability in the SBF after daily acquisition of the CT-scan.

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THE USE OF 3D INTRA-MODALITY ULTRASOUND IMAGING FOR DAILY LOCALIZATION OF THE PROSTATE IN RADIOTHERAPY

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Purpose/Objectif: With the trend towards the use of tight margins for prostate cancer external beam radiation therapy (EBRT), inter-fraction prostate motion became an important source of geometric uncertainties. To ensure the delivery of the prescribed dose to the planned volume, many radiotherapy centers verify the prostate gland position and reposition the patient before each treatment fraction using two-dimensional ultrasound (2DUS) systems, which compare two orthogonal 2DUS images obtained at treatment time to the CT simulator scan images and are, therefore, cross-modality imaging verification systems.
Materials/Methods: Recently, we started to use a novel 3D system that consists of two parts: one system (US Sim) resides in the CT-Sim room and serves to collect the 3D reference image. A second system (US Guide) is based in the treatment room and allows collecting daily 3D images of prostate, bladder and rectal wall. 3D volumes are created from 2D slices by measuring the absolute position in space of the probe. To this end, the probe is outfitted with infrared markers whose motion is measured with a ceiling-mounted infrared camera. By comparing US images at treatment time to the image at CT-Sim, the motion in space of the prostate and its volume change can be determined. The system is an intra-modality system.
Results: To date, the 3D system was used in our clinic to measure daily prostate shifts in 13 patients in an ongoing study. Patients were treated with a 5-field conformal EBRT technique, using 18 MV photon beams. The measured volumes were used to re-assess the daily dose received by the prostate. As four of the five beams enter through the femurs, the dose recalculation was performed with an in-house developed planning system, MMCTP (McGill Monte Carlo Treatment Planning), to fully take the bone heterogeneities into account.

Measured prostate shifts ranged from -1.2 to 1.5 cm (R/L), -2.2 to 2.4 cm (A/P) and -2.1 to 1.4 cm (S/I). The average shifts and their standard deviations were 0.0±0.4 cm (R/L), -0.3±0.8 cm (A/P) and -0.5±0.7 cm (S/I).
The daily dose recalculations indicate that in the case of no corrections of the patient setup, prostates would be underdosed, as measured by a decrease in D_{95} to the PTV, by 10±11% (range -0.9 to 39%), resulting for some patients in very significant cold spots. When the Restitu system is used to reposition the patient, the difference of D95 compared to the prescribed dose reduces to 1.3±1.2% (range -0.6 - 3.4%).
Conclusions: As shown by our results, doses to the PTV may be reduced up to 39% if no system for daily organ localization and alignment is used. It is imperative that the prostate position be verified prior to each treatment fraction, ensuring the reproducibility of treatment planning.

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UNCERTAINTY OF MEGAVOLTAGE CONE BEAM CT (MVCBCT) AND CT ON RAILS (PRIMATOM) FOR SET-UP CONTROL.

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Purpose/Objectif: In 2005 in the Holycross Cancer Centre new accelerator ONCOR AVANTGARD equipped with the MVCBCT and CT on rails Primatom were installed. The 3D registration for set-up control made automatically or manually is possible by means of tools of the Coherence Therapist Workspace (CohThWrk). Humanoid phantom was used for evaluation of uncertainty of 3D registration performed with MVCBCT and PRIMATOM.
Materials/Methods: Alderson Rando phantom was scanned in the pelvis region with Sensation Open CT. Position of the phantom was acquired with 3 radioopaque markers. CT slices were reconstructed with 5 mm separation and 512x512 spatial resolution. Data were send to a virtual simulation station (Dosimetrists, Siemens) and typical box technique was prepared. Treatment plan was send to ONCOR AVANTGARD accelerator. Next two experiments were made. In the first experiment the phantom was placed at the treatment table in the treatment position and 10 times MVCBCT and 10 times examinations with Primatom CT were performed. Low-dose 3D 6 MV MVCBCT image were acquired with total dose of 8 MU. For each MVCBCT image a set of 200 projection images incremented by 1o were made. The CT treatment examination with PRIMATOM were made with the same parameters as for planning. After each scanning with each single modality the 3D image registration with the planning CT images were performed either automatically (auto registration in the CohThWrk) by application of a maximization of mutual information algorithm or manually by aligning multiple coronal slices and sagital and transverse reconstructions. For manual registrations procedure pelvic bony structures and outline contour were used. The 3D displacement vector was obtained. In the second experiment the only difference was that before each scanning humanoid phantom was taken out of treatment table and set-up again.
Results: The first experiment. For Primatom uncertainty of 3D image registration for all directions, left/right (LR), anterior/posterior (AP) and superior/inferior (SI) was less than 0.9 mm and 1.1 mm (1 SD) for auto and manual registration respectively. For MVCBCT uncertainty was less than 0.7 mm and less than 1.1 mm for auto and manual registration respectively irrespective of direction.
The second experiment. For Primatom the uncertainties of 3D image registration were 1.3 mm for the LR direction, 1,9 mm for the SI direction, and 0.8 mm for AP directions for both auto and manual registration. For MVCBCT the uncertainties were 1.2 mm for LR and SI directions and 0.7 mm for AP direction for both auto and manual registrations.
Conclusions: Both methods are reliable and accurate for 3D set-up control however differences in set-up geometry smaller than 2 mm with 95% confidence limit can not be discovered. Manual and automatic procedure give similar results.

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USE OF IN-ROOM CONE-BEAM CT AND EPID TO ASSESS THE `DOSE OF THE DAY`

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The increasing use of IMRT and narrow PTV-margins for tumour dose escalation puts still growing demands on the quality assurance program for dose delivery verification. In our clinic, all routine dosimetrical QA measurements for IMRT are performed with an electronic portal imaging device (EPID), including daily linac QA and patient-specific measurements. For each IMRT patient, portal dose images (PDIs) are acquired with the EPID for all treatment fields prior to the first fraction. Comparison of measured and predicted PDIs may reveal errors in the fluences produced by the linac before any dose is delivered to the patient. Also during treatments, fluences are verified with the EPID, using the SIFT method (Vieira et al. 2004) for accurate fluence verification even in case of strong deviations between the patient anatomy in the planning CT-scan and during treatment. The measured pre-treatment PDIs are also used to reconstruct the 3D patient dose based on the planning CT-scan, allowing a straightforward clinical interpretation of observed fluence deviations. In the present work this portal dose back-projection procedure has been extended for use in conjunction with a kV cone-beam CT-scan acquired in the treatment room (Elekta, Synergy). The combined use of the anatomy of the day as visible in the cone beam CT-scan, and the delivered fluence profiles as derived from EPID measurements, allows assessment of the actually delivered dose distribution in the particular treatment fraction, i.e. the "dose of the day". Accurate dose calculation based on a cone beam CT-scan is hampered by erroneous hounsfield units in these scans, related to scatter. To circumvent this problem an algorithm has been developed for warping of hounsfield units in the planning CT-scan on the cone beam CT-scan. The corrected cone-beam CT-scan and the IMRT fluence profiles derived from the EPID measurements are imported into a treatment planning system for calculation of the 3D dose distribution that was delivered to the patient during treatment. Differences between this dose of the day and the original treatment plan are evaluated. For organs of interest the resulting dose distributions are also analysed using dose volume histograms based on contour information in the cone-beam CT-scan. Currently, evaluations are being performed for various tumour sites. The developed methodology will be explained and evaluated using clinical data. Protocols for broad clinical application will be discussed.

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USE OF LYMPHOSCINTIGRAPHY FOR LYMPHEDEMA RISK REDUCTION DURING RADIATION FOR PRIMARY BREAST CANCER

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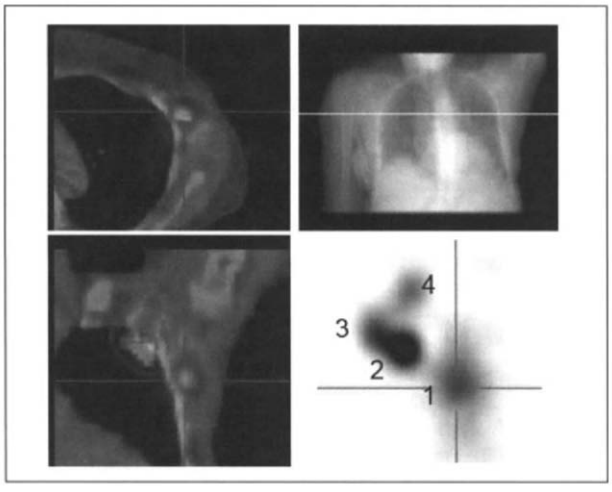
Purpose/Objectif: Lymphedema is an incurable, progressive and debilitating complication of combined modality breast cancer treat-

ment that adversely affects quality of life. Despite surgical sparing of lymph nodes (LNs) with sentinel node biopsy, lymphedema remains prevalent and increases with radiation treatment. Modern treatment techniques may permit modulated dosimetry to LNs considered free of micrometastases. A pilot study was undertaken to determine whether SPECT-CT could be used to localize LNs essential for arm drainage and whether the anatomic coordinates could be used to quantify LN dosimetry.

Materials/Methods: Twenty-eight patients were recruited ≤ 2 weeks prior to radiation treatment for primary breast cancer. To identify LNs draining the arm, 1mCi Tc-99m labeled sulfur colloid was injected subdermally into the dorsal hand and medial cubit ipsilateral to primary breast cancer. A specially designed CT-SPECT scanner (eNTEGRA) was used for scintigraphic and CT imaging ≥ 5 hours after sulfur colloid injection using positioning identical to CT-simulation. These images permitted spatial location of the LNs. The x, y, z coordinates of the lymph nodes were determined. The CT images from eNTEGRA were transferred to the radiation treatment planning system and fused with the CT -simulation images. The LN loci were drawn on the simulation images to quantify dosimetry.

Results: There were 12 left and 16 right breast patients. The treatment planning process included either tangential field (46%) or 4-field treatment (tangents, supraclavicle, and posterior axillary boost) (54%). The node distribution was 1-10 with a mean of 3 LNs/patient distributed through out breast, axillary and supraclavicular LN beds. Subjects receiving 4-field treatment were more likely to have >4 LNs identified on CT-SPECT ($p = 0.006$, X^2). Fig. 1 shows one of the cases. Dosimetry indicates that LNs draining receive the full prescribed dose (46 - 50 Gy) irrespective of location.

Conclusions: Lymphoscintigraphy SPECT data provide unique information allowing radiation fields to be contoured for preservation of lymphatic structures draining the arm. Radiation techniques could be modified to modulate LNs dosages based on scintigraphy.



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VALUE OF RESPIRATORY GATING COMPARED TO INTER-OBSERVER VARIABILITY FOR TUMOURS OF THE LEFT BREAST

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Purpose/Objectif: Technical capabilities of modern CT Linacs now allow irradiation with respiratory gating. While this has been shown to be beneficial in certain cases there still remains an uncertainty as to how much of an advantage gating is during irradiation compared to without and its overall value in comparison to other factors such as PTV variability between different radiation oncologists and setup uncertainty.

Materials/Methods: 9 Patients diagnosed with cancer of the left breast were each given three planning computer tomograms during three different phases of breathing. Scans were done during normal breathing phase, maximum inspiration and maximum expiration. Planning computer tomograms were then transferred to the Focal/Xio Planning system from CMS where the target volumes and critical organs were drawn on all three CT's for each patient by the same radiation oncologist in order to avoid interobserver variability. 3D conformal plans were done for each PTV with maximum individual optimisation and without any compromise to the target volumes. Dose volume histograms were done for each plan to analyse the difference in % volume of heart and lung tissue receiving 20 Gy or more.Another patient with left sided breast cancer had planning target volumes drawn by five radiation oncologists. The differences in irradiated lung and heart volume for each individually optimised treatment plan compared to that obtained between the different breathing phases was evaluated.

Results: For nine patients, 27 dose volume histograms of the 27 treatment plans were analysed for the differences in % volume of heart and lung tissue receiving 20 Gy or more. Results showed a favourable outcome for the inspiration phase, volume of heart recieving 20 Gy or more was 0 - 3 %, which was less than during the normal breathing phase with 0 - 7 % and also during expiration with volumes from 0 - 6 %. A similar trend was observed for the lung volume at 20 Gy with 9 -16 % during inspiration compared to 11 - 22 % during normal breathing and 11 - 23 % during expiration. Central lung distance was also more for plans done during normal breathing and expiration when compared to inspiration. All plans were optimised with 95% PTV recieving at least 95 % dose. There was no difference between plans calculated using Clarkson Algorithm and Convolution.

For the patient with five treatment plans of PTV's drawn by 5 different radiation oncologists, lung volume at 20 Gy had a median value of 14% (range 3 - 17 %) and a central lung distance between 2 and 3.5cm. % of heart volume at 20 Gy had a median of 9% (1 - 16 %). Overall there was a difference of up to 37% in volume of PTV.

Conclusions: Studies have been done to show that respiratory gating is beneficial when irradiating certain tumours such as breast and lung. In this study, there seems to be an advantage to treating the breast during maximum inspiration when compared to normal breathing and expiration. The maximum difference is 8% between inspiration and normal breathing phase for lung volume at 20Gy or more. The maximum difference in heart volume between the different phases was 5%. For the different PTV`s drawn for the same patient by five staff radiation oncologists, the maximum difference was 15% for heart volume at 20Gy and 14% for lung volume at the same dose. PTV delineation of the breast varied by up to 37% in volume most significantly in location and shape. However if such data can be confirmed in a larger study, then PTV delineation would be more important than dynamic gating techniques. This would imply that increased efforts for teaching, imaging and quality control for PTV delineation by radiation oncologists is required.

561 poster

VARIOUS PROCEDURES FOR THE REDUCTION OF CUPPING ARTIFACTS IN MEGAVOLTAGE CONE-BEAM CT

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Purpose/Objectif: MegaVoltage Cone-Beam CTs (MVCBCTs) offer a 3-D anatomy model of a patient during or prior to treatment. To use MVCBCTs for dose calculations, electron densities must be extracted as accurate as possible. For MVCBCT, this extraction is hampered by phantom scattered photons reaching the detector, inhomogeneous response of the flat panel and the poly-energetic spectrum of the linear accelerator. These phenomena result in a cupping artifact. A correction is necessary in order to use MVCBCT scans for dose calcu-

lation purposes. The goal of the present study is to develop a model for cupping artifact correction.

Materials/Methods: MVCBCT scans were acquired using a Siemens Oncor linear accelerator equipped with an a-Si Siemens OptiVue 1000 AG9 Electronic Portal Imaging Device (EPID). Projections were acquired and corrected for dead pixels, gain and offset by default. Three strategies are evaluated to correct for cupping artifacts. First, a correction was performed to eliminate the influence of scattered photons from a patient to the portal imager using pencil beam scatter kernels. Second, the beam profile was restored in the flood field corrected projection data. Third, a correction for changes in the energy spectrum due to beam hardening and off-axis beam softening was applied. The various approaches were tested using cylindrical water equivalent phantoms with various diameters positioned in the isocenter plane. Results of the cupping artifact are expressed as a standard deviation (SD) calculated in the central sagittal and axial slices of the phantoms.

Results: Preliminary results of a cylindrical phantom (16 cm diameter x 30 cm length) showed that reconstructed electron densities without correction showed a cupping artifact of 6.8% and 10.5% (1 SD) for the sagittal and axial slices respectively. Using the scatter correction these differences were reduced to 6.5% and 8.5% (1 SD) respectively. Correcting the image for the beam profile, values of 6.2% and 5.6% (1 SD) were observed respectively.

Conclusions: Corrections to projection images prior to MegaVoltage Cone-Beam reconstructions can reduce cupping artifacts significantly, allowing more accurate dose calculations.

562 poster

VERIFICATION KILOVOLTAGE CONE BEAM CT (CBCT) IN MONITORING DELIVERED DOSES AND DOSE GUIDED RADIOTHERAPY IN OESOPHAGO-GASTRIC CANCERS

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Purpose/Objectif: Organ motion and setup errors can have a profound effect on the delivered dose, leading to differences between the planned and delivered doses. We hypothesize that measurement of the cumulative dose delivered to the target and organs-at-risk (OAR) can be achieved using verification CBCTs.

Materials/Methods: 12 patients were treated with radical chemoradiotherapy for OG junction cancers(50Gy in 25 fractions).Off-line CBCTs(Elekta Synergy™, Elekta Systems, Crawley,) were used to correct for the systematic setup errors using bony anatomy(spine) according to departmental protocols. Patients had CBCTs on days 1-5,8,15,22&29, immediately after radiotherapy, in the treatment position. Translational displacements in *x,y,z* coordinates obtained from bony co-registration of CBCTs with the planning scan were used to shift the beam and recalculate the dose in the planning scan. We assumed the target & OAR move collectively and rigidly.The cumulative equivalent uniform dose (EUD) delivered to the CTV & OAR was used to compare with the planned dose. The CTV was divided into 4 equal longitudinal sections (CTV1-4) to provide spatial information on dose distribution. Temporal & hot/cold spot changes ($V_{>105\%}$ and $V_{<95\%}$ respectively) were recorded.

Results: The cumulative delivered dose to the CTV was generally within ±5% of the planned dose. The lowermost part of the CTV (CTV4), corresponding to the OG junction and proximal stomach showed considerable dose variation(mean=0.54%;1.96SD=8.8%) and was most susceptible to cold spots(1.96SD=35cm^3).Individual variations were marked in the heart, lung & spinal cord doses and hot and cold spot volumes (note 1.96*SD in table). In one patient there was over dosage to the spinal cord (+8%) and an increase in the lung dose (+4%).There were no strong temporal patterns during the treatment period and no significant changes in shape of the target volumes to indicate treatment response. The mean and the standard deviation of differences when compared to the planned dose were:

Organ	Mean Difference between cumulative delivered and planned dose	±1.96*SD (95% confidence intervals)
CTV	+0.46%	3.78%
HEART V_{45Gy} (as % of total heart vol)	-11%	17.35%
SPINAL CORD (as% of cord in field)	+1%	8.68%
LUNG V_{20Gy} (as % of total lung -PTV vol)	+0.37%	8.27%
CTV $_{<95\%}$ in cm^3 (cold spots)	-0.52 cm^3	12.74 cm^3
CTV $_{<105\%}$ in cm^3 (hot spots)	+2.77 cm^3	*

* Verification CBCTs can provide accurate delivered dose information across the irradiated volume. This could be used to correct for significant dose variations from planned(eg:boost in case of underdosage). Dose guidance may be a useful tool in the implementation of adaptive strategies to improve accuracy and to evaluate highly conformal treatments such as IMRT.

Posters Anal Colorectal Cancer

563 poster

AN ANALYSIS OF FAILURES AFTER RADIATION THERAPY FOR SQUAMOUS CARCINOMA OF ANAL CANAL: IMPLICATIONS FOR RADIOTHERAPY TECHNIQUE

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Purpose/Objectif: The radiation doses and volume of electively treated area are a matter of controversy in the treatment of squamous carcinoma of anal canal.

Materials/Methods: The stage distribution of our consecutive series of 82 patients was: I - 6%, II - 52%, IIIA - 16% and IIIB - 26%. Chemoradiation was given for 85% of patients. The remaining 15% of patients, due to the comorbidity, received irradiation alone. In majority of patients, the total dose for gross tumour was 50.6 - 54.6 Gy and for electively treated lymph nodes 30.6 Gy delivered in 1.8 - 2 Gy per fraction. For patients treated with irradiation alone the total doses were usually 10 Gy higher. The upper border of electively treated area was usually set at S2-S3 level. Chemotherapy consisted of 2 courses of 96 hours continuous infusion of 5-fluorouracyl 1000 mg/m^2 per day and bolus Mitomycin 10 mg/m^2 in first course.

Results: The median follow-up was 57 months. Local-regional recurrences occurred in 24 patients (29%). There were 11 regional failures: 4 in the boost volume; 3 in electively treated volume and 4 in common iliac lymph nodes outside irradiation volume. All 3 patients who failed in electively treated volume did not receive full elective radiation dose or chemotherapy. All 4 patients who failed outside irradiation volume had T3-4 disease. Failure in high dose volume occurred more often in patients with partial response at the end of irradiation as compared to those with complete response, 37%

(17/46) vs. 10% (3/30) respectively, p=0.008.
Conclusions: The elective dose of 30.6 Gy is sufficient, if chemotherapy is delivered in full doses. For patients with T3-4 disease, the electively treated volume should encompass common iliac lymph nodes. For patients with partial response, the increase of total dose should be considered.

564 poster

APPLICATION OF PET FOR TUMOUR RESPONSE ASSESSMENT IN PRE-OPERATIVE CHEMORADIATION IN RECTAL CANCER

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Purpose/Objectif: To evaluate tumour response and pathological correlation of 18F-FDG-PET (PET) using pre-operative chemo-radiation therapy (CRT) for locally advanced (T3) rectal cancers.
Materials/Methods: Twenty rectal cancer patients were analyzed with pre and post CRT PET scans. Pre-operative CRT (radiation therapy of 50.4-54 Gy in 1.8 Gy per fraction weeks with continuous infusion of 5-Fluorouracil infusion) was delivered to all patients with histologically confirmed locally advanced adenocarcinoma of the rectum. All patients underwent surgical resection (5 abdominoperineal resections and 15 anterior resections) 4-8 weeks following the completion of the CRT. All patients were clinically staged prior to commencement of CRT with EUS+/or MRI, CT and PET. Initial staging revealed T3N0M0 in 16 cases, T3N1M0 in 2 cases and T3N0M1 in 2 cases where each case had only 1 solitary liver metastasis.
The PET and pathological response were scored from 0-2 i.e. 0=no response, 1=partial response and 2=complete response. The pre and post CRT PET scans were compared by a nuclear medicine physician specialized in PET to determine the PET response. The PET response was classified as a complete response if the tumor was FDG avid on the pre-CRT scans and this returned to normal as assessed qualitatively and with respect to background and rectal SUV values on post-CRT scans. No response was scored when there was no change or progression on the post-CRT scans compared to pre-CRT scans from a qualitative and quantitative (SUV) perspective. All other responses were scored as a partial PET response. Similarly the pathological response was scored as a complete response when no viable tumor was seen on the histological examination, no response was concluded if no therapeutic response was viewed and all others were scored as incomplete. The PET response was compared to the surgical pathological response to assess correlation.
Results: There were 14 males and 6 females. The average and median age was 58 years (range 37-79 years). Following CRT there was no PET response in 3 patients, incomplete in 10 and complete in 7. The pathological outcome following surgery was no response in 9 patients, incomplete response in 3 and complete response in 7.
All 3 PET non responders correlated with no pathological response.
3 of the 10 PET incomplete responders correlated with the pathological incomplete response. Of the remaining 7 PET incomplete responders, the PET overestimated the response in 5 and underestimated the response in 2.
6 of the 7 PET complete responders were shown to be pathological complete responders. The remaining PET complete response was shown to have no response pathologically and thus PET overestimated the response.
Conclusions: In this study a complete PET response and no PET response was shown to correlate well with the pathological outcomes. However in the partial PET response group there was a tendency for PET to overestimate the pathological response. A larger study is warranted to further evaluate these findings

565 poster

AUDIT OF MANAGEMENT OF PATIENTS (PTS) PRESENTING WITH NON-METASTATIC RECTAL CANCER (NMRC) TO A SINGLE CENTRE OVER A 6-YEAR PERIOD.

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Purpose/Objectif: From its establishment in 1998, the BOCOC, a not-for-profit organization, has provided non-surgical oncology services for up to 80% of the island's newly diagnosed cancer pts in the context of site specialization.
Materials/Methods: A retrospective review of the management of pts with NMRC, referred from September 1998 to December 2004 was performed.
Results: Fourty surgeons referred 117 pts (73 M, 44 F) to the BOCOC; 97% were referred postoperatively; their median age was 66 years (range 34-81). The median follow-up was 30 months (range 11-79). Preoperative pelvic imaging with CT/MRI and CEA estimation was available in 23/117 and 22/117 pts, respectively. Surgical treatment included: an anterior resection in 62 (53%), an abdominoperineal resection in 46 (39%) and a Hartman's procedure in 9 (8%) cases. Distribution of surgical stage was: UICC-0 in 2 (2%), UICC-I in 23 (20%), UICC-II in 51 (44%) and UICC-III in 41 (34%) pts. Involved resection margins were reported in one case, and intra-operative inadvertent perforation in another. The median number of reported lymph nodes was 9 (range 1-31). Adjuvant radio-chemotherapy was offered to 64/117 pts; 14/117 received adjuvant radiotherapy and 4/117 chemotherapy alone. The median interval between surgery and the start of chemotherapy was 52 days (range 4-165) and the median interval between surgery and the start of radiotherapy was 110 days (range 32-241). In 51/68 pts, who received chemotherapy, a total of 219 courses of bolus 5-fluorouracil plus leucovorin ("MAYO regimen") were administered. There were 21/82 treatment interruptions due to Gr. III-IV toxicity or patient refusal; 33 pts received no adjuvant treatment (early stage disease or co-morbidities/refusal). Three-year disease-free survival (DFS) was 65%: UICC-I 100%, UICC-II 65%, UICC-III 43 % (UICC II vs UICC III $p<0.09$). Overall 3-year survival was 84%: for UICC-I 100%, UICC-II 93%, UICC-III 58 % (UICC II vs UICC III $p<0.03$). In 30/117 (26%) pts recurrence was recorded during follow-up. Sites of first recurrence were: pelvis in 7 pts (6%), lung in 13, liver in 8, para-aortic nodes in 3 and bones in 1 case. In 3/30 pts salvage surgery was performed.
Conclusions: Our survival- and local-control data are consistent with those reported in other series from the pre-TME era using adjuvant radio-chemotherapy for "high-risk" rectal cancer. In the future, efforts will be directed towards individualised management in pts with NMRC, in the context of a multidisciplinary approach.

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CONCURRENT ADMINISTRATION OF URASIL-TEGAFUR AND FOLINIC ACID WITH RADIATION FOR LOCALLY ADVANCED RECTUM CANCER: TOLERABILITY AND QUALITY OF LIFE ASSESSMENTS

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Purpose/Objectif: The objective of present phase II prospective study was to evaluate the feasibility of urasil-tegafur (UFT)/folinic acid (FA) as a concomittant chemoradiotherapy (CRT) administration for rectal cancer in adjuvant setting.
Materials/Methods: Between October 2003 and December 2005 thirty-one (10 female; 21 male) patients were treated. All the patients were locally advanced (T2N1-2M0 (2), T3N0M0 (12), T3-4N1M0 (9), T3-4N2M0 (7)) and median age was 62 (range, 21-85). Inclusion criteria were WHO 0-1, age ≥ 18, complete tumor resection as low anterior resection (LAR) or abdomino-perineal resection (APR), stage T3/4 or N+, adequate CBC, liver function tests and signed informed consent form. RT was performed in 8 weeks following the surgery and the total dose was 50.4 Gy in conventional course (1.8Gy x 28). Chemotherapy was consisted of UFT (300 mg/m^2/day) and FA (30 mg/day) during week-days of radiotherapy and continued 4 cycles with same dose (D1-28/35days) after CRT. Acute toxicity was assessed according to CTC 2.0 criteria. QLQ-C30 and QLQ-CR38 were done at begining and at the end of CRT.
Results: Median follow-up for all patients was 12 months (between 3-27 months). No toxic death occurred. CRT related side effects were diarrhea Gr 2 (25 %) and Gr 3 (25 %); emesis Gr 2 (29 %) and Gr 3 (10 %); dysuria Gr 2 (10 %) and Gr 3 (10 %). All patients completed radiotherapy but 21 out of 31 (67 %) continued with UFT/LV until the end of concurrent treatment. The full compliance to the adjuvant CT part was 63 %. During the adjuvant CT period there were diarrhea Gr 3-4 (10 %), emesis Gr 3 (10%) and no Gr 3-4 hematological toxicity observed during the whole treatment. During the study period none of the patients failed locally, 3 patients developed distant metastases (2 liver, 1 bone), and 3 patients died (1 with disease, 2 without). Two-year disease-free and overall survival rates were 84% and 91%, respectively.
Conclusions: The acute and subacute toxicity of CRT with UFT/FA is acceptable and seems comparable to infusional 5-FU based combined modality treatments. The QLQ-C30 and QLQ-CR38 results also will be represented during presentation.

567 poster

CONCURRENT CHEMOTHERAPY AND RADIATION THERAPY FOLLOWED BY SURGERY FOR RECTAL CANCER: A MODERATELY HIGH PELVIC RADIATION DOSE AND GOOD LOCAL CONTROL

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Purpose/Objectif: To determine the incidence of toxicities, complete resection rate, sphincter preservation rate, and survival in patients treated with concurrent chemotherapy and radiation therapy (CCRT) followed by surgery for rectal cancer.
Materials/Methods: Fifty-seven patients with histologically proven adenocarcinoma of the mid to lower rectum were treated with preoperative CCRT and curative resection. Median radiation dose to pelvis was 5400 cGy (5040~5580 cGy). The concurrent chemotherapy was done at the first and fifth week of radiation with bolus intravenous 5-fluorouracil 400 mg/m^2 and Leucovorin 20mg/m^2 for 5 days each. The surgery was attempted 6~8 weeks after completion of preoperative CCRT. Post-operative adjuvant chemotherapy was added for 4 cycles.
Results: The toxicities during CCRT were generally mild and manageable: grade 1/2 anemia, 3.5%; grade 1/2 leucopenia, 45.6%; grade 3 leucopenia, 3.5%; grade 1/2 diarrhea, 22.8%; grade 1/2 abdominal discomfort, 7%; and perianal skin reaction, 5.3%. There were no late complications requiring surgical intervention. Complete surgical resection rate with negative resection margin was 98.2% of the patients, and the down-staging rate was 59.7% (34/57). The complete pathologic response was found in 3.5% (2/57), and in other 2 patients, only some nests of tumor cells were noted in the surgical specimen. The sphincter preservation rate for the total patients was 77.2% (44/57). Among 30 patients with tumors located within 5 cm from anal verge, sphincter preservation was possible in 60.0% (18/57). With a median follow-up duration of 40 months, the overall and disease free survival rates for 3 years were 91.8% and 79.7%, respectively. Local and distant failure rates were 5.3% and 21.1%, respectively.
Conclusions: Preoperative CCRT demonstrates encouraging rates of tumor down staging and facilitates complete resection and sphincter saving in distal rectal cancer with acceptable toxicity. Further studies involving this moderately high radiation dose to pelvis should be warranted to improve local control.

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DOES PREOPERATIVE HYPERFRACTIONED RADIOTHERAPY INCREASE THE RISK OF ANASTOMOTIC LEAKAGE FOLLOWING TOTAL MESORECTAL EXCISION FOR RECTAL CANCER?

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Purpose/Objectif: Preoperative radiotherapy results in lower local recurrence rate and improved survival of patients with stage II and III rectal cancer, but its impact on anastomotic leakage risk after anterior resection with total mesorectal excision remains unclear.
Materials/Methods: From January 2000 to December 2003 ninety-four consecutive patients (age: range 37-88, mean 60.2) with stage II and III rectal cancer were operated on with sphincter-preserving total mesorectal excision and studied prospectively. Double-stapled end to end anastomoses were done in all cases. Forty-nine patients underwent neoadjuvant short-course 25 Gy radiation in 5 x 5 Gy schedule followed by surgery within one week and postoperative chemotherapy with 5-fluorouracil 325 mg/m^2 and folinic acid 20 mg/m^2 (six cycles, bolus i.v.). Forty-five patients received adjuvant radiochemotherapy: 25 x 1.8 Gy + 5.4 Gy boost irradiation combined with chemotherapy (as above). The study end point was the rate of symptomatic anastomotic leak. Associations between leakage incidence and radiation schedule, clinical parameters (gender, age, stage, tumor site), surgical protective procedures (pelvic drainage, defunctioning stoma, omental wrapping) were evaluated in uni- and multivariate analysis.
Results: Anastomotic leakage was noticed more frequently after preoperative radiation (12 vs 9%) but without statistical significance. The leakage rate was higher in females (11 vs 10%), patients older than 60 years (12 vs 9%) and cancers in stage III (11 vs 10%) but also with the lack of significance. Among clinical features only tumor site below 7 cm from the anal verge influenced an enhanced leak incidence with statistical importance (18 vs 5%). Defunctioning stoma significantly protected patients from symptomatic dehiscence of anastomosis (3 vs 25%). Neither pelvic drainage (10 vs 11%) nor omentoplasty (10 vs 12%) was effective for reduction of leakage rate. In multivariate analysis the only important factor enhancing the risk of leakage was the lack of proximal diversion.
Conclusions: Preoperative hyperfractioned radiotherapy does not significantly increase the risk of symptomatic anastomotic leakage following total mesorectal excision. The most important clinical factor influencing the leakage rate is the level of primary tumor. Proximal diversion with temporary stoma remains the most effective sur-

gical method for anastomosis protection.

569 poster

DOWNSTAGING, SPHINCTER PRESERVATION AND TUMOUR REGRESSION GRADING IN PATIENTS WITH RECTAL CANCER TREATED WITH PREOPERATIVE RADIOCHEMOTHERAPY–FIRST RESULTS OF INTERDISCIPLINARY TREATMENT IN WIESBADENY

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Purpose/Objectif: Retrospective analysis of tumour downstaging, sphincter preservation and tumour regression grading (TRG) after preoperative simultaneous radiochemotherapy in patients with rectal cancer.

Materials/Methods: From 2000 to March 2005 preoperative radiochemotherapy was performed on 50 patients with UICC-stage II (n=13), III (n=32) and IV (n=5) rectal carcinoma. Pretreatment stages were determined as T3 in 39 and T4 in 10 patients using endorectal ultrasound and magnetic resonance imaging. One patient with a regional lymphonodal recurrence was treated. The pelvis was irradiated with daily fractions of 1.8 Gy, 5 times a week to a total dose of 50.4 Gy. Chemotherapy was performed on day 1-5 and 29-33 of radiotherapy with continuous infusion of 5-fluorouracil (5-FU) (1000 mg/m^2/d). TRG following radiochemotherapy was determined by the amount of viable tumour versus the amount of fibrosis, ranging from no evidence of any treatment effect (grade 0) to a complete response with no viable tumour identified (grade 4). The five point TRG was categorized as poor regression (TRG 0+1), intermediate regression (TRG 2+3), and complete regression (TRG 4).

Results: All 50 patients with a median age of 61.5 years (range 32-84) completed therapy, assessment of TRG was available in 46 patients. Downstaging of at least one T-category was found in 23/49 patients (46.9%) (p=0.0001, Wilcoxon-test). A complete pathological regression was found in 5 patients (10.9%), intermediate regression in 36 Patients (78.2%), and poor regression in 5 patients (10.9%). A R0-resection was achieved in 45 patients (90%). Sphincter preservation was achieved in 41.6% of patients with tumours located at or below 6 cm from the anal verge.

Conclusions: Downstaging, sphincter preservation rate in tumours of the distal rectum and distribution of TRG are comparable to results of other studys. This schedule is feasible and highly effective in the treatment of patients with rectal cancer.

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EFFECTIVENES AND TOXICITY OF PERIOPERATIVE RADIATION THERAPY IN RECTAL CANCER: REPORT ON 123 CONSECUTIVE CASES OF A SINGLE INSTITUTION EXPERIENCE.

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Purpose/Objectif: Radiotherapy increases local control of surgical treatment for stage II-III rectal cancer. In this retrospective study we evaluated local control (LC), disease free survival (DFS), and toxicity in patients having stage II-III rectal cancer treated by either preoperative (NRT) or postoperative (ART) regimens.

Materials/Methods: One hundred and twenty-three consecutive patients with histologically established rectal cancer were treated at the Radiation Oncology Department of the University "Federico II" of Naples between April 1999 and January 2006 (53 patients were treated with NRT and 70 with ART). One hundred and fifteen patients (93%) were also treated with antiblastic chemotherapy. Median age at diagnosis was 64 years (range 36-86). Fourty-five (36.6%) patients were female and 78 (63.4%) male. Radiotherapy was administered by a three field technique with 25 daily fraction of 1.8 Gy over 5 weeks for a total dose of 45 Gy.

Results: At a median follow up of 18 (range 2-76) months 7 patients relapsed locally, 2 locally and at distance, and 13 relapsed distantly. LC and DFS resulted respectively 93% (90% for ART and 96% for NRT) and 82% (83% for ART and 81% for NRT). According to RTOG toxicity score, in the course of treatment; 40 patients (32.5%) experienced G1, 44 (35.8%) G2, 2 (1.6%) G3 and 1 (0.8%) G4 gastrointestinal (GI) toxicity. Late GI toxicity of grade 3 was registered in two patients (1.6%), while 3 (2.4%) and 28 (22.8%) were affected by respectively G2 and G1 toxicity.

Conclusions: The data of our retrospective study, although the follow up is still short, suggest that a multidisciplinary approach can cure most part of patients affected by stage II-III rectal cancer without unacceptable risk of toxicity.

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EXPRESSION OF TUMOR INFILTRATING T LYMPHOCYTES, EGFR, VEGF AND P53 IN RECTAL CARCINOMA TREATED BY ADJUVANT POSTOPERATIVE RADIOCHEMOTHERAPY

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Purpose/Objectif:
To evaluate retrospectively the expression of tumor infiltrating T lymphocytes (TIL), EGFR, VEGF and oncoprotein p53 in rectal carcinoma treated by adjuvant postoperative radiochemotherapy (RCT).

Materials/Methods:
Between March 2000 to May 2004, 40 patients (pts), 28 males and 12 females, median age 64 (36-78) years, with rectal adenocarcinoma were treated. All pts had histology of adenocarcinoma: 2 pts grade 1, 23 pts grade 2 and 15 grade 3. Pathologic TNM stage was as follows: 27 (67.5%) pts stage II and 13 (32.5%) pts stage III. Anatomic sublocalization were as follows: 10 (25%) pts low rectum (0-5 cm), 15 (37.5%) pts middle rectum (5-10 cm) and 15 (37.5%) pts upper rectum (upper than 10 cm). Adjuvant postoperative RCT follows after R0 resection in 32 pts, R1 resection in 3 pts and R2 resection in 5 pts. RCT consisted of external beam radiotherapy 45 - 50.4 Gy in 25 - 28 fractions, 1.8 Gy daily, with concomitant 5-fluorouracil 200 mg/m^2 /day in continuous infusion. In all pts were immunohistochemically investigasted TIL, EGFR, VEGF and p53. The number of CD3 positive TIL in tumor tissue was evaluated quantitatively (number of lymphocytes in 1 mm^2 of tumor) and the expression of EGFR, VEGF and p53 semiquantitatively.

Results: Median of pretreatment level of hemoglobin was 131 (43-167) g/l, leucocytes 9.2 (3.88-24.3) 10^9/l, thrombocytes 242 (151-405) 10^9/l and CEA 4.22 (0.17-916.19) mg/l. Median of nadir during RCT was as follows: hemoglobin level 126 (87-159) g/l, leucocytes 4.6 (1.6-14.19) 10^9/l and thrombocytes 185 (136-278) 10^9/l. At the date of evaluation (April 15th, 2006) 29 pts were alive. Twelve pts had recurrence: 5 local recurrence, 6 distant metastases and 1 pt synchro-

nous local recurrence and distant metastases. Median number of TIL in 1 mm^2 was 722, mean 842, range (188-2000). Median percentage of tumor cells membraneous and cytoplasmic EGFR positive was 22.5%, mean 37%, range (0-97%), median grade of membraneous positivity of EGFR was 2.5, mean 2, range (0-3), median percentage of tumour cells membraneous EGFR positive was 5%, mean 17%, (range 0-80%), median percentage of tumor cells cytoplasmic EGFR positive was 27.5%, mean 32%, (range 0-90%), median percentage of VEGF expression was 95%, mean 72%, range (0-100%), median percentage of p53 was 75%, mean 53%, range (0-100%).

Conclusions: The results of this pilot study demonstrates the expression of TIL, EGFR, VEGF and p53 in rectal carcinoma treated by adjuvant postoperative radiochemotherapy.

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MODERATELY LOW ALPHA/BETA RATIO FOR RECTAL CANCER BEST EXPLAINS THE OUTCOME OF THREE FRACTIONATION SCHEDULES OF PREOPERATIVE RADIOTHERAPY

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Purpose/Objectif: To estimate the alpha/beta ratio for rectal cancer based on the outcome of three fractionation schedules of preoperative radiotherapy.

Materials/Methods: Between 1998 and 2002 166 patients with locally advanced operable, rectal cancer were treated in Gliwice with preoperative radiotherapy. Three fractionation schemes were used: 51 patients were treated with 25 Gy in 5 Gy per fraction (group A), 45 received 30 Gy in 3.0 Gy per fraction, and 70 were treated with accelerated hyperfractionation 42 Gy, 1,5 Gy per fraction, twice a day with an inter-fraction interval of 8 hours. The groups were comparable with respect to tumor stage, surgical treatment, follow-up, age and sex. Surgery was performed shortly after radiotherapy with a median interval of 6, 10 and 4 days in groups A,B,C respectively. The actuarial data on loco-regional tumor control were analyzed using Cox model in which the total radiation dose and the quotient of total dose and dose per fraction were considered as independent variables. Crude data were analyzed using linear-quadratic model.

Results: The actuarial 5-year tumor control rates in groups A,B,C were 83%, 70%, and 97% respectively. Cox model provided alpha estimate of 0,276 (std. error 0.103), and beta estimate of 0,059 (std. error 0.026), which resulted in alpha/beta ratio of 4.7 Gy with 95% confidence limits -0,7 and 10,1 Gy. The alpha and beta estimates were statistically significant (p=0,007 and p=0,024 respectively). The crude rate of recurrences were: A- 7/51 (13.7%), B- 11/45 (24,4%), C - 3/70 (4,3%), which provides similar alpha/beta estimates to those obtained using Cox model. In all three schemes the overall treatment time was short (medians of 6, 14 and 20 days respectively) which limits rationales for incorporating time effect into the model. If, however, time was incorporated (assuming no lag period for tumor repopulation) the alpha/beta ratio was 8,2 Gy, while the dose increment required to compensate for repopulation was 0,11 Gy/day. In such case the estimate of beta was, however, not significant due to strong correlation between the dose per fraction and the overall treatment time.

Conclusions: While due to the retrospective character of the study, non-randomized selection of fractionation and uncontrolled quality of surgery the present results can be regarded as hypothesis generating only, the control rates obtained in the pelvis are consistent with moderately low alpha/beta ratio for rectal cancer.

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NEOADJUVANT RADIOCHEMOTHERAPY OF LOCALLY/REGIONALLY ADVANCED RECTAL CANCER IS A STANDARD TREATMENT OPTION

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Purpose/Objectif: Resectability, down-staging and acute adverse events (AEs) were evaluated in locally/regionally advanced rectal cancer patients receiving neoadjuvant RCT.

Materials/Methods: Forty-two consecutive pts with a median age of 66 years (range: 50-83) were treated for T3-4/N1-2 M0 (stage II: 20 pts, stage III: 22 pts) rectal adenocc. with neoadjuvant RCT between January and December 2005. The clinical stage was determined by CT (42), transrectal US (16) and MRI (4). For 3D radiotherapy planning, spiral CT-scans were taken with the belly board in the prone position, with 10-mm increments between the top of the L3 vertebral body and the upper-middle third plane of the femur. The planning target volume (PTV) encompassed the macroscopic tumor with 3-5-cm margins in the cranio-caudal and a 3-cm margin in the lateral directions; perirectal, presacral and internal ilacal lymph nodes, and a portion of the sacrum were included. The 3 or 4, 18 MV field plans were carried out with a 1.8-Gy daily dose, using a linear accelerator. During RCT, a 500 mg/m^2 5-fluorouracil continuous infusion and a 30 mg/m^2 folinic acid bolus on days 1-5 of weeks 1 and 5 of radiotherapy were applied. Four weeks after RCT completion, the pts were restaged by CT according to the RECIST criteria. Curative resection was performed 6-9 weeks following RCT. The pathologic down-staging was evaluated by the pT or pN definition and the 5-score tumor regression grade (TRG) of Mandard. AEs were recorded with CTCAE v3.0.

Results: The mean 1516 cm^3 (range: 1118-2187 cm^3) PTV was irradiated with a mean total dose of 45.2 Gy (range: 36-48.5 Gy). Forty pts received 2 cycles and 2 pts 1 cycle of chemotherapy. Acute grade 4 AE was not observed during RCT, whereas one patient experienced a grade 4 small bowel injury, detected during surgery. Grade 3 gastrointestinal and hematological toxicity were found in 5 (12%) and 4 (9.5 %) pts, respectively. Following RCT, clinical restaging revealed 1 (2.5 %) complete remission (CR), 24 (57%) partial remission, 11 (26%) stable disease and 4 (9.5%) progressive disease (2 pts were not evaluated). Curative resection was performed in 32 (76%) cases. Surgery was not initiated in the remaining cases due to disease progression (2), a decline in performance state (3), pt refusal (3) or a loss to follow-up (2). The surgical intervention was low anterior (24 pts, 57%) or abdomino-perineal (8 pts, 19%) resection, with an R0 rate of 88% (28 pts). Pathology revealed CR in 2 pts (4.7%, including the patient with clinical CR), and down-staging in 14 cases (33%) for T and 11 cases (26%) for N categories. The numbers of TRG 1, 2, 3, 4 and 5 cases were 3 (7%), 12 (28%), 10 (23%), 7 (16%) and 0, respectively.

Conclusions: Neoadjuvant RCT in locally/regionally advanced rectal cancer is a standard treatment option that results in a high curative and R0 resection rate, and a low incidence of acute AEs.

574 poster

PREOPERATIVE CHEMORADIATION USING ORAL CAPECITABINE IN LOCALLY ADVANCED RECTAL CANCER

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Purpose/Objectif: Capecitabine is an oral 5-FU pro-drug (fluoropyrimidine carbamate), which was rationally designed to affect as a tumor activated and tumor selective chemotherapy. We attempted to evaluate the efficacy and toxicity of preoperative chemoradiation (CRT) using capecitabine in locally advanced rectal cancer.
Materials/Methods
Between September 2004 and January 2006, 22 patients (12 male, 10 female) with locally advanced rectal cancer (cT2-T4 N0-N2) received neoadjuvant CRT with a total irradiation dose of 50.4 Gy with 1.8 Gy daily dose in approximately 5.5 weeks (45 Gy delivered to the pelvis followed by a 5.4 Gy boost to the primary tumor). Capecitabine was administered concurrently with radiotherapy, 825mg/m^2/day, and 7 days/week. Surgery was performed 5-6 weeks after chemoradiation. Pretreatment stage was determined both with Computed Tomography (CT) and Endorectal Ultrasound (ERUS) according to the RECIST criteria.
Results: Two patients were excluded from the study. Primary tumor downstaging and node downstaging occurred in 12/20 (60%) and 10/14 (71%) respectively. Pathological complete response occurred in 3/20 (15%). All of the patients, except for the two who were excluded from the study, treated with surgery after CRT, 16/20 (80%) achieved sphincter preservation. No Grade 3 or 4 toxicity developed. Most significant toxicities were as follows: nausea 13 (65%), anemia 5 (25%), diarrhea 5 (25%), leukopenia 4 (20%).
Conclusions: The concurrent preoperative combination of radiotherapy and capecitabine is a well-tolerated treatment with a considerable downstaging effect on the tumor. This fact can increase the possibility of sphincter preservation for LARC.
These findings encouraged us to proceed to clinical trials in collaboration with the University of Athens Medical School, Greece. Further research will include factors that affect the therapeutic response of the treatment. These enzyme factors are Thymidine Phosphorylase (TP), Thymidylate synthase (TS), Dihydropyrimidine Dehydrogenase (DPD) and Tumor Necrosis Factor-a (TNF-a) which, consist of the "enzymatic profile" of each patient. This profile is probably critical for the therapeutic response, tumor resistance and toxicity of the therapy. Our clinical trial is on going.

575 poster

PREOPERATIVE CHEMORADIOTHERAPY AND SURGERY FOR RECTAL CANCER: A SINGLE INSTITUTION EXPERIENCE

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Purpose/Objectif: To report the outcome of preoperative radiotherapy (RT) combined with oral tegafur-uracil (UFUR) plus leucovorin (LV) and surgery for rectal cancer.
Materials/Methods: Sixty-eight patients with rectal adenocarcinoma (MRI staged T2-4N0-2) without distant metastases received pelvic RT of 45 Gy in 20 fractions over 28 days. Concurrent chemotherapy consisted of UFUR (200 mg/m^2/day) and LV (45 mg/day) on days 1 to 28. UFUR (250 mg/m^2/day) and LV were continued on days 36 to 63. Surgery was performed on day 70. Patients were followed up regularly to evaluate tumor control.
Results: After concurrent chemoradiotherapy (CCRT), 47 patients received LAR, 18 received APR and 3 transanal excision. T-downstaging occurred in 38 (56 %), pathological complete response in 19 (26 %), and sphincter preservation was achieved in 28 of 41 (68 %) with lower-seated tumors. With a median follow-up time of 32 months, locoregional failure developed in 6 (9 %), and distant metastases occurred in 11 (16 %). The 5-year overall survival was 81 % and disease-free survival 68 %. Lower pathological T (p=0.02) or N stage (p=0.01), higher T-downstage score (pathology minus MRI stages, p=0.03) are associated with fewer recurrences.
Conclusions: Oral UFUR + LV administered with pre-operative RT are effective in tumor downstaging, pathological complete response and sphincter preservation. Good response to CCRT predicts durable tumor control.

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PREOPERATIVE MULTIMODALITY THERAPY FOR LOCALLY ADVANCED RECTAL CANCER IN PAKISTAN

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Purpose/Objectif: In contrast to West the incidence of colorectal cancer in Asia is low. The efficacy of preoperative chemoradiation (CRT) in reducing local recurrence in rectal cancer has been demonstrated in randomized trials. The data on preoperative CRT in Asian population is limited. The present retrospective analysis was performed to document the effect of preoperative CRT and recurrence among patients with locally advanced rectal cancer treated in Shaukat Khanum Memorial Cancer Hospital Lahore
Materials/Methods: 53 medical records of rectal cancer patients treated between January 2001 and December 2005 at our institution were retrospectively analyzed. Mean age was 40 years (range 20 - 71). Male: Female ratio was 1.9:1 They were all in good clinical condition (ECOG 0 -1). Pre treatment stage as assessed on MRI pelvis: cT2N+ 4%, cT3 83%, cT4 13%. The site of tumor within rectum was upper 15%, middle 21% and lower 64%. Tumor size was < 5 cm in 32% and > 5 cm in 68%. Pelvic radiation therapy was administered with multiple fields on megavoltage equipment as 1.8 Gy/day, 5 days/week, up to a dose of 50.4Gy. 5FU based chemotherapy was given as bolus IV injection during week 1 and 5 of radiation treatment. Total mesorectal excision was planned 6 - 8 weeks after completion of CRT. Pathological complete response (pCR) was defined as either no evidence of viable malignant cells in specimen or scattered isolated malignant cells without gross residual disease.
Results: 79% patients underwent abdominoperineal and 27% had low anterior mesorectal resection. Circumferential margins were negative in 55% (R0), positive 19% (R1) and unknown in 26% of the patients. Post treatment tumor stages were ypT1-2N0 in 24%, T3N0 in 22%, T1-2 N+ in 6%, T3N+ in 42% and unknown in 6% of cases. A pCR was evident in 18% (complete response 6%, microscopic foci 12%), pathological tumor regression > 50% regression occurred in

51% and < 50 regression or no response in 38%. To date 28% have recurred; isolated pelvic recurrence 8% and distant metastases 20%. The median overall survival was 3.17 years (95% CI: 2.74 - 3.60) with a 50% 5 year survival. The median disease free survival was 3.43 years (95% CI (1.67 - 5.18) with a 40% 5 year survival.
Conclusions: Pathological response to preoperative 5FU based CRT and survival following total mesorectal excision in our population is similar to other reported series.

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PREOPERATIVE RADIATION TREATMENT FOR RECTAL CANCER: COMPARISON OF TARGET COVERAGE AND SMALL BOWEL NTCP IN CONVENTIONAL VERSUS 3D-CONFORMAL PLANNING.

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Purpose/Objectif: A prospective study was undertaken to evaluate the improvement in rectal cancer radiation treatment achieved with the implementation of target delineation for conformal radiotherapy replacing conventional technique using standard radiological anatomy for target volume definition.
Materials/Methods: In 10 patients receiving preoperative pelvic irradiation because of rectal cancer a three field technique was designed by a 3-D planning system (XIO, CMS). Two plans were simulated for each patient, one with the fields designed in conventional way based on radiological anatomy (Martenson JA et al. in Treatment planning in Radiation Oncology. Baltimore, Williams and Wilkins, 1998), and the other with the fields designed on the basis of a delineated PTV (1 cm + CTV according to Gunderson et al., Clinical Target volumes in conformal and intensity modulated radiation therapy. Springer -Verlag, 2004). A total dose of 45 Gy in 25 daily fractions of 1.8 Gy in five weeks was planned. Dose-volume histograms (DVH) of PTV, small bowel and urinary bladder were analyzed to compare plans. The normal tissue complication probability (NTCP) was determined by the radiobiological model of Lyman and Kutcher using the tolerance data of Emami.
Results: NTCP for small bowel (conventional 0.4% vs. conformal 0.6%) and urinary bladder (conventional 0.0% vs. conformal 0.0%) resulted not statistically different while the PTV coverage resulted significantly lower with conventional treatment relatively to conformal (95% isodose covering respectively 91% vs. 100% of the volume, $p < 0.05$).
Conclusions: 3D-conformal treatment plan for preoperative radiotherapy for rectal cancer allows a better target coverage without significantly affect small bowel and urinary bladder NTCP. In our study the conventional treatment planning technique resulted in a not adequate coverage of PTV in rectal cancer treatment.

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PREOPERATIVE RADIOCHEMOTHERAPY IN RECTAL ADENOCARCINOMA. RESULTS OF 154 PATIENTS

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Purpose/Objectif: Neoadjuvant radiochemotherapy produce downstaging increasing resectability and the number of an sphincter sparing procedure, improving local control. To assess downstaging, types of surgery, complications, acute and late toxicity, local control and survival of preoperative radiotherapy ± chemotherapy in patients with rectal cancer.
Materials/Methods: From January -00 to December-05, 154 patients, (100 men and 54 women), with a mean age of 66,2 ±9,5 years, and diagnosed of rectal adenocarcinoma received preoperative radiotherapy ± chemotherapy. Histologic diagnoses was made according to a endoscopy and biopsy, and showed in all cases Adenocarcinoma. Mean distance from the anal verge was: 6,8 ±3,3 cm . Staging confirmation was made according to a CT scan or an endorectal ultrasound. Tumours were classificated according to the TNM classification: 59 T3 N0, 4 T4 N0, 6 T2 N1, 78 T3 N1, and 7 T4 N1. Radiotherapy was delivered using high energy photons from a linear accelerator of 6 MV in 114 cases, and with 18 MV in 40 patients. Mostly, patients were treated in a prone position with a three field technique in 126 cases, and a four field technique in 28. Only 7 patients did not receive concomitant chemotherapy. After 1,3 ± 1,1 month, surgery was performed.
Results: Acute toxicity was mild in most patients. There were only 13 local relapses and 26 metastases .Types of surgical procedure were anterior resection in 106 patients (68,8%), and an abdominoperineal resection in 48 patients (31,2%). In 138 the specimen found no residual disease, 4 microscopic residual and 12 macroscopic residual disease. From the 28 patients with tumours localized < 5 cm from anal verge; five of them (17,9%) had an anterior resection . Histologic specimen showed: 23 complete remission, (15%) 78 partial response, 41 estabilizations and 12 progressions.
Most of the patients did not present any kind of toxicity post surgery. There were 43 patients with wound dehiscence or infection. There were 17 reinterventions. The median of the hospitalization days were 10 (9-15). Overall and specific survival at 3 years were: 70,2 ± 9,3 %, and 77,5 ± 8,9 % respectively. The local and distance disease free survival at 3 years was 89,2± 5,7% and 75,6 ± 8,7 % and the disease free survival at 3 years was 73,7 ±8,9%.
Conclusions: Preoperative radiotherapy ± chemotherapy, increases local control, produce mild toxicity, important downstaging, increasing the safety of an sphincter saving procedure.

579 poster

RADICAL DEFINITIVE EXTERNAL BEAM RADIOTHERAPY FOR RECTAL CANCER

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Purpose/Objectif: Definitive radiotherapy is uncommonly used in the management of rectal cancer. The purpose of this retrospective study was to assess preliminary results of this treatment in patients with rectal cancer who refused or were unfit for surgery or had unresectable lesions.
Materials/Methods: Between 2000 and 2005, 25 patients (9 with primary tumour and 16 with pelvic recurrence after surgery) underwent radical external beam radiotherapy (22 had 3D treatment planning). The maximal tumour dimension ranged from 2 to10 cm, median 5 cm; in 8 patients on rectal examination the tumour was fixed. The total dose varied from 55 to 68 Gy, median 64 Gy; 1.8-2.5 Gy per fraction. In 9 patients irradiation was combined with 5-fluorouracyl and Leucovorin. The follow-up for living patients ranged from 2 to 67 months, median 19 months. One patient was lost to follow-up.
Results: Local control, defined as lack of tumour progression, was observed in 13 (52%) patients. Distant metastases were detected in 5 patients. Nine patients were alive and free of cancer from 2 to 47 months after treatment, median 14 months. In these patients the maximal tumour dimension ranged from 2 to10 cm, median 4.7 cm; in 3 patients the tumour was fixed on rectal examination. Two-year disease-free survival was 46% (95% CI 24% - 68%). Severe late toxic-

ity occurred in 1 patient.
Conclusions: Our preliminary results suggest that radical radiotherapy for primary or recurrent rectal cancer provides an opportunity for cure.

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RADIOCHEMOTHERAPY AND EXTENDED SPHINCTER-PRESERVING SURGERY IN CURATIVE TREATMENT OF RECTAL CARCINOMA INFILTRATING FEMALE GENITALIA

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Purpose/Objectif: Females with non-resectable rectal carcinoma have a dismal prognosis. In tumors infiltrating adjacent organs resectability, sphincter preservation and adequate local control are difficult to achieve but multimodal management may result in improved long-term patients survival.
Materials/Methods: From January 1997 to December 2003 thirty-two female patients with histologically confirmed rectal cancer with involvement of internal reproductive organs were treated by combined radiation, chemotherapy and extended sphincter-saving surgery. Eleven women underwent palliative resection, twenty-one multivisceral excision with curative intent. In curatively treated group in eighteen females anterior resection of the rectum with hysterectomy and bilateral salpingo-oophorectomy was performed. In three women additional excision of posterior vaginal wall had to be made. Surgical resection was combined with 50.4 Gy irradiation (25 x 1.8 Gy + 5.4 Gy boost) and six five-days cycles of chemotherapy (bolus i.v.) with 5-fluorouracil (325 mg/m^2) and folinic acid (20 mg/m^2).
Results: The R0 resectability rate was 65%. Following curative resection two-year recurrence-free survival rate was 53%. Neither patient's age, intraoperative blood loss nor tumor differentiation was significantly related to prognosis. Factors significantly influencing poor survival were: radial margin < 2 mm (P=0.011), distal margin < 1 cm (P=0.014) and lymph nodes metastases (P=0.026). Eight of ten females with distal margin ^{3} 1 cm, ten of fourteen women with radial margin ^{3} 2 mm and six of seven lymph node-negative patients survived two years without any evidence of recurrent disease.
Conclusions: Multimodal treatment results in prolonged survival for females in whom curative resection can be achieved despite the malignant infiltration of adjacent internal genitalia. The ability to obtain adequate radial and distal resection margins is the strongest predictor of enhanced recurrence-free survival. The presence of lymph node metastases remains a significant indicator of poor prognosis.

581 poster

RADIOTHERAPY ALONE IN THE ANAL CANAL CANCER: RESULTS OF TREATMENT AND PATTERN OF FAILURE

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Purpose/Objectif: Radiotherapy (RT) has been the standard treatment of anal canal cancer for many years. But, there are still many open questions such as optimal radiation technique, boost dose and how to boost or best chemotherapy concomitant regimen. The aim of our study was to evaluate the efficacy and toxicity of radical RT in the treatment of anal canal cancer.
Materials/Method: In the Institute for Oncology and Radiology of Serbia from February 1995 to September 2005, 52 pts with squamos cell cancer of the anal canal were included in prospective non-randomized clinical study. Mean age of pts was 57, 7 years (range 28- 82 years) with male: female ratio 8: 44. According to TNM classification, stage distribution was as follows: T2- 16 pts (30, 8%), T3- 25 pts (48, 1%) and T4- 11 pts (21, 1%). Inguinal positive lymph nodes were revealed in 14 pts (26, 9%). All patients received initially external beam RT on Linear electronic accelerators (10- 18MeV) by two widened pelvico-ingvinal parallel opposed fields and dose ranged from 40-50 Gy, followed usually after a 2- weeks gap in some pts or in continuity, by local external beam or brachytherapy boost (intraluminal or interstitial). The total tumor dose ranged from 55-75 Gy.
Results: Acute complications were noticed in 37pts (71, 1%). The most frequent complications were moist skin perineal desquamation in 26pts (50%). On the first follow up (2 months after the RT) 32 pts or 61, 5% were in complete remission (CR), 19 pts in partial remission (36, 5%), while in one pts (1, 9%) locoregional progression (PD) was registered. On the second follow up (4 months after RT) 12 pts moved from PR in CR group i.e. CR was registered in 44 pts (84, 6%). With a mean follow up time of 41, 7 months (range 6- 112 months) 43 pts (82, 7%) were disease free, while local or distant progression was diagnosed in 9 pts (17, 3%). Local disease control was achieved in 45 pts (85, 1%). The 5- year overall survival was 69, 3% and disease free survival was 81, 8%. Late sequelaes, which were of low grade (1 and 2), were registered in 25 pts (48, 1%).
Conclusions: A good local control of the disease can be achieved by a radical RT with an acceptable rate of acute and late sequelaes. For more precise quantification we need more investigations in order to optimize different irradiation techniques and boost dose, possible benefits and complications with or without chemotherapy.

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RALTITREXED AND RADIOTHERAPY AS ADJUVANT TREATMENT FOR STAGE II-III RECTAL CANCER: A PHASE II STUDY.

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Purpose/Objectif: Adjuvant 5-FU plus radiotherapy (RT) represents the standard treatment for radically resected rectal cancer at high risk for relapse according to the NIH Consensus Conference. This regimen was associated to severe treatment-related toxicity and a suboptimal patient compliance with this regimen. Raltitrexed is a specific thymidylate synthase inhibitor with a convenient administration schedule, acceptable toxicity and radiosensitizing properties. The aim of this study was to evaluate the overall and disease-free survival in rectal cancer patients (pts) treated with raltitrexed and RT.
Materials/Methods: From September 2000 to June 2004, 50 patients with radically resected stage II-III rectal adenocarcinoma were treated. Forty-seven pts were evaluable for survival. Patient characteristics. Gender: M/F 26/21; median age 63 (range 38-75); site of disease: upper 23, middle 14, lower rectum 10 pts; type of surgery: anterior resection 43, abdominoperineal resection (APR) 4 pts; stage II 27, stage III 20 pts. Within 60 days from surgery, each patient underwent adjuvant treatment. RT was administered to the pelvis (plus perineum after APR) with photon beam energy ^{3} 5 MV, 3-4 fields technique, 45 Gy/25 fractions/5 weeks plus a boost delivered to the site of resected disease with 3-4 fields, 9 Gy/5 fractions/1 week to a total dose of 54 Gy. The boost dose was administered after complete exclusion of the small bowel from the treatment volumes; if this was not possible a total dose of 50.4 Gy was given. Raltitrexed was administered intravenously at a dose of 3 mg/m^2 as a bolus injection

on days 1 and 22 of RT one hour before treatment, for a total of two cycles. Each patient underwent weekly clinical evaluation and laboratory tests. Toxicity was assessed by the WHO scale.
Results: After a median follow-up of 42 months (range, 13-70), local relapse was reported in 3/47 (6%) and distant metastases in 11/47 pts (23%). The principal sites of distant metastases were liver and lung, while for local relapse were anastomosis and presacral space, with a median time to relapse of 15 months (range, 8-56 months). Five-year overall (OS) and disease-free survival (DFS) were 88% and 66%, respectively. The stage of disease (II vs. III) does not represent a statistically significant difference nor for OS (96% vs 77%, p = 0,07), neither for DFS (78% vs 52%, p = 0,47).
Conclusions: We demonstrated the feasibility, the low toxicity and the optimal patient compliance of raltitrexed-RT combination (M.Lupattelli et al Tumori 2005,91:498-504). As regard OS and DFS our data were similar to those obtained by standard treatment (M.Lupattelli et al Tumori 2001,87:240-248).

583 poster

RESULTS OF CONCOMITANT CHEMO-RADIOTHERAPY OF THE SQUAMOUS CELL ANAL CANCER

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Purpose/Objectif: Assessment of the effectiveness of concomitant chemo-radiotherapy in patients with squamous cell anal cancer treated in the Oncology Center in Cracow between 1995 and 2004.
Materials/Methods: Clinical material consists of 48 patients with squamous cell anal cancer in stage: T1 - 2%, T2 - 50%, T3 - 40%, T4 - 8%. Regional lymph nodes involvement was revealed in 6% of patients only. Median age was 62 years. All patients received chemotherapy with fluorouracil and mitomycin concomitantly with radiotherapy. In 71% two cycles was given, 29% received only one cycle because of toxicity. In 67% patients split course radiotherapy was given with break after 40Gy, treatment was continued after 4 weeks to the total dose of 60 - 70 Gy. The rest of patients received continuous conventional radiotherapy do the dose 60 - 70 Gy.
Results: The median follow-up time was 60 months. The 5-year , loco-regional control (LRC), disease free survival (DFS) and overall survival (OS) rates were 71%, 66% and 68% respectively. LRC rates were higher in patients with T1 - T2 than in T3 - T4: 74% and 68% respectively. Patients who received two cycles of chemotherapy had significantly higher 5-year LRC, DFS and OS comparing to those who received only one cycle: 86% vs 70%, 80% vs 65% and 76% vs 67% respectively. Improvement in LRC, DFS and OS was also observed in patients who received continuous radiotherapy instead of split course radiotherapy: 88% vs 63%, 81% vs 58% and 73% vs 66% respectively. Salvage surgery was performed in 7 patients.
Conclusions: Concomitant chemo-radiotherapy is effective treatment method in patients with anal cancer. Application of two cycles of chemotherapy concomitantly with continuous high dose radiotherapy improves treatment results.

584 poster

RETROSPECTIVE AUDIT OF SHORT COURSE PREOPERATIVE RADIOTHERAPY IN THE TREATMENT OF LOW RECTAL ADENOCARCINOMA REQUIRING ABDOMINOPERINEAL RESECTION AT THE EDINBURGH CANCER CENTRE MARCH 1996-MARCH 2004

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Purpose/Objectif: There is conflicting evidence regarding the role of short course preoperative radiotherapy in the management of operable low rectal adenocarcinoma requiring abdominoperineal resection, with many advocating long course combined chemoradiotherapy for these patients.
Materials/Methods: Eighty three patients with operable rectal adenocarcinoma received short course preoperative radiotherapy (25Gy/5#) followed by abdominoperineal resection at the Edinburgh Cancer Centre from March 1996 - March 2004. A retrospective audit of outcome was performed.
Results: The median age of the patients was 67 (range 32-87) of whom 17 were female and 66 were male. 14 patients had a positive or close (<1mm) circumferential margin. The remaining 69 patients had clear margins, median 4mm (range 1-20). The pathological staging of the patients was - 9 Duke A, 30 Duke B, 41 Duke C. 3 had metastatic liver disease diagnosed at the time of abdominoperineal resection. The median follow up is 22 months (range 0-74). The median disease free and overall survival has not yet been reached.
3 patients developed local regional recurrence (LRR); of these two had positive circumferential margins. 19 patients developed metastatic disease of whom 3 had positive margins. 26 patients received adjuvant single agent 5FU based chemotherapy - 5 Dukes B, 21 Dukes C. 1 patient died of LRR, 18 of metastatic disease (10-liver, 5-lung, 1-peritoneal, 1-brain, 1-caecal). There were 5 deaths not attributable to rectal adenocarinoma or its treatment.
Conclusions: The above audit demonstrates an acceptable rate of local recurrence in patients treated with short course preoperative radiotherapy. For the patients in this cohort their risk of metastatic disease is higher than that of local failure. Therefore for patients with low rectal cancer in whom clear surgical margins are predicted on preoperative staging short course preoperative radiotherapy remains an appropriate strategy.

585 poster

SALVAGE TREATMENT FOR LOCALLY RECURRENT RECTAL CANCER

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Purpose/Objectif: To evaluate the treatment outcome according to the salvage treatment modalities and identify the prognostic factors influencing survival.
Materials/Methods: Fifty patients with locally recurrent rectal cancer treated with salvage aim between October 1994 to December 2004 at Department of Radiation Oncology, Samsung Medical Center were reviewed retrospectively. There were 31 (62%) men and 19 (38%) women whose ages ranged from 29 to 72 years old (median: 60). Median time to diagnosis of local recurrence, estimated from initial surgery, was 16 months (range: 3-73 months). Of these patients, 27 (54%) showed recurrence at presacral and/or perirectal space, 16 (32%) at anastomosis site, 4 (8%) at perineum and 3 (6%) at pelvic wall. Fifteen out of 20 patients who received salvage surgery were treated with postoperative chemo-radiotherapy and remaining five were treated with postoperative radiotherapy. There were 30 patients who were treated other than surgery. Nineteen of them were treated with chemo-radiotherapy and 11 were treated with radiotherapy alone. Total dose of radiotherapy was ranged from 37.5 to 65.0 Gy (Median 51 Gy) with daily dose of 1.8-3 Gy. There were 16 patients with history of previous pelvic irradiation. Patients with and without history of previous irradiation were treated with total radiation dose of median 47.5 Gy (range: 37.5-60 Gy) and 51 Gy (range: 40-65.0 Gy), respectively.
Results: Median follow up period was 32 months (Range: 2-104

months). 5-year overall survival rate (OSR) and locoregional progression free survival rate (LRPFS) of all patients were 28.7% and 40.2%. Patients who received salvage surgery showed OSR and LRPFS of 45.1 % and 77.4%, which was significantly better than 22.4 % and 20.0 %, 0% and 0% of patients with chemo-radiotherapy, radiotherapy alone, respectively (p= 0.0015 and 0.0002). OSR and LRPFS were significantly affected by initial stage. When the patients were divided into two groups, A-B3 and C1-C3 according to Modified Astler-Coller stage, OSR and LRPFS were 43.4% and 61.2% vs 0% and 0%, respectively (p=0.0246 and 0.0365). OSR and LRPFS were also significantly different according to group of patients with disease free interval less than 24 months or more. Patients who diagnosed to have recurrence earlier than 24 months from initial surgery showed OSR and LRPFS of 13.3% and 31.4% and that of whom diagnosed to recurrence later than 24 months was 62.6% and 55.9%, respectively (p=0.0105 and 0.0879). There was no significant difference in OSR and LRPFS by re-irradiation in 30 patients treated with other than surgery (p=0.6885 and 0.6800).

Conclusions: Surgical resection should be considered most preferably for patients with locally recurrent rectal cancer. In case of patients with unresectable recurrent lesion, combined chemo-radiotherapy may achieve higher locoregional progression free survival and overall survival than radiotherapy alone.

586 poster

SPIRAL COMPUTED TOMOGRAPHY IN ASSESSING RECTAL CANCER DOWN- STAGING WITH PREOPERATIVE RADIOTHERAPY

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Purpose/Objectif: Accurate disease staging in patients(pts) with rectal cancer is very important, because the optimal therapy depends on it. Spiral computed tomography (CT) plays significant role in rectal cancer staging and it is widely used. The primary limitations of CT are the difficulties in detecting minimal invasions of perirectal fat tissue and great prevalence of metastases in lymph nodes which are of normal size. The aims of our study were to present treatments results after preoperative radiotherapy (preopRT), assess the accuracy of CT in downstaging of rectal cancer after therapy and also in comparison of CT verified clinical with pathohistological stage of disease.

Materials/Methods: In the Institute for Oncology and Radiology of Serbia between January 2003 and October 2005 clinical prospective nonrandomized study was performed in 55 pts with locally advanced rectal cancer (stage T3- 37 pts, stage T4-18 pts). All pts were treated with preopRT with total tumor dose of 45- 50 Gy on Linear accelerators (10- 18 MeV). In the aim of accurate initially staging and adequate preopRT treatment planning CT was performed in all pts. Four to six weeks after preopRT (before the operation) CT examination was done again in order to assess tumor regression on performed treatment. CT results after preopRT were compared with pathohistological results according to TNM classification. Optimal surgery was performed in 50/55 patients.

Results: Out of 55pts, complete regression (CR) after preopRT was detected in 5 pts (9, 3%), partial regression (PR) in 29 pts (54 %) and stabile disease (SD) in 21 pts (38, 9%). Disease progression didn't appear in any of the pts. The response rate (RR) was noted in 33 pts (61, 2%). Most irradiated lesions were overstaged by radiological assessment. Pathohistological analyses showed that 17 pts were overstaged by CT,11 pts were downstaged and 22 pts had complete agreement between clinical and pathohistological stage of the disease. CT showed sensitivity of 44% in comparison with pathological stage of the disease or 22 precisely staged patients.

Conclusions: In our study, we confirmed good treatment results which are obtained after preopRT in pts with locally advanced rectal cancer. CT has a significant role in initial diagnosis and rectal cancer staging, planning preopRT, but moderate assessment of tumor response (downstaging).

Posters Benign Disease

587 poster

ANTI-INFLAMATORY RADIOTHERAPY FOR REFRACTORY DEGENERATIVE JOINTS (OSTEOARTHRITIS)

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Purpose/Objectif: To evaluate the effectiveness of radiotherapy for pain relief in patients with long term osteoarthritis of the extremities in a one year follow-up

Materials/Methods: From 1999 to 2004, 170 treatments of anti-inflamatory radiotherapy were given to patients suffering from osteoarthritis. 89 cases were evaluated: 69 females, 20 males; mean age 70 (52-86). 68 cases corresponded to treatment of lower extremities and 21 upper extremities. In the majority of the cases 6 Mv photons were used and the total dose administered 6 Gy with the exception of three cases where Rx of 180 KV was used and a total dose of 10 Gy. The dose per fraction was 1 Gy. Response was assessed using the visual analog scale (VAS) in the 89 cases, at the end of treatment, at 2 months and at 1 year.

Results: At the end of treatment 30 cases (33.7 %) showed improvement, 59 showed no change. At two months 64 cases (71.9%), of which 8 were asymptomatic, showed improvement. In the case of upper extremities, the improvement was 76.2%.

At 1 year 52 cases (58.4%), of which 16 were asymptomatic, showed improvement. In upper extremities it was 85.7%.

Conclusions: Antiinflammatory radiotherapy in osteoarthritis of the extremities can be a valid tool in older patients and/or patients with long term processes where other treatments are not effective. It is a well-tolerated treatment with improvement in 65 % of the cases beginning at the 2 month follow-up.

More complete studies should be carried out in order to determine the results in the reduction of rigidity, of incapacity as well as assessing pain relief.

588 poster

EFFECTIVENESS OF LOW DOSE RADIOTHERAPY IN THE TREATMENT OF DIABETIC AND ARTERIOSCLEROTIC INFLAMMATORY FEET DISEASE

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Purpose/Objectif: Following long time clinical experiences in our department we evaluated the effect of low dose X- ray radiotherapy on the healing of feet soft tissue lesions caused by diabetes and arteriosclerosis.

Materials/Methods: A total of 253 patients treated between 1997 and 2001 were analysed retrospectively and studied prospectively (n=87 patients in 107 radiotherapy series) since 2001 as case observations. Treatment was performed with low dose X- ray radiotherapy (150 kV) with daily single doses of 30 cGy respectively 50 cGy up

to total doses of 750 cGy five times weekly. We divided the lower limb lesions into their causes (diabetic feet, arteriosclerosis or mixed disease) and specifyed for each cause separatly the response of the ulcer and the surrounding inflammation using a newly offered score system. We evaluated clinical aspects (pain, drugs, blood circulation, bone resorption), neurological symptoms and frequency of amputation 3 weeks and 2 months after radiotherapy.
Results: Complete remission was achieved in 9.3% (n=10) and partial remission in 58,9% (n=63). Besides a slight benefit for diabetic feet lesions there were no differences between the etiologys of feet lesions. The ulcers showed partial remission in 29% (n=31). There was no influence of the single dose used. The risk for minor and major amputation was 14% respectively 21,5% mainly in the mixed disease group.
Conclusions: In lack of randomised clinical trials we see also presently in the antibiotic era the advantage of low dose radiotherapy underestimated. Using low dose radiotherapy for this kind of benign diseases is well tolerated, without side effects and with a well moderate risk. The clinical effect should be investigated in more detail.

589 poster

FINAL RESULTS OF A RANDOMIZED TRIAL OF 30 GY/3 FRACTIONS VERSUS 40 GY/4 FRACTIONS IN POSTOPERATIVE STRONTIUM-90 RADIATION THERAPY (RT) FOR PTERYGIA

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Purpose/Objectif: Postoperative adjuvant treatment by strontium-90 RT is a proven technique for reducing the recurrence of pterygium. This randomized trial was conducted to evaluate whether a total dose of 40 Gy provides a better local control rate than a total dose of 30 Gy for surgically resected pterygia.
Materials/Methods: A single institutional randomized trial was conducted in 70 patients with 74 pterygia between July 1999 and July 2003. Only fresh pterygia resected by a bare sclera method within 3 days of RT were included. Postoperative RT was given by a strontium-90 eye applicator of 1 cm in diameter. Treatment was performed once a week. The reference point was the surface of the eye, and a dose of 10 Gy per fraction was delivered. Pterygia were randomly treated either by 30 Gy/3 fractions/15 days (group A) or by 40 Gy/4 fractions/22 days (group B). Pterygia treated with mitomycin C at the time of resection were excluded. Written informed consent was obtained from all patients. During the same period, 40 Gy/4 fractions/22 days was given for patients who refused to enter the trial (group C). Local control rate was calculated from the date of operation, and statistical analysis between local control curves was assessed by the log rank test.
Results: Of the 70 enrolled patients, one patient with a pterygium was excluded from the analysis, because he refused to come to our hospital after one fraction of RT. The remaining 69 patients with 73 pterygia were analyzed. There were 36 men and 32 women. The median age was 60 years old. Of the 73 pterygia, 41 pterygia were allocated into group A, and the remaining 32 into group B. There were no statistical difference in sex, age, and the interval time between operation and RT between group A and group B. The two-year local control rates of group A and group B were 85% and 75%, respectively, without significant difference. In addition, 22 patients with 25 pterygia who met the inclusion criteria of the trial but refused to enter the trial were also analyzed (group C). There were no statistical difference in sex, age, and the interval between operation and RT between group B and group C. The two-year local control rate for group C was 80%, which was not significantly different from that of group A or group B. No serious late complications that may be associated with strontium-90 RT were noted for groups A, B and C.
Conclusions: As a similar local control rate of postoperative pterygia was obtained by either 40 Gy/4 fractions or 30 Gy/3 fractions, our new standard fractionation for postoperative pterygia is 30 Gy/3 fractions. A randomized trial comparing 30 Gy/3 fractions and a single fraction of 25 Gy is now ongoing.

590 poster

LINAC-STEREOTACTIC RADIOSURGERY (LSRS) IN THE MANAGEMENT OF TRIGEMINAL NEURALGIA

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Purpose/Objectif: Stereotactic Radiosurgery (SRS) with the Gamma Knife (GK) has been used successfully in the treatment of Trigeminal Neuralgia (TN). Results have been comparable to open surgery. There have been few reports with the use LSRS in the management of TN. We report our updated results with LSRS in the treatment of TN.
Materials/Methods: Between 2000 and 2006, 43 patients with medically refractory TN were treated with LSRS. Prior neurosurgical intervention had been performed in 34 patients. Nineteen patients had one procedure, 12 patients two, and 3 patients three interventions. All patients had typical TN. LSRS was given to the cranial nerve V entry root zone into the brainstem. Targeting was defined by CT and MRI Scans, and CT Cisternogram, utilizing axial and coronal images. Treatment planning was accomplished thru Radionics Treatment Planning System. The dose was 87 Gy to Dm, in one fraction using the 5 mm collimator and 6 arcs with the 20% Isodose line just touching the brainstem. This dosimetry is similar to Gamma Knife. The dose rate was 400 MU/min. Average Arc length was 130 degrees. Response to treatment was defined as excellent (no pain, off analgesics), good (no pain, with analgesics), and poor (continued pain despite analgesics).
Results: With a median follow-up of 43 months (range 6-78 months), 74.4% (32/43) of patients have reported an excellent or good result after LSRS. One patient has sustained permanent ipsilateral facial numbness.
Conclusions: LSRS offers comparable results to Gamma Knife SRS in the management of TN.

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NOVEL RADIOTHERAPEUTIC MANAGEMENT OF PAINFUL FLARE UPS IN CHRONIC PANCREATITIS

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Purpose/Objectif: Patients with chronic pancreatitis may present repeated painful flare-ups of pancreatitis and even unrelenting pain. Current management options are limited to analgesics and surgery, in selected cases. We reasoned that radiotherapy, which appears to be effective in other inflammation based painful disorders of the body, might prove valuable to severely symptomatic patients with chronic pancreatitis.
Materials/Methods: We studied prospectively over a 4-year period till Nov. 05, the efficacy of single dose radiotherapy in 12 consecutive patients with chronic pancreatitis (ethanol related in 7, idiopathic in 4 and cystic fibrosis in one) who fulfilled the following criteria: either 2 flare ups of pancreatitis in the previous 6 months (all 12 patients) and/or continuous pain for more than 3 months (2 of the 12). Median age was 41 years (range 32-80), there were 9 males and 3 females; diagnosis of chronic pancreatitis (6 months to 16 years,

median 5 years) and number of prior attacks (2 to >15, median 6). Treatment consisted in a single dose of radiation of 8 Gy, with accelerator lineal of 6Mv and 3-dimensional conformal radiation plan. Before and after radiation we assessed: exocrine function by fecal elastase, endocrine function by c peptide, quality of life (EuroQol) and clinical outcomes. Response was defined as no further pain or flare-ups of pancreatitis.

Results: During follow up (median 26 months, range 4 to 53 months) 9/12 patients had no further pain or flare-ups. One patient required a second radiation dose after 1 year and has been well since (31months), and other patient required a second radiation dose after 6 month. One patient did not respond and had a pancreaticojejunostomy at 1 month. Before radiation 4 patients had exocrine (fecal elastase<100 mg/g) and 2 endocrine (c peptide<0.50 ng/ml) dysfunction. Post treatment 1 additional patient developed exocrine (at 25 months) and endocrine (at 13 months) insufficiency. The responder group (11/12) gained 4 to 20 Kg in weight during follow up (median 6 Kg) and EuroQol improved significantly from 0.572 before till 0.817 after treatment ($p<0.01$).

Conclusions: Radiation treatment of severely symptomatic chronic pancreatitis is effective and could potentially substitute or delay surgery.

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RADIOTHERAPY FOR PEYRONIE`S DISEASE – RESULTS OF A NATIONAL PATTERNS OF CARE STUDY

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Purpose/Objectif: After a general Patterns of Care Study (PCS) the German Cooperative Group on Radiotherapy for Benign Diseases initiated a multicenter cohort study in order to analyse the radiation practice for Peyronie's disease.

Materials/Methods: In 2005 and 2006 a PCS was conducted in all German radiotherapy (RT) institutions by mailing a standardized structured questionnaire in order to assess patients' accrural, pretreatment, treatment indications, dose and target volume concepts for irradiation. In addition, the treatment outcome of individual patients was evaluated. The PCS was structured and analysed according to the model for quality assessment by Donabedian in three major components: structure, process and outcome evaluation.

Results: Data sets from 204 institutions (95% of the German radiotherapy institutions, 3440 patients) could be obtained. 61 (30%) of the institutions have reported experience with the treatment of Peyronie's disease, 60/61 institutions sent sufficient data for further analysis. 22% of the institutions used orthovoltage machines (50-330kV), 2% performed brachytherapy, the remaining 76% used electrons and photons of a linear accelerator. Total doses ranged from 8 to 40Gy (majority: 20Gy) applied in single doses of 1 - 4Gy (majority 2Gy) two to five times a week. 20 institutions gave an estimation of their therapy results. According to the majority, deviation, pain and the size of the foci improved in 50% of the patients. Ten further institutions evaluated their results meticulously. The number of patients of these institutes ranges from 1 to 101 (in total 167) patients. The detailed results were as follows: Deviation: complete relief 2%, partial relief 31%, no change 37%, progression 29% of the patients. Size of the foci: complete remission 2%, partial remission 23%, no change 48%, progression 27%. Relief of pain in 32% of the patients. In one institution an analysis of prognostic factors was attempted. There was no statistical correlation of the primary stage with the outcome. Acute side effects were very rare, long-term side effects almost missing. Secondary malignancies have never been reported.

Conclusions: Nearly 30% of the German radiotherapy institutions perform radiotherapy for Peyronie's disease regularly. The results are well within the range of those reported in the literature. Radiotherapy for Peyronie's disease appears to be a reasonable treatment alternative with very mild and rare side effects.

Posters Biological Dose Planning

593 poster

A BIOLOGICAL COMPARISON OF EPITHERMAL NEUTRON BEAMS FOR BNCT

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Purpose/Objectif: The biological effects of epithermal neutron beams, used for Boron Neutron Capture Therapy, are expected to vary between centres due to the differing mix of high and low LET dose components. A transportable system has been developed, involving the clonogenic assay of V79 cells, allowing a direct comparison between epithermal neutron beams. Irradiations at an existing and a proposed clinical facility were compared at various depths in a phantom.

Materials/Methods: Irradiations were carried out at the Swedish BNCT Facility based on the 1 MW R2-0 reactor Studsvik and the proposed accelerator-based BNCT facility at the University of Birmingham, UK. The reactor facility used an aluminium and PTFE $[(C_2F_4)n]$ filter to extract the appropriate energy epithermal neutrons. At the accelerator facility, neutrons were generated via the $^7Li(n, p)^7Be$ reaction and filtered by a composite material, made of a mix of Al, AlF and LiF. V79 cells were irradiated in suspension in vials at depths of 20, 35, 50 and 65 mm in a water-filled phantom. In order to prevent the repair of sublethal damage during irradiation and eliminate the effects of marked differences in dose-rate from the incident and induced g-ray dose component, which varied from 5-71 minutes at Studsvik and 80-470 minutes at Birmingham, the water temperature was kept at 4°C. The elimination of the dose-rate effect at this temperature was demonstrated by irradiating cells with 250kVp X-rays.

Results: X-irradiation at 0.7 and 0.027 Gy/min at 4°C produced identical cell survival data. The corresponding dose-rate of the γ-ray component was between 0.23 and 0.13 Gy/min for the of the Studsvik beam, and between 0.015 and 0.0092 Gy/min for the Birmingham beam, depending on the depth in the phantom. The γ-ray component contributes between 85.2 - 93.9% and 88.7 - 95.4% of the total physical dose in the Studsvik and Birmingham beams respectively, the remaining dose arising from incident fast neutron contamination and thermal neutron capture in nitrogen, the later yielding 580keV protons. The cell survival data at 50 and 65 mm, in the two epithermal neutron beams, were comparable and were combined. At all depths and all cell surviving fractions, the Studsvik beam was more biologically effective than the Birmingham epithermal neutron beam. The ratio of the total dose, on the two beams, required to give a surviving fraction of 1% was independent of depth in the phantom, being 1.30, 1.30 and 1.33 at 20, 35, and 50/65 mm respectively. However, the ratio of doses did depend on the level of cell survival.

Conclusions: The expected dose-rate effect, due to the marked difference in the γ-ray component of the two beams, was avoided by irradiating at 4°C. The greater biological effectiveness of the Studsvik

beam is only partially explained by the greater high LET dose component, suggesting the differing energy spectra of the fast neutron components of the two beams has biologically significance.

594 poster

COMPARISON OF DOSE DISTRIBUTIONS FROM TOMOTHERAPY AND IMRT TREATMENT PLANS USING THE BIOLOGICALLY EFFECTIVE UNIFORM DOSE

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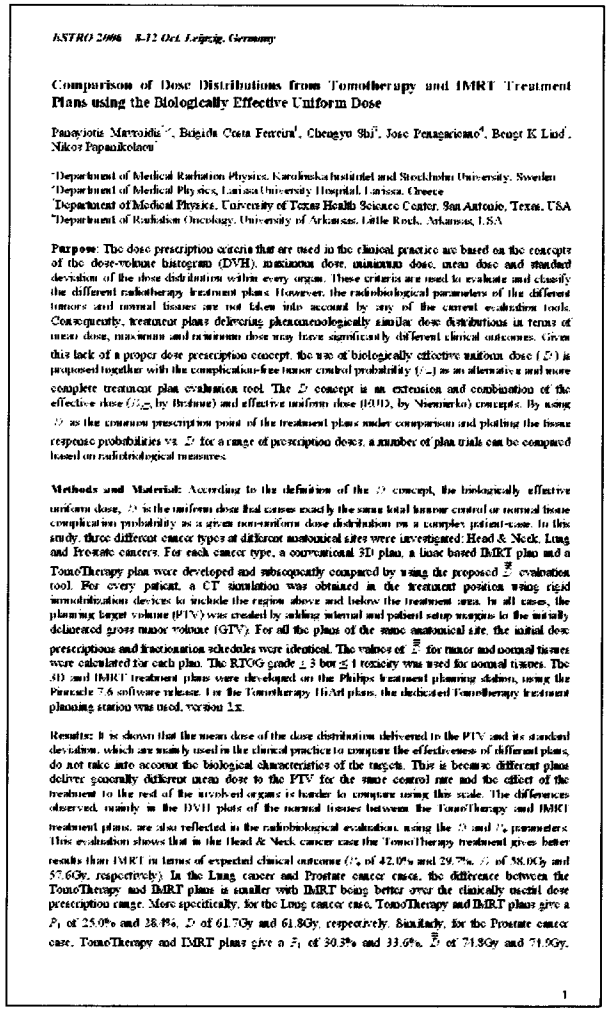
Purpose/Objectif: The radiobiological parameters of the different tumors and normal tissues are not taken into account by any of the current dose prescription criteria such as the dose-volume histogram (DVH), maximum, minimum, mean and standard deviation of the dose distribution. Given this lack of a proper dose prescription concept, the use of biologically effective uniform dose (*D*) is proposed together with the complication-free tumor control probability (*P+*) as an alternative and more complete treatment plan evaluation tool.

Materials/Methods: By using D as the common prescription point of the treatment plans and plotting the tissue response probabilities vs. D for a range of prescription doses, a number of plan trials can be compared based on radiobiological measures. In this study, three different cancer types at different anatomical sites were investigated: Head & Neck, Lung and Prostate cancers. For each cancer type, a conventional 3D plan, a linac based IMRT plan and a TomoTherapy plan were developed. The 3D an IMRT treatment plans were developed on the Philips treatment planning station, using the Pinnacle 7.6 software release. For the Tomotherapy HiArt plans, the dedicated Tomotherapy treatment planning station was used, version 2.x.

Results: The proposed plan evaluations shows that in the Head & Neck cancer case the TomoTherapy treatment gives better results than IMRT in terms of expected clinical outcome (P_+ of 42.0% and 29.7%, BEUD of 58.0Gy and 57.6Gy, respectively). In the Lung cancer and Prostate cancer cases, IMRT plans are better over the clinically useful dose prescription range. More specifically, for the Lung cancer case, TomoTherapy and IMRT plans give a P_+ of 25.0% and 28.4%, BEUD of 61.7Gy and 61.8Gy, respectively. Similarly, for the Prostate cancer case, TomoTherapy and IMRT plans give a P_+ of 30.3% and 33.6%, BEUD of 74.8Gy and 74.9Gy, respectively. If a higher risk for complications (>than 5%) could be allowed then the complication-free tumor control could increase to over 40%, 70% and 60% for the three cancer cases, respectively.

Conclusions: Radiobiological evaluation of treatment plans should provide a closer association of the delivered treatment with the clinical outcome by taking into account the dose-response characteristics of the irradiated targets and normal tissues. There may exist clinical cases, which may look dosimetrically similar but in radiobiological terms to be quite different. In such situations, traditional dose based evaluation tools can be complemented by the use of BEUD to effectively evaluate and compare treatment plans.



ESTRO 2006 8-12 Oct. Leipzig, Germany

Comparison of Dose Distributions from Tomotherapy and IMRT Treatment Plans using the Biologically Effective Uniform Dose

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Purpose: The dose prescription criteria that are used in the clinical practice are based on the concepts of the dose-volume histogram (DVH), maximum dose, minimum dose, mean dose and standard deviation of the dose distribution within every organ. These criteria are used to evaluate and classify the different radiotherapy treatment plans. However, the radiobiological parameters of the different tumors and normal tissues are not taken into account by any of the current evaluation tools. Consequently, treatment plans delivering phenomenologically similar dose distributions in terms of mean dose, maximum and minimum dose may have significantly different clinical outcomes. Given this lack of a proper dose prescription concept, the use of biologically effective uniform dose ($\bar{D}$) is proposed together with the complication-free tumor control probability (P_+) as an alternative and more complete treatment plan evaluation tool. The $\bar{D}$ concept is an extension and combination of the effective dose (D_{eff}, by Brahme) and effective uniform dose (EUD, by Niemierko) concepts. By using $\bar{D}$ as the common prescription point of the treatment plans under comparison and plotting the tissue response probabilities vs. $\bar{D}$ for a range of prescription doses, a number of plan trials can be compared based on radiobiological measures.

Methods and Material: According to the definition of the $\bar{D}$ concept, the biologically effective uniform dose, $\bar{D}$ is the uniform dose that causes exactly the same total tumour control or normal tissue complication probability as a given non-uniform dose distribution in a complex patient case. In this study, three different cancer types at different anatomical sites were investigated: Head & Neck, Lung and Prostate cancers. For each cancer type, a conventional 3D plan, a linac based IMRT plan and a TomoTherapy plan were developed and subsequently compared by using the proposed $\bar{D}$ evaluation tool. For every patient, a CT simulation was obtained in the treatment position using rigid immobilization devices to include the region above and below the treatment area. In all cases, the planning target volume (PTV) was created by adding internal and patient setup margins to the initially delineated gross tumor volume (GTV). For all the plans of the same anatomical site, the initial dose prescriptions and fractionation schedules were identical. The values of $\bar{D}$ for tumor and normal tissues were calculated for each plan. The RTOG grade ≤ 3 bor ≤ 4 toxicity was used for normal tissues. The 3D and IMRT treatment plans were developed on the Philips treatment planning station, using the Pinnacle 7.6 software release. For the Tomotherapy HiArt plans, the dedicated Tomotherapy treatment planning station was used, version 2.x.

Results: It is shown that the mean dose of the dose distribution delivered to the PTV and its standard deviation, which are usually used in the clinical practice to compare the effectiveness of different plans, do not take into account the biological characteristics of the targets. This is because different plans deliver generally different mean dose to the PTV for the same control rate and the effect of the treatment to the rest of the involved organs is harder to compare using this scale. The differences observed, mainly in the DVH plots of the normal tissues between the TomoTherapy and IMRT treatment plans, are also reflected in the radiobiological evaluation, using the $\bar{D}$ and P_+ parameters. This evaluation shows that in the Head & Neck cancer case the TomoTherapy treatment gives better results than IMRT in terms of expected clinical outcome (P_+ of 42.0% and 29.7%, $\bar{D}$ of 58.0Gy and 57.6Gy, respectively). In the Lung cancer and Prostate cancer cases, the difference between the TomoTherapy and IMRT plans is smaller with IMRT being better over the clinically useful dose prescription range. More specifically, for the Lung cancer case, TomoTherapy and IMRT plans give a P_+ of 25.0% and 28.4%, $\bar{D}$ of 61.7Gy and 61.8Gy, respectively. Similarly, for the Prostate cancer case, TomoTherapy and IMRT plans give a P_+ of 30.3% and 33.6%, $\bar{D}$ of 74.8Gy and 74.9Gy.

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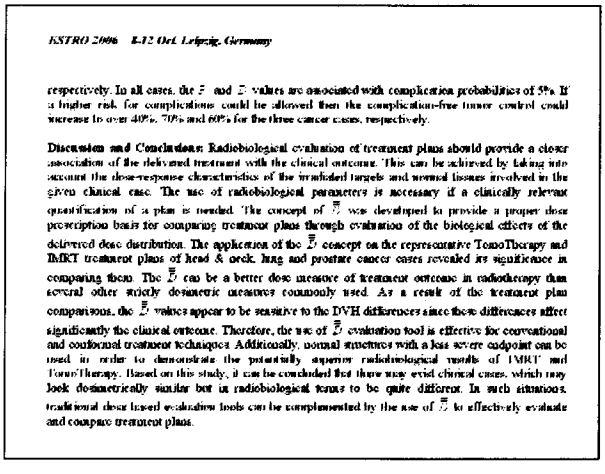

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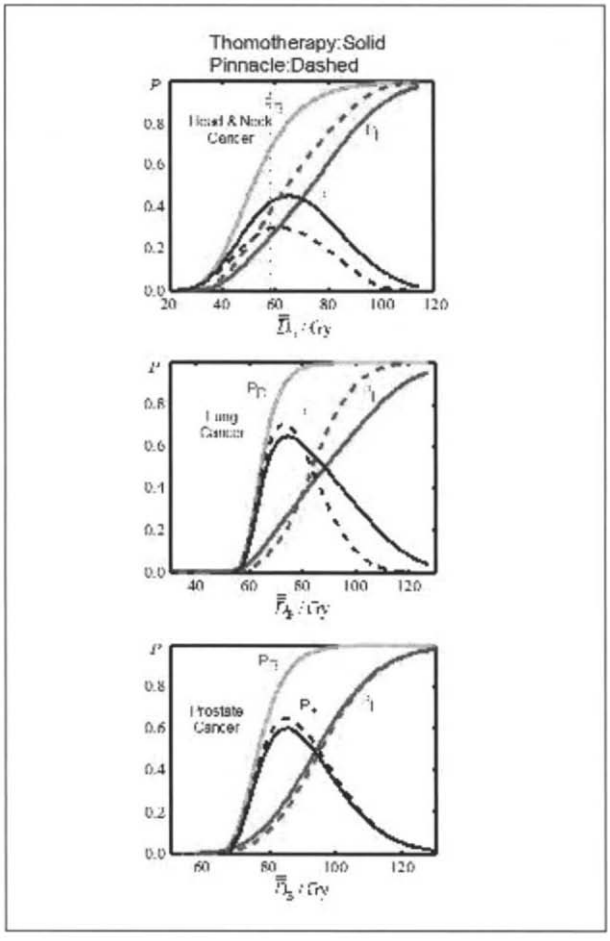
respectively. In all cases, the $\bar{D}$ and P_+ values are associated with complication probabilities of 5%. If a higher risk for complications could be allowed then the complication-free tumor control could increase to over 40%, 70% and 60% for the three cancer cases, respectively.

Discussion and Conclusions: Radiobiological evaluation of treatment plans should provide a closer association of the delivered treatment with the clinical outcome. This can be achieved by taking into account the dose-response characteristics of the irradiated targets and normal tissues involved in the given clinical case. The use of radiobiological parameters is necessary if a clinically relevant quantification of a plan is needed. The concept of $\bar{D}$ was developed to provide a proper dose prescription basis for comparing treatment plans through evaluation of the biological effects of the delivered dose distribution. The application of the $\bar{D}$ concept on the representative TomoTherapy and IMRT treatment plans of head & neck, lung and prostate cancer cases revealed its significance in comparing them. The $\bar{D}$ can be a better dose measure of treatment outcome in radiotherapy than several other strictly dosimetric measures commonly used. As a result of the treatment plan comparisons, the $\bar{D}$ values appear to be sensitive to the DVH differences since these differences affect significantly the clinical outcome. Therefore, the use of $\bar{D}$ evaluation tool is effective for conventional and conformal treatment techniques. Additionally, normal structures with a less severe endpoint can be used in order to demonstrate the potentially superior radiobiological results of IMRT and TomoTherapy. Based on this study, it can be concluded that there may exist clinical cases, which may look dosimetrically similar but in radiobiological terms to be quite different. In such situations, traditional dose based evaluation tools can be complemented by the use of $\bar{D}$ to effectively evaluate and compare treatment plans.



595 poster

HYPOFRACTIONATED RADIOTHERAPY (HF-RT) OF LUNG AND LIVER METASTASES USING HELICAL TOMOTHERAPY (HT): ANALYSIS OF DOSE-ESCALATION PROTOCOLS BY MEANS OF RADIOBIOLOGICAL MODELS (RBMS)

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Purpose/Objectif: In patients (PTs) affected by lung and liver METs, the use of HF-RT offers opportunities of improving clinical outcomes by means of higher radiation doses and significant\\notable reduction in overall treatment time. HT provides a better dose painting (target coverage and sparing of healthy tissues) compared with CRT and Linac-based IMRT; the daily acquisition of a MV_CT reduces random and systematic set-up errors. Any HF dose-escalation protocol has to evaluate dose and volume limitations in order to maintain the risk of complications at an acceptable level. The use of RBM offers a robust way to NTCP in defining the appropriate RT schedule.

Materials/Methods: 10 PTs with lung or liver METs were scheduled to receive a HF treatment in 5 (liver) or 6 (lung) fractions over a two-week period. In this analysis the dose per fraction was varied from 7 to 15 Gy (BED10: 70-200 Gy). All PTs were immobilised by means of a vacuum pillow, CT/PET scans were acquired during free breathing, and a 4D procedure based on a Varian RPM system was used to define target volumes and to estimate the respiratory cycle related margins. Small margins (3-5 mm) were added for set-up errors. The treatment planning was obtained by HT inverse planning with highest priority PTV coverage. The LKB model of NTCP was applied; each DVH bin was corrected for fractionation using the Withers formula. The original Emami data for the model parameters were used except for lung (radiation pneumonitis, De Jaeger 2003) and liver (RILD, Dawson 2002).

Results: The PTV volumes were 40"b33 cc and 227"b158 cc for lung and liver diseases respectively. In these 5 liver PTs, the NTCP values for spinal cord and kidney remained < 5% up to BED10=200 Gy. The normalized mean liver dose (mean liver-CTV dose divided by the prescribed dose) was 26"b6 %. The mean liver NTCP was 5.1"b7% and 26"b30% for BED10 equal to 132 and 168 Gy respectively. In PTs with small tumour volume or normalized mean liver dose < 20%, the risk of RILD remained < 10% up to BED=150 Gy. The liver NTCP showed a steep increase when BED10 > 130 Gy in PTs with normalized mean liver dose > 25%. For all 5 lung PTs the PTV had a very small volume and was far from "serial" OARs. The normalized mean lung dose was 13"b6%; the risk of radiation pneumonitis remained < 15 % up to BED10=200 Gy

Conclusions: As they are able to deal with both fractionation effects and healthy organ behaviour ("serial/parallel"), RBMs are considered to be quite a useful tool in the design of HF treatments.

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IRRADIATION ADAPTATION TO THE TUMORAL ACTIVITY WITH THE HELP OF IMRT FOR HEAD AND NECK CANCERS

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2 - Centre de Recherche en Automatique de Nancy, *UMR 7039 CRAN CNRS-UHP-INPL, Nancy, France*

3 - Varian Medical Systems, *Buc, France*

4 - Laboratoire de Chimie Bioinorganique Médicale, Imagerie thérapeutique et diagnos, *CNRS FR2599-UPS, Toulouse, France*

Purpose/Objectif: The purpose of this study was to index deposited doses of irradiation to the tumoral activity and not only to the tumoral geometry. This tumoral activity (biological heterogeneities) is given by PET imaging or Magnetic Resonance Spectroscopy Imaging. The idea is to administer a higher dose to a tiny volume (around 1cm of diameter), included in a larger Planning Target Volume (PTV). The long-term objective is to offer to the radiation oncologist the possibility to irradiate a hyperfixation with a higher dose within a PTV, while improving the tumoral control.

Materials/Methods: Dose calculations were performed on Eclipse/Helios, Varian Medical Systems treatment planning system. Two IMRT head and neck phantoms developed in the Centre Alexis Vautrin, were used with various detectors to either perform 1D dosimetry (ionisation chamber), 2D dosimetry (radiographic film) or 3D dosimetry (dosimetric gel, Glucogel). Software characterization was realized studying the influence of different parameters (factor of priority, smoothing, number of beams, prescribed dose…) and according to different treatment plans. Two models were used: - a "simplistic" model, with a non realistic geometry: spherical fields for PTV and Organs At Risk (OAR) with or without conditions on OAR, - an anatomically realistic model containing target volumes, hyperfixation and OAR such as spinal cord, parotids…

Results: For volumes of hyperfixation superior to 2cm^3, the conformation number was superior to 0.7; the target volume conformation by the reference isodose was thus satisfactory. One or several hot spots outside PTV, unfavourable to the treatment, appeared when the OAR was too close to the hyperfixation (distance inferior to 0.8cm). The Conformal Index was lower than 0.53. No influence was noticed when the 2 structures were separated by 2.6cm or more. The detector choice was as important as its location in the phantom, for this reason we used several types of detectors. In absolute dosimetry, the difference between measured and calculated values were in the order of 4% at the isocentre (area of low gradient), and reached 15% at areas of high gradients. In relative dosimetry with films, 89% of pixels had a gamma index inferior to 1, for isodoses superior to 20% and with 3mm and 4% of tolerances. Also with the gel, 90.5% of

voxels had a gamma index inferior to 1 at isocentre.
Conclusions: Highly precise radiotherapy in limited zones is possible with IMRT depending on various conditions: such as localization, number of OAR, distance between PTV and OAR, presence of hyperfixation, volume of this hyperfixation, its localization within the tumour, localization of the tumour as well as its volume within the zone to be treated and the number of fields. According to our results, a precise geometry will thus be recommended to use this method of irradiation adapted to the biological heterogeneities.

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OPTIMIZATION IN IMRT: EUD CONCEPT REVISITED FOR VOXEL BASED EVALUATION

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Purpose/Objectif: Treatment optimization comes to find the treatment parameters, such as map fluence for IMRT, which minimize a score function.The score function is a mathematical tool checking the relevance of a treatment plan according to the dose constraints for the target volume and normal tissues involved in the irradiation. Dose constraints are currently introduced inside commercial TPS by DVHs points. DVHs are 2D representation of 3D physical dose distribution and do not take into account the spatial information or the non-linear dose response of the volumes of interest.To overcome this lack of information, we are developing a biology based score function which takes into account the spatial information at the voxel level.
Materials/Methods: The Equivalent Uniform Dose (EUD) concept is based on radiobiological principles and is a measurement of dose weighted for biological effects. Nevertheless, EUD is defined at the structure level and the spatial information is loss.We have developed a dedicated application to IMRT treatment plan evaluation and optimization within the MathLab framework.Spatial information and fractionation effect are taken into account by applying on dose matrices a filter based on local linear quadratic EUD (LQ EUD) values for each voxel. Compensation for hot and cold spots is a weakness for EUD models and it was compared by calculating the resultant LQ EUD. This limitation is overcome using this methodology.
Results: The filter was applied on a dose distribution corresponding to a target volume of 93.2cm^3, prescription dose 44Gy.Hot spots and cold spots were defined according to ICRU report 50.The target includes 7 isolated cold spots (12-41 Gy): 6 smaller than 1cm^3 (2.3% of the whole volume) and another one representing 3.7% of the volume. 69% of the volume is overdosed (47-60 Gy) leading to EUD and LQ EUD values of 48Gy.Filtered LQ EUD is less sensitive to the compensation for hot and cold spots. We found LQ EUD value of 45 Gy when the volume element analysis is 2cm^3.
Conclusions: The calculation of local EUD is a way to summarize the strength of heterogeneous spots. Our analysis at the voxel level is a way to keep LQ EUD concept and to overcome DVHs restrictions.The introduction of a biological model could lead to better plans and the development of such treatment plan evaluation is the beginning of a biological based treatment optimization project.

598 poster

QUANTIFYING TUMOUR HYPOXIA FROM PET FOR THE BIOLOGICAL OPTIMISED TREATMENT PLANNING

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2 - Norrland University Hospital, Department of Radiation Physics, Umea, Sweden
3 - Karolinska Institutet, Department of Medical Radiation Physics, Stockholm, Sweden

Purpose/Objectif: Hypoxia has been shown to be a strong microenvironmental factor which modulates the response to treatment through the radioresistance it confers to the affected cells and their malignant selection. Several markers are now available and could therefore be used in clinical PET investigations to image tumour hypoxia. This study will present a theoretical assessment of the hypoxia information provided by various markers and the impact of various calculation models for tumour hypoxia.
Materials/Methods: Biologically relevant tissue oxygenations were calculated for ranges of physiological tumour parameters. They were then used to simulate PET images in combination with experimental binding curves for different hypoxia markers. The resulting marker concentration maps were quantified with various methods in order to calculate the corresponding optimal dose distributions needed to counteract the effect of the hypoxic regions. The results were compared in terms of their impact on the predictions of treatment outcome.
Results: A tumour model has been constructed having heterogeneous oxygenations obtained from simulations of oxygen diffusion from blood capillaries and consumption in tissue. Distributions of PET markers throughout the tumour were calculated from the individual oxygen tensions with various assumptions regarding the uptake of the marker. It was found that different markers yield different images both in terms of the apparent oxygenation distribution and in terms of the magnitude of activity relative to the oxic tissues. This could lead to some potential problems in interpreting the images obtained with various markers as well as in including the information they contain into treatment planning. These aspects have to be taken into consideration when physiological information is used to customize radiation delivery by adapting it to the individual features of each patient in the attempt to improve radiation therapy.
Conclusions: The results of this study contribute to the understanding of the most influential factors for the inclusion of imaging information into the simulation of radiation response. Thus, the accuracy of the predictions was found to be related to the uptake of the hypoxic tracer as well as to the tumour vascularisation that modulates the amount of tracer available for uptake.

599 poster

UNCERTAINTY LEVELS EVALUATION IN THE NTCP DETERMINATION

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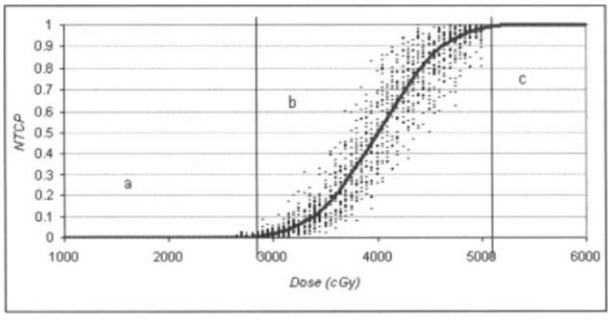
Purpose/Objectif: Nowadays the calculation of NTCP and TCP values are useful to scoring alternative treatment plans, and it is common that treatment planning systems incorporate different radiobiological models. In this work, we evaluate the uncertainty level of NTCP parameter as function of the uncertainties of the variables associated. A quality assurance of the values calculated by our treatment planning system is performed.
Materials/Methods: We have assumed a sigmoidal dose response model for NTCP, depending of equivalent uniform dose (EUD), m and D_{50} parameters. The Kutcher-Burman reduction method is used to calculate the EUD. We suggest that m and D_{50} follow a Poisson probability distribution, and we apply Monte Carlo method of propagation of uncertainties to derive the distribution probability of NTCP. A number of sets of parameters values for different organs have been gathered in databases. We have developed a Visual Basic application to carry out an independent calculation of NTCP based on dose-volume histograms automatically exported from the treat-

ment planning system and these values are compared with those calculated by the Philips Pinnacle³ (v. 7.4f) planning system.
Result: The uncertainty analysis of the NTCP shows three different regions: a. NTCP near to zero, b. Slope zone, and c. NTCP near to one. In a. and c. the parameters uncertainties does not affect to the NTCP uncertainty because the value of NTCP reaches a saturation region. The more important uncertainty is obtained in region b, because is mostly sensitive to the uncertainties of both m and D_{50}.
Conclusions: We conclude that, though parameters of the NTCP model could be affected by relevant uncertainties, clinical acceptable uncertainties are achieved if the NTCP value is kept in the saturation region. The comparison between our model and the planning system shows an agreement in all the cases studied when using the same dataset of parameters.



Posters Brachytherapy

600 poster

^{125}I PROSTATE BRACHYTHERAPY TOXICITY IN 80 CONSECUTIVE PATIENTS

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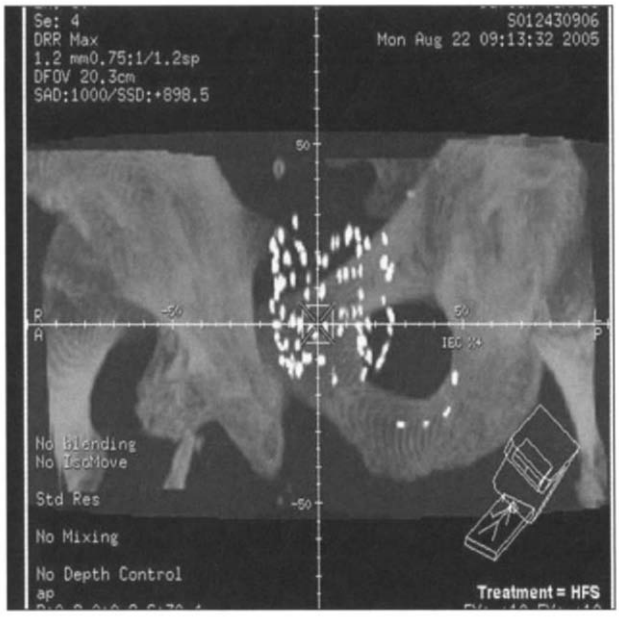
1 - Centre Oscar Lambret, Department of Radiotherapy, Lille, France
2 - Centre Oscar Lambret, Department of Radiology, Lille, France

Purpose/Objectif: To present pre- and post-implant dosimetric results. To collect acute and chronic toxicity trends and to identify clinical and dosimetric predictive factors for urinary morbidity.
Materials/Methods: Eighty consecutive patients with biopsy-proven T1-T2 prostate adenocarcinoma whom underwent brachytherapy between 08/2002 and 11/2005 were evaluated. An ultrasound-guided transperineal permanent seed implantation (pre-implant technique) with stranded ^{125}I sources (RAPIDstrand©) was performed. The prescription dose was 145 Gy to the planning target volume. Post-implant dosimetry was performed 1 day and 1 month later on the basis of CT imaging. The pre-implant, day 1 and day 30 prostatic (V200, V150, V100, D90), urethral (V150, D30, D5) and rectal (V110) parameters were calculated. The median time of follow-up was 19 months (range 2-38). Urinary, rectal and sexual toxicity was classified by the RTOG toxicity scale at 2, 6, 12, 18 and 24 months. Clinical, treatment and dosimetric parameters were evaluated in univariate and multivariate analyses to identify independent predictors for urinary morbidity.
Results: The mean pre-implant prostate volume was 32.8 cm³. Day 1 and 30 mean CT prostate volume were 49.3 cm³ and 37.5 cm³. The mean (SD) prostatic dosimetric values at day 1 post-implant were: V100: 85 % (8), D90: 90 % (17) and at day 30: V100: 90 % (6), D90: 102 % (16). The mean (SD) urethral dosimetric values at day 1 post-implant were: V150: 6 % (10), D5: 136 % (26), D30: 122 % (18) and at day 30: V150: 21 % (21), D5: 163 % (39), D30: 143 % (31).
Because of urinary retention, 8 (10 %) patients required a pubic catheter and two of them needed surgical transurethral resection. Median time of onset and duration were 10 days (range 12 hours - 6 months) and 6 months (range 2 - 12 months). Urinary retention was linked to non treatment related as well as technical factors: prostatic volume (p = 0.02), number of needles (p = 0.005) and number of seeds (p = 0.01). Neither clinical factors, nor treatment related or dosimetric factors predicted pollakiuria, nocturia or incontinence.
Compared to the initial clinical status, dysuria at 2 months increased in almost half of the patients, decreasing to 30% after 1 year. The dosimetric parameters V100 and D90 at day 1 and day 30 predicted (p < 0.04) dysuria grade 2 or 3, 2 months after treatment. Nocturia worsened in 25 % of the cases after 2 months and decreased to 16 % after 1 year. Pollakiuria and incontinence were negligible (<5%). No rectal toxicity was demonstrated. Impotence was increasing with time of follow-up.
Conclusions: Our data suggest that post brachytherapy toxicity profile is acceptable. Retention, dysuria and nocturia are the most common symptoms and decrease with increasing time of follow-up. Prostatic volume, number of needles and seeds predict the risk of retention.



601 poster

A CASE OF STRAND MIGRATION AFTER PROSTATE SEED IMPLANT

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Purpose/Objectif: I-125 seeds are available for use as within strands (i.e. spaced at a fixed distance within an absorbable suture). Strand technique is often employed for prostate seed implants in order to improve seed spacing and inhibit and seed migration
Materials/Methods: An I-125 seed implant was executed with a total of 87 seeds implanted using 28 needles. All the seeds were accounted for by fluoroscopic images obtained at the end of the case. Cystoscopy showed no seeds or strands in the bladder. The activity per seed was 0.42 Units, the total activity was 37.41 units or 29.46 mCi. The prescribed dose was 145 Gy and the prostate volume was 34.4 cc.
Results: Post-plan evaluation performed four weeks after the implant demonstrated that one strand was found to have migrated to the anterosupero-lateral margin of the ischiorectal fossa (adjacent to the ischium; see figure). Dosimetric parameters were found to be adequate as follows: The D90 was 135.0 Gy or 93%, the V150 was 10.3 cc or 30% of the implanted volume, the V100 was 82% or 28.2 cc. The V90 was 92% or 31.6 cc and the V80 was 98% or 33.7 cc. Average dose to the urethra was 147.4 Gy, maximum dose to the urethra was 159.2 Gy. Average dose to the rectum was 109 Gy and maximum

dose was 134 Gy. The patient did not report any symptoms related to the strand migration.
Conclusions: Strand migration may occur after seed implant using this technique. The mechanism of strand migration to this particular location in this case remains unclear. Dosimetric parameters were not dramatically affected and the patient had no related symptoms.

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A COMPARISON BETWEEN POST-PLANNING PROCEDURES AFTER SEED IMPLANTATION

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3 - Klinikum Leverkusen, *Klinik für Urologie, Leverkusen, country*

Purpose/Objectif: Comparison of post-plannning procedures done independent with Variseed and Pinnacle.
Materials/Methods: For 17 patients we have done post-planning procedures after seed implantation with the Variseed and the Pinnacle treatment planning system. All patients were treated according to the recommendation of ESTRO and EAU. The treatment was done with the intraoperative dynamic treatment realtime treatment planning module of the Variseed 7.1 planning system. The median activity of the seeds were at 0,634mCi/seed. The post-planning CT was done with a slice thickness of 3mm and 3mm increments as well. We have done automatic seed-finding with Variseed and manually with Pinnacle. The region of interests were defined independently by the same radiation oncologist on both systems. Then we compared the volume, the D90 and V100 of the prostate and the Dmax of the urethra.
Results: The deviations between the two treatment planning procedures have the following average values.Volume of the prostate: 6.6% standard dev 4.7% D90 prostate: 7.9% standard dev 4.3% V100 prostate: 2.9% standard dev 1.2% Dmax urethra: 16% standard dev 13.7%
Conclusions: It is possible to make post-planning procedures with both planning systems. The large differences for Dmax of the urethra is caused by the small distances to the seeds and the enormous influence of the definition of the urethra.

603 poster

A DOSIMETRY STUDY OF VAGINAL ^{192}IR BRACHYTHERAPY APPLICATIONS WITH A SHIELDED CYLINDRICAL APPLICATOR SET

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Purpose/Objectif: Shielded vaginal cylinders are used in the brachytherapy with Ir-192 for special treatments. The dose distribution can be modified by the use of shielded segments from tungsten (90° segments). An example is the protection of the rectum during vaginal treatments. In this work the precision of the calculated dose distribution of the treatment planning system is examined. From the result conclusions are derived for the clinical use.
Materials/Methods: The treatment planning system (Plato BPS, Nucletron B.V., Veenendal, The Netherlands) calculates the dose at point P corresponding to the AAPM TG 43 formalism. If point P is located behind a shielding segment the weakening of the radiation is taken into account by a factor. In the concrete case the factor is 0.17. Changes of the dose distribution on the open side due to absorption and backscattering are disregarded. The dose distribution of the source is measured in an automated scanning water phantom (Blue Phantom, Scanditronix-Wellhöfer). The used ionization chamber was the CC01(Scabditronix-Wellhöfer) with a measurement volume of only 0.01cm^3. The rate of charge collection by the ionization chamber is measured using an electrometer (Farmer-Dosemeter Typ 2570) set in the dose rate mode. The effective centre of the source is determined empirically by scanning the detector in the x-, y- and z-directions past the source. The effective centre is located at the dose rate maxima of the three orthogonal scans. The following measurements are carried out at two different distances (35 and 50mm) from the source axis in the level of the effective centre. The dose rate is measured in steps of 5° from 0 to 360° around the radioactive source. We examined our results with the Monte-Carlo method (EGSray).
Results: The results are investigated in three separate categories: (Open side, protected side and transition zone). A relatively good agreement appears on the open side between calculated and measured values. The measured results deliver generally higher dose rates. However, the deviation is clinically acceptable with max. 5%. The measured results on the protected side reveal up to 10% lower dose rates than the calculated ones. Arising deviations in the area of transition are up to 20%. The monte carlo simulation confirms our result. We observed a good agreement with our results.
Conclusions: Changes of the dose distribution in the near area of the source due to the use of tungsten segments are not negligible. The backscattering-effect should particularly taken into account on the open side. The appearance of backscattering causes an intensification of the radiation on the open side. It could be shown, that this complex system can be adequately described with a very simple computational model. The transition zone must receive special attention. No critical structures should occur.

604 poster

A NEW TECHNIQUE OF STEREOTACTIC PERMANENT BREAST SEED IMPLANTATION

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Purpose/Objectif: To evaluate the feasibility of a new technique to use permanent seed implants in the breast. This first experience was based on 15 patients treated in the context of a boost after external beam radiotherapy.
Materials/Methods: Patients were selected based on risk factors for local recurrence (mainly age <50y, or insufficient resection margins). The patient was immobilized and the breast fixed with a thermoplastic sheet at a simulation procedure during external classical whole breast radiotherapy. A template bridge was applied, mildly compressing the breast and consisting of 2 identical thick needle guiding templates with holes every cm. It was placed in such a way that the tumor bed was covered by the template under fluoroscopic and clinical control. Reference points were placed on the sheet and patient, to reposition the sheet during the next steps. A thoracic CT/MRI scan was obtained and the image set rotated to get images perpendicular to the implant axis. A 4 to 5 mm thick skin layer, the whole heart in case of left sided treatments, the ipsilateral lung and the CTV were delineated. The CTV was defined as the tumor bed plus a margin of at least 2 cm, amounting in practice to the volume of a breast quadrant which is considered appropriate in this boost series. A preplan was made prescribing a 50 Gy boost to the CTV, and limiting if possible skin doses to below 30 Gy. In the operating theatre the breast was immobilized in the same position using the marked reference points. Under general anaesthesia 8-20 needles were placed and 29-80 0.3 mCi Iodine125 seeds in strands were implanted through the template, similar to prostate implants. A short fluoroscopy at the end of the implant was done to check implant consistency. The implant results were verified with a postplan 2 weeks later on which the CTV was not contoured because of a different breast orientation and the absence of visible markers in most patients.

Results: The simulation, scanning and implant procedure were feasible and well tolerated: no short term toxicity over grade I after a mean follow up of 10 months (range 1-15) except for one case of transient grade III arm neuropathy. Fluoroscopic control showed a good strand insertion, with the exception of a mild shift in a few strands. The pre plan and dose volume histogram showed a good CTV coverage (CTV V100% = 97±3.8%). Organs at risk were well spared: the mean post plan skin, heart and lung V30Gy were 2, 0, 4 ml respectively. The post plan showed a mild seed dispersion because of breast oedema and relaxation after sheet removal, leading to a slightly lower V100% (96±37 ml versus 105±41 ml, p=0.007) and trend for a lower V200% (34±16 ml versus 37±20 ml, p=0.45).
Conclusions: The described technique is feasible but to be able to use it for partial breast irradiation we need to select patients with good markers helping to identify the target volume. A trial testing this approach for PBI is due to start.

605 poster

A SIMOLE ANALYTIC EXPRESSION FOR MULTIPLYING FACTOR (MF) IN HDR BRACHYTHERPAY GYNECOLOGICAL TREATMENTS

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Purpose/Objectif: Comparing different Brachytherapy gynecological treatments is an old and unsolved problem. The big dose gradients inside treatment volumes, different dose rates used and different fractionations hinder an easy obtaining of radiobiological comparisons parameters. R. Dale has proposed the use of a Multiplying Factor (MF) to solve these difficulties but the calculation of this factor is not mathematically simple. The MF associates an equivalent BED with a reference BED ($BED_{eq} = MF * BED_{ref}$).
Materials/Methods: Obtaining the MF can only be carried out through a calculation "voxel by voxel" in a certain dose distribution. This dose distribution in gynecological brachytherapy depends essentially on used applicator.
Since 1992 in our center we have treated more than 1000 patients with gynecological HDR brachytherapy using the ring applicator. For all the possibilities of this applicator (combining rings of 26, 30 and 34 mm with tandems of 20, 40 and 60 mm) and for a certain distribution of dwell positions the MF was calculated using as reference BED value the BED in point A.
For our purpose we develop a software that obtains the dose distribution considering the applicator geometry and the active well positions, and it gives the MF as final result.
81 different situations were analyzed and through a fiting technique an analytic expression between BED_{eq} and BED_{ref} was obtained.
Results: With our analysis we obtained a simple analytic expression for the MF as a function only of the treatment volume, the number of fractions, the reference dose per fraction and the parameters a and b of the linear quadratic model.
In all analyzed cases treated with standard protractation, the difference between the value calculated by the software "voxel by voxel" and the analytic expression was smaller than 5%. This difference is acceptable for radiobiological comparison.
Conclusions: These results suggest that the obtained equation is acceptable for clinical use, and that it can permit the comparison among different institutions allowing by this way the analysis of the biological effectiveness of different HDR brachytherapy treatments. The present work has been developed with ring applicator because it is today the more frequently used. The results can be perfectly applied to treatments carried out with Fletcher applicator wich is also broadly used in the practice of the gynecological brachytherapy in many centers of the world.
The same analysis could be made in bachytherapy LDR.

606 poster

ACUTE AND LATE URINARY TOXICITY IN 606 PROSTATE BRACHYTHERAPY PATIENTS – THE BC CANCER AGENCY EXPERIENCE.

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Purpose/Objectif: To describe acute and late urinary toxicity and associated predictive factors in 606 uniformly treated consecutive prostate brachytherapy (PB) patients.
Materials/Methods: Pts were implanted July 1998 - January 2003. Median follow was 49.5mo (range 34 - 89). Baseline and post-treatment IPSS, urinary QOL (scale from 0=delighted to 6 = terrible) were prospectively collected. Acute urinary toxicity was measured at 6 weeks, subacute at 6 months and late on > 12 months after PB using the RTOG scale. Logistics regression was used for probability of RTOG grade 2+ and Cox proportional hazards regression for time to IPSS normalization.
Results: Median baseline IPSS was 5. Median IPSS at 6 weeks, 6, 12 and 60mo were 19, 11 and 8 and 6 respectively. Of the entire cohort, 83% had an IPSS that returned to baseline with 31%, 62% and 75% by 6, 12 and 24mo respectively. Patients not attaining IPSS normalization had lower pre-treatment IPSS scores (p<0.001). For all pts, baseline median QOL score was 2 and have improved (decreased) to 1 at 24mo. Percentage of pts having acute (at 6 weeks), subacute (at 6 months) and late (at > 12 months) RTOG grade 2 toxicity was 37%, 20% and 23%; RTOG grade 3: 16%, 4%, and 5%. One patient developed grade 4 toxicity at 36-month follow up. The proportion of patients experiencing grade 2+ toxicity at any particular 12-60 month follow-up remained stable (9-5% grade 2, <2% grade 3).
Factors predictive for late RTOG > 2 urinary toxicity were: baseline IPSS (p<.001), pre-implant prostate volume (p=0.027), diabetes (p=0.044), prostate D90 (p=.03) and V150 (0.05). Factors predictive for time to IPSS normalization after prostate brachytherapy were: baseline IPSS (p<.001), androgen suppression (p<.001), pre-PB prostate volume (p=0.016), prostate V100 (p<.001), V150 (p=.011) and D90 (p=.002).
Conclusions:
Most urinary symptoms resolve within 12 months after PB. We have observed a low rate of severe late urinary toxicity (7% RTOG > 2) at 5 years. Two years after PB and onwards, most patients have the same urinary QOL compared to baseline. Baseline urinary symptoms (iIPSS), prostate size pre implant and prostate dosimetry (V100, V150 and D90) predict for worse urinary symptoms after the procedure.

607 poster

ACUTE TOXICITY IN LOW RISK PROSTATE CANCER TREATED WITH LOW DOSE (125)I BRACHYTHERAPY: PROSPECTIVE ANALYSIS.

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Purpose/Objectif: The morbidity associated with brachytherapy

is mainly rectal, urinary and sexual. The objective of this study is to analyse the acute toxicity (12 months after treatment) in a prospective study and the statistics significance of several risk factors.

Materials/Methods: Between September 2003 and December 2005, 66 patients with low risk prostate cancer (<T2b, Gleason<7 and PSA≤10ng/ml) and mean preimplant prostate volume of 34±10 cc, have received radical treatment with (125)I brachytherapy, using an intraoperative real time, peripheral loading technique and a prescribed dose of 145 Gy. Alpha-blockers was initiated 10 days before the implant, and antibiotic and NSAIDs were prescribed for a week after. We evaluate urinary, rectal and sexual toxicity

Results: Mean follow-up is 18 months. Urinary toxicity: I-PSS and QoL values pre-implant were 7.5 and 2 respectively; 12 months after the implant, the values were 6.8 and 1.5. The incidence of dysuria went down from 48% (one month after the implant) to 19% 12 months after. Haematuria post-implant was reported in 27%. Acute urinary retention (AUR) was detected in 11% of the patients, with an average duration of 42 days. The only significant risk factor to urinary retention was the preimplant prostatic volume (0.047); presence of median lobe and pre-treatment I-PSS not found significantly related to the incidence of AUR. Rectal toxicity: Rectal tenesmus and/or urgency were found in 11%, all of them cured at 6 months. Initial discharge of mucus or blood was detected in 6.1%, all of them solved at 6 months. Sexual toxicity: Excluding patients in androgen deprivation therapy, adequate erectile function was seen in 72% and partial dysfunction in 21%. Twelve months after the implant 16% of patients referred impotence, partial disorder in 28% and normal rigidity in 56%, being the previous erectile function the most important predictive factor. Haemospermia and painful ejaculation (9% and 7% after the month 1) disappeared at 6 months.

Conclusions: In our initial experience (125)I brachytherapy has low morbidity focused in urinary symptoms and in less proportion rectal toxicity. After 12 months, however, I-PSS recovered preimplant values. This procedure maintains an excellent erectile function, mainly in patients with previous normal erectile response. We want to stress the need to selection adequately patients with no large prostates regarding to avoid AUR

608 poster

CLINICAL FEASIBILITY OF A NEW ROBOTIC NEEDLE INSERTION METHOD TO MINIMIZE PROSTATE MOTION DURING IMAGE GUIDED PROSTATE INTERVENTIONS

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Purpose/Objectif: The purpose of this study is to investigate the efficacy of a new needle insertion method (tapping instead of pushing) in reducing attendant prostate motion. This can be useful in applications where tissue motion due to needle insertion is problematic such as e.g. MRI-guided prostate brachytherapy and breast biopsies.

Materials/Methods: Prostate motion due to needle insertion was measured in 30 patients, who were transperineally implanted with fiducial gold markers for position verification in prostate intensity modulated radiotherapy. In total 32 needles were manually pushed into the prostate and 29 were tapped with a prototype robotic system. This system makes it possible to insert a needle with a certain, well-defined, amount of momentum and a high velocity. Due to this high needle insertion velocity, we expect the prostate motion to be minimal. The needle insertion velocity is adjustable by changing the air pressure of a pneumatic cylinder. After the first 5 patients the air pressure was increased from 6 to 8 bar.The prostate motion in the cranio-caudal direction was measured on the video record of the ultrasound images. Differences in prostate motion between the two needle insertion methods were analysed with SPSS using the t-test and the Mann-Whitney test.

Results: No problems or complications occurred during needle insertion with the tapping device. The group of patients who had the needles tapped into the prostate seemed to have less pain during needle insertion compared to the group who had the needles pushed into the prostate, likely because of the high needle insertion velocity.The mean prostate motion was 5.6 mm (range 0.3 - 21.6) when the needle was pushed and 0.9 mm (range 0 - 2.0) when the needle was tapped into the prostate ($p < 0.001$). After increasing the air pressure from 6 to 8 bar the mean prostate motion decreased from 1.4 mm to 0.7 mm ($p = 0.002$).

Conclusions: We have shown that our new robotic needle insertion method is feasible and significantly reduced the prostate motion compared to the old method of pushing the needle into the prostate. The optimal air pressure might be somewhat higher than the used 8 bar, resulting in even less prostate motion.

609 poster

COMPARISON BETWEEN CT AND ORTHOGONAL BASED CALCULATION OF ICRU RECTAL AND BLADDER DOSES DURING INTRACAVITY BRACHYTHERAPY FOR UTERINE CERVIX CANCER - ARE ORTHOGONAL FILMS NOW OBSOLETE?

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Purpose/Objectif: To compare the accuracy of the ICRU-38 dose points defined for cervix brachytherapy when planned using conventional 2D or image guided 3D protocols.

Materials/Methods: The study included 26 consecutive patients receiving intrauterine brachytherapy for cervix cancer using a single intrauterine tube and 2 colpostats with a conventional Manchester type applicator. Cases were from 17/06/2005-28/04/2006. For their first fraction of intracavity brachytherapy, after insertion of the applicator, bladder catheter and vaginal packing, all patients had a CT scan of the pelvis at 2mm slice intervals and digitalised A-P and lateral orthogonal films. Using the Varian brachytherapy planning system (BrachyVision) standard plans were applied to these images with the dose defined at point A. The ICRU-38 rectal and bladder points were also identified and doses at these points recorded. To exclude inter-observer variation the points were determined by a single person. The paired-t test was used to determine if there was a significant difference between the doses calculated in an individual patient using CT- or orthogonal-based imaging.

Results: Of the 26 patients 2 were excluded, resulting in 24 patients. For the rectum, the mean difference between CT and orthogonal film calculations of the dose at the ICRU point was 4.02% (1.43-6.60%; $p<0.01$). Similarly for the bladder the mean difference was 3.81% (1.48-6.15%; $p<0.01$%).

Conclusions: There is a statistically significant difference of dose when calculated using the two techniques of about 4%. HDR brachytherapy doses are more damaging than the same dose given at LDR. Correction factors of 0.54 are advised. This suggests that the LDR radium equivalent difference in dose calculations for our study would be 4.02 x 1/0.54 = 7.44%, which could be of real clinical significance for future toxicity.

At present, many radiotherapy centres are changing several steps of their cervix brachytherapy protocols; dose rate (LDR or MDR to HDR), applicator design (Manchester type to ring design), dose calculation (2D orthogonal radiographs to CT planned 3D). Both American Brachytherapy Society and ESTRO guidelines mandate that, for continuity, we continue to report doses at the ICRU-38 "point A" , "bladder" and "rectal" points during this period of change. We believe that radiotherapists need to be aware that a change from

2D to 3D estimation of Organ at Risk dose points may be of clinical significance. Each centre may need to repeat a study such as this to maintain similar ICRU-38 points during the transition to new 3D planning.
In addition approximately 6% of patients who receive radical radiotherapy for gynaecological malignancy, despite being within dose constraints for ICRU rectal and bladder points, develop significant bowel or bladder toxicity. It is possible that some of this toxicity is due to inaccuracy in measurement of the ICRU bladder and rectal point using orthogonal films.

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COMPARISON OF A PRE PLANNED DOSE DISTRIBUTION WITH A REAL TIME DOSE DISTRIBUTION IN ULTRA SOUND GUIDED 3D CONFORMAL BRACHYTHERAPY OF PROSTATE CANCER

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Introduction: Since 1998 the University Hospital in örebro has been treating prostate cancer with HDR brachytherapy in combination with external radiotherapy. The dose in external radiotherapy is 50 Gy (2 Gy/frac) and in brachytherapy 20 Gy (10 Gy/frac). The treatment was based on a pre planned dose distribution. 235 patients were treated between may-1998 and feb-2004. Since mars-2004 a real time dose planning system "SWIFT"(Nucletron B.V.) is used for ultra sound guided 3D conformal brachytherapy for our prostate treatments. To the present time, 90 patients have been treated with the system.
In the brachytherapy treatment, the needles can diverge from the preplanned positions and this will cause some uncertainness in the dose distribution. For the old method this was not fully corrected for.
The aim of this study was to evaluate the influence of the needle divergence between the old method, the pre planned dose distribution and the new real time dose planning. As a measure, we used the DVH (dose volume histogram) data.
Materials/Methods: The real time dose planning system, SWIFT, for brachytherapy of prostate cancer was used. This system gives us the possibility to make ultra sound guided corrections of the needle configuration and displacement in real time. The needles are placed accordingly to a preplan and we can then acquire US images and perform longitudinal and transversal corrections of the needles in relation to the target.
To simulate the old technique we used a pre planned dose distribution, in the real time dose planning system, based on the same (+/- 1,5 %) DVH data as for the live plan given to the patient. This dose distribution, dwelltimes/dwell weights, was then transferred into the live plan needle positions. This will give us a dose distribution without corrections for eventually transversal displacement. This was done for 40 patient treatments. We also determined the actual displacement of the needle tip or the first dwell position for the needles in the 40 treatments.
Results: The mean DVH data for the target with and without corrections was for D90: 111% and 103% and for V100: 99% and 92% respectively. For urethra and rectum the numbers are D10: 113% and 108% and D10: 73% and 73% respectively.
The determined lateral displacement of the first dwell positions in the live plan compared to the pre planned position was found to be 2,4 mm.
Discussion: Considering the dose distribution we found that it was the inner part of the prostate volume that received a somewhat lower dose using the old approach with no needle displacement correction. This explains why urethra received a lower dose. However, we also noted that two patients received high dose values (D10>125%) with the old technique. For the prostate, 20% of the treatments with the old technique resulted in a D90 which was less than 15% of the prescribe dose.
Conclusion: With the real time dose planning system corrections for needle divergence can be performed. We consider it to be important to use this kind of real time dose planning tool to be able to make individual dose plans more accurate.

611 poster

COMPARISON OF LOCAL CONTROL, SURVIVAL, AND LATE MORBIDITY BETWEEN CONTINUOUS LOW-DOSE-RATE BRACHYTHERAPY AND PULSED-DOSE-RATE BRACHYTHERAPY IN CERVICAL CANCER PATIENTS.

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Purpose/Objectif: To compare outcome in terms of local control, survival, and late morbidity between two groups of cervical cancer patients who received continuous low-dose-rate brachytherapy (LDR) or pulsed-dose-rate brachytherapy (PDR).
Materials/Methods: In 1996 our manually loaded intracavitary 137-Cs tube and box equipment for cervical cancer was replaced with 192-Ir remote afterloading PDR. A review of all patients treated between February 1994 and March 2000 was performed. The study endpoints were local control rate, overall- and disease-free survival rates and late morbidity. All patients were treated as part of a protocol (NOCECA) with radiotherapy without concomitant chemotherapy. For tumours £ 8 cm, the pelvis (CTV-E) was treated with 45Gy/25fx while the tumour and uterus (CTV-T) was treated with 50Gy/25fx. Brachytherapy (BT) was given after 10, 20, and 25 fractions of EBRT each time delivering 10Gy (dose rate 1Gy/h) to point-A. For tumours > 8 cm, CTV-E was given 45Gy/25fx and CTV-T 60Gy/30fx. BT was given after 15 and 25 fractions of EBRT each time delivering 10Gy (dose rate 1 Gy/h) to point-A. Outcome and morbidity (RTOG) was prospectively recorded.
Results: A total of 90 patients were given EBRT and BT. Forty patients (44%) and 50 patients (56%) were treated with LDR and PDR, respectively. The equivalent dose in 2 Gy fractions (EQ2) delivered to the CTV-T was the same in each period. In all patients, median follow-up was 4.08 (0.36- 6.95) years. In the LDR and PDR group median follow-up was 4.44 (0.36-6.95) years and 3.69 (0.61-5.46) years, respectively. The group of patients treated with PDR had significant larger tumour sizes (P-value 0.03) and lower hemoglobine (P-value 0.03), while other patient and treatment characteristics were equally distributed between the two groups. The 5-year local control rate, disease-free survival rate, and overall survival rate was 82%, 63%, and 62% for the LDR group and 75%, 49%, and 46% for the PDR group. These differences were not statistically significant. Moreover, no significant difference in late actuarial bladder, bowel and vaginal toxicity was found between the two groups.
Conclusions: Treatment outcome for LDR was equivalent to PDR. Considering the advantages of PDR in terms of dose optimisation and patient friendliness the present data support the use of PDR in the treatment of cervical cancer.

612 poster

CONJUCTIVAL CARCINOMA TREATED BY BRACHYTHERAPY WITH 90SR/90Y

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Purpose/Objectif: Conjuctival carcinomas are rare and there is no uniform method of their treatment. After local excision various therapeutic procedures could be performed, such as brachytherapy, cryotherapy and external beam irradiation.

Materials/Methods: We treated 7 patients with squamous cell carcinoma of the conjuctiva. There were 6 man and one woman with mean age 75 years (range from 70 to 85 years). One male patient was treated 5 years before because of the breast carcinoma. He was treated by mastectomy, postoperative irradiation and chemotherapy and was NED at the appearance of conjuctival carcinoma.

All patients were operated upon. Histopathological examination confirmed invasive squamous cell carcinoma with minimal residual tumor (R1) in 4 pts and macroscopic residual tumor (R2) in two pts. In one patient only biopsy was done because of extensive carcinoma of the bulbar conjuctiva and conjuctiva of eyelids.

All pts were irradiated postoperatively by ophthalmic applicator 90 Sr/90 Y. Dose at the surface was 60 Gy, given in 4 fractions for R2 tumors and for R1 tumors 40 Gy also in four fractions. In patient with extensive tumor, brachitherapy was combined with ortovoltage X-ray therapy for tumor of the eyelids with shielding of the bulbar conjuctiva treated by ophthalmic applicator. The dose to the lid conjuctiva was 70 Gy.

Results: There were no local reccurences or distant metastases with minimum follow-up for at least 1 year for all pts. (range from 1 to 4 years).

Conclusions: Brachitherapy with 90Sr/90Y ophthalmic applicator is effective treatment modality in management of conjuctival carcinomas. Photograps of the tumors before and after brachytherapy will be presented.

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CONSERVATIVE TREATMENT OF CHOROIDAL MELANOMA WITH 125-IODINE BRACHYTHERAPY

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Purpose/Objectif: To evaluated the results of 125-I plaque brachytherapy in our institution and identify prognostic factors associated with local control (LC), free metastatic survival (FMS) , overall survival (OS) and evaluated visual acuity (VA) postreatment for ocular melanoma (OM) 125-I.

Materials/Methods: From March 2001 to October 2004, 79 patients underwent 125-I episcleral plaque (Collaborative Ocular Melanoma Study [COMS] design) for the treatment of choroidal melanoma. The median tumor height was 5 mm (range 5- 11 mm). Doses and dose rates at the tumor apex, base, and sclera were calculated. Visual acuity was scored with Snellen eye chart and a visual acuity of 20/200 as used as cut off point. Patient age and the presence of hypertension (HAS), diabetes (MD) or smoking(S) tobacco were noted.

Results: With a median follow-up of 28 months, the 4-year actuarial OS and LC rate were 94.6% and 81%, respectively. The median time to visual loss after therapy was 18.7 months. The 4-year actuarial rate of visual preservation better than 20/200 was 44%. Dose rates to the tumor apex smaller than 90 Gy, age older than 60 years, tumor diameter more than 9.6 mm and height tumor more than 5mm were associated with reduced LC. Patients older than 60 years were associated reduced OS.

Conclusions: Patients in our series experienced excellent OS, FMS and satisfactory LC, but with a measurable incidence of visual decline. Age, tumor height, tumor diameter and dose at tumor apex were independent prognostic factors associated with LC.

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CONTEMPORARY RADICAL TREATMENT FOR PROSTATE CANCER USING BRACHYTHERAPY OR EXTRAPERITONEAL LAPAROSCOPIC RADICAL PROSTATECTOMY: 18 MONTH OUTCOMES INCLUDING URINARY FUNCTION, INCONTINENCE AND ERECTILE DYSFUNCTION

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Purpose/Objectif: The reported biochemical outcomes of brachytherapy and radical prostatectomy from contemporary studies seem similar within the first 5-10 years post therapy. Symptomatic ptient reported outcomes have rarely been reported from contemporary, prospective, longitudinal studies using validated questionnaires, particularly when radical prostatectomy has been performed using the laparoscopic route. Erectile Dysfunction (ED), urinary problems (UP) and urinary incontinence aid bother (UIAB) from brachytherapy (BXT) and laparoscopic radical prostatectomy (LRP) are reported from UK centers (2 performing LRP & 1 BXT centre).

Materials/Methods: EORTC-PR25 and IIEF-5 questionnaires were completed before treatment (BXT n=189, LRP n=101) and at 3/6/12/18months. LRP Nerve-Sparing was Bilateral (BNS)-35%, Unilateral (UNS)-12% and not-attempted (NNS)-53%. Potency was defined as IIEF-5>11.

Results: BXT potency preservation (PP) was: 53% at 12m and 58% at 18m. Changes of 'Moderate' clinical significance in the UP domain occurred up to 6m with changes of 'a little' significance thereafter. No significant changes in UIAB score occurred.

Overall PP was 30% at 12 and 18m for all LRP patients, but 67% at 12m and 43% at 18m after bilateral nerve-sparing LRP. No significant change in the UP domain occurred following LRP. Clinically significant deterioration in UIAB of at least 'moderate' intensity occurred at every follow-up; similar changes occurred at 3 and 6m in the BNS group (no patients who reported UIAB problems in the BNS group had 12 or 18m data yet).

Conclusions: Both treatments significantly adversely affect potency rates. Incontinence is a 'moderate' problem after LRP and these changes persist up to 18m. 'Moderate' changes in the urinary problem domain after brachytherapy improve to 'a little' clinical significance after 6m.

	Potency For Patients Potent Preop (IIEF>11)		EORTC PR25 Urinary Problems (UP) Mean (SD)				EORTC PR25 UIAB Mean (SD)			
	12m FU	18m FU	Pre	3m	12m	18m	Pre	3m	12m	18m
All LRP	30% (n=20)	30% (n=10)	8.3 (19.3)	6.8 (13.4)	4.9 (13.1)	6.6 (12.3)	5.6 (19.2)	27.6 (30.6)	21.4 (21.1)	19.1 (26.2)
BNS LRP	67% (n=9)	43% (n=7)	7.4 (21.4)	5.1 (9.2)	4.0 (11.4)	3.0 (6.7)	13.3 (29.8)	20.5 (21.6)	0	0
All BXT	53% (n=28)	58% (n=19)	8.1 (9.6)	23.9 (16.5)	15.9 (13.2)	15.9 (14.7)	0	0.8 (6.4)	0.4 (3.5)	0

615 poster

CONVENTIONAL SOURCE DWELLING UP TO THE UTERINE FUNDUS MAY NOT BE MANDATORY IN INTRACAVITARY RADIOTHERAPY FOR CERVICAL CANCER

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Purpose/Objectif: It is essential to identify target volume clearly in modern radiotherapy (RT). Intracavitary radiotherapy (ICRT) for cervical cancer, however, has conventionally been applied regarding the entire uterus as target volume because tumor extension up to the corpus is normally not estimable by the gold standard of physical examination. We investigated whether conventional tandem-source dwelling up to the uterine fundus is still mandatory today when tumor extension is estimable by magnetic resonance (MR) imaging.

Materials/Methods: This retrospective study consisted of 95 patients with stage IB1-IVB cervical squamous cell carcinoma treated by high-dose-rate ICRT (3-6 insertions per patient) after pelvic external RT with central doses ranging from 12.0 to 50.0 Gy (median, 30.6 Gy) with or without chemotherapy betwe en 1993 and 2003. Reduction of source-dwell length at the uterine corpus was applied optionally to 46 of 105 patients treated before April 2001 and routinely to 49 to 50 patients treated thereafter. Target volume was assessed by MR images obtained before traetment and immediately before or during ICRT. A tandem applicator was inserted to reach the uterine fundus after sounding the uterine cavity. Source-dwell length was carefully tailored referring to the MR-assessed target volume so that the target volume is sufficiently encompassed by the reference dose envelope (6.0 Gy). Acceptability of reduction of source-dwell length was analyzed in terms of pelvic failure at the uterine corpus.

Results: Reduction of source-dwell length was put into practice in 248 of 368 total insertions and in all individual insertions for 38 patients. The reduced length ranged between 5 and 50 mm. Pelvic failure was identified in 21 patients between 3.7 and 25.0 months after the treatment, and there was no evidence of pelvic failure in the remaining 74 patients with the follow-up period between 1.2 and 128 months. In none of these 21 patients, failure was identified at the uterine corpus by MR imaging at the time of pelvic failure.

Conclusions: Our clinical practice of ICRT performed after external RT, which could have contributed to eradicate subclinical disease in the corpus, suggested that reduction of source-dwell length in accordance with MR-assessed target volume is acceptable from the standpoint of local disease control.

616 poster

DOSE VOLUME HISTOGRAM ANALYSIS OF NORMAL STRUCTURES ASSOCIATED WITH ACCELERATED INTRACAVITARY PARTIAL BREAST IRRADIATION DELIVERED BY HIGH DOSE RATE BRACHYTHERAPY

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Purpose/Objectif: To assess the radiation dose delivered to the heart and ipsilateral lung during delivery of accelerated intracavitary partial breast brachytherapy using a MammoSite™ applicator.

Materials/Methods: In the context of an institutional review board approved feasibility study, dosimetric analysis was conducted on patients receiving accelerated intracavitary partial breast irradiation using the MammoSite™ applicator following wide local excision and negative sentinel lymph node biopsy for T1 ductal breast carcinoma. Dose to the heart was evaluated for all patients with left breast tumors who had a CT scan encompassing the entire heart. Dose to the lung was evaluated for all patients for whom the entire lung was scanned. Structures of interest were contoured. The treatments were planned using 7 to 9 dwell positions with 5mm spacing. The dwell times were chosen so that the prescription dose of 3400cGy was 1cm from the surface of the MammoSite™ balloon.

A number of dose parameters, such as the volume of the structure receiving 10Gy or more (V10) and the dose received by 20 cc of the structure (D20), were calculated as well as the maximum and mean doses received.

Results: Fifteen patients were in the study. Five had complete CT data for the lungs, ipsilateral lung volumes ranged from 925 to 1380 cc. The median lung D_{mean} was 4.7 Gy [range 2.1-5.6 Gy] and the median lung D_{max} was 37.5 Gy [range 6.3-45.7 Gy]. The median V20 as a percentage of the lung volume was 0.9% [range 0-2.5%] while the median lung V10 was 7.3% [range 0-13.3%]. Six patients had complete heart data for left breast treatment, cardiac volumes ranged from 337 to 551 cc. The median cardiac D_{mean} was 3.7 Gy [range 3.1-4.8 Gy] and the median cardiac Dmax was 15 Gy [range 10.6-27.2 Gy]. The V20 for the heart was zero for all but one patient while the V10 was 0.01%. The median cardiac D20 was 7.9 Gy [range 6.4-11.9 Gy].

Conclusions: This small subset study gives low values for V10 and V20 for both heart and lung. In all cases less than 25% of the ipsilateral lung received less than 20 Gy. Though not directly comparable to external beam dose parameters, it appears that the dose to ipsilateral breast and heart do not give any indication against partial breast irradiation based on high dose rate brachytherapy.

617 poster

DOSIMETRIC COMPARISON OF ORTHOGONAL X-RAY AND CT BASED MULTI-CATHETER INTERSTITIAL INTRAOPERATIVE IMPLANT FOR ACCELERATED PARTIAL BREAST IRRADIATION (APBI) USING DOSE VOLUME INDICES.

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Purpose/Objectif: CT based dosimetry provides a clinically realistic evaluation of interstitial implant as compared to traditional orthogonal radiograph technique. In this study dosimetric outcome of X-ray and CT based planning of multi-catheter intestinal implant used for APBI were compared using different dose volume indices. The potential of interactive isodose optimization algorithm was tested for improved tumor coverage

Materials/Methods: Intra-operative placement of flexible nylon tubes were performed on ten consecutive patients of early stage breast cancer using the Paris system. For each patient an enface radiograph and axial CT images were taken and dosimetry was carried out on Plato Sunrise TPS. Lumpectomy cavity, CTV and ipsilateral breast were delineated on axial CT images following RTOG 0413 guideline. Catheter reconstruction was done on CT images. For each patient three plans were generated using active loading length measured from a) the X-ray [P1] and b) based on the CTV [P2]. In both P1 and P2 geometrical optimization was done on volume. The reference prescription isodose of P2 was subsequently optimized interactively using graphical optimization tool and this yielded the plan P3. Dosimetric outcome were evaluated qualitatively and quantitatively using the dose volume indices which include coverage index (CI), external volume index (EI), relative dose homogeneity index (DHI), overdose volume index (OI) and conformal index (COIN)

Results: The median volume of lumpectomy cavity was 66.3 cc (range 39.4 to 87.6 cc), while the volume of CTV ranged from 98.2 to 179 cc (median 138 cc). The median (SD) CI of lumpectomy cavity

estimated from P1, P2 and P3 was 0.85 (0.06), 0.88 (0.08) and 0.97 (0.04) respectively. The corresponding value for CTV was 0.69 (0.11), 0.73 (0.11) and 0.91 (0.05). The 33% (w.r.t P1) and 25% (w.r.t.P2) increase in the median CI of CTV observed in graphically optimized plan (P3) lead to decrease in DHI from 0.84 to 0.77. In all patients V_{150} and V_{200} was lesser than 60 cc and 19 cc respectively; highest being observed in P3. Highest median OI of 0.1 (SD 0.02) was observed in P3 as compared to 0.04 of P1 and P2. EI was highest in P1 (median 0.24) as compared to 0.14 of P2 and 0.18 of P3. Significant improvement of COIN (median 0.75, SD 0.02) was observed in P3 over 0.47 and 0.61 of P1 and P2 respectively.

Conclusions: Dosimetry based on the active length measured from X-ray provides excessive irradiation of normal breast. Interactive graphical optimization allows the shaping of prescription isodose to the shape of target at the cost of high dose volume and dose inhomogeneity. Use of dose volume indices allow quantitative evaluation of different plans and can be use as a tool to correlate dosimetry with clinical outcome.

618 poster

DOSIMETRIC EVALUATION OF INTERSTITIAL HIGH-DOSE-RATE IMPLANTS FOR LOCALISED PROSTATE CANCER

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Purpose/Objectif: We use transrectal ultrasound-guided interstitial prostate brachytherapy as a boost treatment in combination with teletherapy to patients with localised intermediate- or high-risk prostate cancer. Dose distributions of the implants performed with a high-dose-rate Ir-192 source were evaluated.

Materials/Methods: Treatment plans of 134 implants for 126 patient were evaluated using dose-volume histograms. Geometrical optimization was applied, and 10 Gy dose was prescribed to surface of the prostate. The tolerance dose to urethra and rectum was 125% and 80%. Graphical optimization was used when the dose coverage needed improvements. The volume of the prostate was measured, and its fraction receiving 90%, 100%, 150% and 200% of the prescribed dose was calculated (V90, V100, V150, V200). The dose delivered to 90% of the prostate volume (D90), the minimum dose in the prostate (Dmin), maximal dose to rectum (D_r) and urethra (D_u) reference points, dose to volume of 2cm^3 of the rectum (D_2) and 0,1cm^3 and 1% of the urethra ($D_{0,1}$, D1) were determined. Correlation analysis was performed between point and volume doses. The dose non-uniformity ratio (DNR) and the dose homogeneity index (DHI) were calculated to quantify the dose homogeneity. The coverage index (CI) was determined, and the dose conformality to the target volume was assessed with the use of the conformal index (COIN). In most patients in-vivo dose measurement was performed in the rectum with semiconductor detectors.

Results: The median number of needles was 16 (range: 7-23), the mean prostate volume was 24.6cm^3 (6-65,4cm^3). The mean V90, V100, V150 and V200 were 98%, 94%, 43% and 15%, respectively. The mean D90 was 106% (71-118%), and the Dmin was 81% (44-96%). The mean dose to rectum and urethra reference points was 74% (37-116%) and 121% (83-134%), respectively. The mean volume doses were D_2=47% (23-77%) for the rectum, $D_{0,1}$=129% (86-147%) and D1=145% (93-253%) for the urethra. The correlation coefficients were: R(D_r,D_2)=0,69, R(D_u,$D_{0,1}$)=0,55, R(D_u,D1)=0,23. The mean DNR was 0.40 (0.22-0.58), while the DHI was 0.54 (0.27-0.81). On average, 94% of the target volume received at least the prescribed dose, CI=0.94 (0.68-0.98), and the mean COIN was 0.64 (0.42-0.82). The mean maximal measured dose in the rectum was 2.7Gy (0.3-6Gy).

Conclusions: The treatment plans based on the real positions of catheters provided acceptable dose distributions. In the majority of our cases the dose to urethra and rectum was kept below our tolerance level. The dose to rectum can be estimated correctly by the reference point dose but for urethra dose determination the D1 volumetric parameter is recommended to use. To find correlations between dose-volume parameters and side effects requires further analysis.

619 poster

DOSIMETRIC VERIFICATION OF THE DOSE DISTRIBUTION IN PULSED DOSE RATE BRACHYTHERAPY

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Purpose/Objectif: The aim of this study was the dosimetric verification (in-phantom) of doses calculated with the Plato treatment planning system (TPS) by using the GafChromic films and thermoluminescent detectors (TL) in PDR brachytherapy.

Materials/Methods: Absorbed doses in chosen points were measured with the TL detectors; while dose distributions were measured with GafChromic films. Dose measurements were made in 14 reference points in a specially designed, tissue equivalent phantom. All 14 TL-detectors were placed in the selected dosimetric points and GafChromic film was placed between the two pieces of phantom. The treatment plan was calculated using Plato TPS. Integrated Brachytherapy Unit was used to verify the applicator and detectors positions. On the basis of received images the treatment plan was made. The prescribed doses were compared with the measured doses. The fusion of images with dose distributions was made. The Image read from the dosimetric films after its digitalization was fused to the one received from TPS. The qualitative analysis of this fusion was performed.

Results: Wilcoxon Test and Sign Test (dependent samples) were used to compare the doses calculated with those measured with TL detectors. Calculated p-value was analyzed at confidence level α = 0.05. The statistical comparison of doses calculated and measured revealed the insignificant differences, between the range of -14.7% and 12.6%. These results fitted well to results of qualitative analysis made using images' fusion made for calculated and measured dose distributions.

Conclusions: Both quantitative and qualitative analysis proved correctness of the calculation algorithms used by Plato planning system in a phantom study for PDR brachytherapy.

620 poster

DYNAMIC DOSIMETRY IN PROSTATE BRACHYTHERAPY IMPROVES POSTPLAN DOSIMETRY, LOWERS THE NUMBER OF SEEDS REQUIRED PER PROSTATE VOLUME AND AT THE SAME TIME SIGNIFICANTLY REDUCES TOXICITY

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Purpose/Objectif: After more than 500 implants we introduced dynamic dosimetry to our prostate brachytherapy pogram in 2003. Dynamic dosimetry enables us to constantly control the dosimetry of the implant after every single needle implanted and react to any misplacement of the seeds in changing the plan for the remaining seeds.

Materials/Methods: We compared 3 groups of patients: the first group was being treated at the beginning of our prostate program

(1999) the second group 2001 and the third group after introducing dynamic dosimetry 2003. The number of seeds needed per cm^3 were compared. Furthermore postplan dosimetry data esp. D90, V100, V200, D10 were evaluated for all 3 groups. For groups 2 and 3 long term toxicity data (10-21 mths) could be acquired and compared.
Results: Seeds needed per cm^3 could be reduced from 1.5 seeds to 1.4 and 1.3. For an average prostate of 35 grms a reduction of 7 seeds could be achieved. At the same time the average coverage of the prostate with the prescription isodose (V100) was increased from 89% to 94% and 96 %. High activity regions within the prostate were reduced from 450 Gy to 430 Gy and 400 Gy (D10) as well as 35%, 33% and 30% (V200) respectively. Nycturia > 3 times per night was reduced from 22% to 6% (p=0,01), obstructive symptoms from 15% to 9% (p=0,03) and erectile dysfunction from 15% to 9% (p=0,01).
Conclusions: Using dynamic dosimetry two main issues of quality control in prostate seed brachytherapy could be addressed even in a centre with experience of more than 500 implants. Less seeds were needed to achieve better postplan parameters such as V100 and D90. High dose regions could be limited. This was not only more cost effective using less seeds but also proofed to be advantageous in significantly reducing side effects. We believe that our results clearly show that dynamic dosimetry should become the standard planning method for safe and effective seed implants.

621 poster

ESTIMATION OF THE OPTIMAL EXPOSURE TO URETHRA IN CT-GUIDED BRACHYTHERAPY OF PROSTATE CANCER

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Purpose/Objectif: Together with rectum and urinary bladder urethra is treated as one of the critical organs in the computed tomography (CT) -guided brachytherapy for prostate cancer with micro-sources iodine-125 (^{125}I). Proper treatment planning of radiotherapy taking into account optimal radiation exposure to urethra plays significant role both in terms of radiotherapy results and patients' life quality.
Purpose research was as follows:
- to analyze of radiation exposure to urethra while performing CT-guided brachytherapy for prostate cancer;
- to estimate optimal exposure to urethra which involves the dual problem. The coverage of the prostate should not be less than 95% of target dose and that coverage should not hit of patients' life quality.

Materials/Methods: Data on 48 patients with localized prostate cancer were included in this study. During 2004-2006 they were treated with CT-guided interstitial brachytherapy using micro-sources ^{125}I in the Center of Brachytherapy for prostate cancer of Medical Radiological Research Centre of RAMS, Obninsk. Bar graphs exposure-volume were analyzed to make conclusion on absorbed dose load to urethra region. Qualitative showings on influence of radiation exposure to urethra region and grade of developed urinary symptoms were estimated. For this purpose patients were interviewed to find out their quality of living.
Results: It was found out radiation exposure to urethra region more than 165% of treatment dose for prostate (145 Gy = 100%) of usual treatment dose causes deterioration of patients' quality of live. They revealed dysuria, nycturia and increasing in frequency of urination. They become most obviously in the critical period which lasts first 4 weeks after the treatment. From the other hand the exposure less than 145% of the target dose (145 Gy) decreases target coverage which is limited with the 100% isodose.
Conclusions: Optimal dose to urethra region was determined during the research. It lays in the range from 145 to 165% of treatment dose for prostate (145 Gy). At the same time 100% dose coverage keeps to be not less than 95% of the target volume and patients' quality of life is not hit.

622 poster

ESTIMATION OF BRACHYTHERAPY DOSE-VOLUME PARAMETERS FROM PROJECTION IMAGES

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Purpose/Objectif: When treating gynaecological cancer patients with brachytherapy using a vaginal cylinder, we verify the correct fitting of the applicator within the vagina using a contrast agent. Imaging is performed on the treatment simulator, since demarcation of the region with contrast is clearer on the simulator than on CT. Two mutual orthogonal radiographs show possible existence of voids between cylinder and vaginal mucosa. Such voids result in a displacement of the vaginal wall from the cylinder, hence leading to underdosage (Huizenga, ESTRO 2006). Studying the influence of these voids on dosimetric aspects of the treatment requires a quantitative analysis in terms of dose-volume parameters, i.e., the volume of the target that is underdosed when a void is present. The aim of the present work is to obtain a method for estimating the volume receiving a specific dose.
Materials/Methods: The volume is estimated by summation of surface area estimates of cross-sections perpendicular to the common axis of the simulator radiographs. The estimation of these surface areas assumes the cross-sections are rectangular, with dimensions obtained from the projection images. The accuracy of this approach depends on the shape of the volume. It will give an overestimation of the true volume value, which is partially compensated by assuming ellipsoidal shapes.
Estimation of volumes receiving a dose less than a specified value is performed by excluding volume elements that project within a cylinder on both images. This cylinder contains the area where the dose is higher than the specified value.
Results: The method was validated using three different phantoms created from dental wax, wrapped around a vaginal cylinder with a diameter of 30 mm. Seven sets of two mutual orthogonal images were taken, at a range of gantry angles, digitized and processed with in-house written software (Matlab, The Mathworks). The estimated volumes were compared with actual wax volumes, and an agreement of 97% ± 3% was obtained.
Conclusions:
Our estimation algorithm of a volume from two projection images can at best be approximate. The method is extended to account for exclusion of cylindrical structures, thereby producing dose-volume parameter values. These are of clinical relevance for the study of the influence of voids between applicator and vaginal wall.

623 poster

ESTIMATION OF DOSE RECEIVED BY BLOOD VOLUME DURING THE INTRAVASCULAR BRACHYTHERAPY WITH AN USE OF 32P SOURCE

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Purpose/Objectif: Restenosis of coronary vessels is a frequent (around 50%) complication of angioplasty. Intravascular brachy-

therapy reduces this risk to 10%. Steep dose gradient of brachytherapy protects nearby organs. However, the blood flowing through the vessel is not being protected at all. There are few data on doses received by blood volume during this procedure. The aim of this study was to estimate a dose received by blood during intravascular brachytherapy using 2 different methods.

Materials/Methods: Seventeen patients treated with intracoronary brachytherapy for restenosis after angioplasty were evaluated. For irradiation sealed beta emitting phosphorus 32 - ^{32}P source was used. The dosimetric data (activity, radiation characteristics, diameter of angioplastic baloons) delivered by the manufacturer together with the radiation source ^{32}P (and home verified) were used. All patients received 20 Gy normalized 1 mm from the inner vascular wall. Data on vessel diameter, length treated (2 cm for all), exposition time, and speed of blood flow were taken into account for each patient. Two evaluating models were applied: in the first the geometry of the set-up was assumed as perfectly symmetrical (2-D method), the second approximated the set-up and calculated dose using voxels (3-D method).

Results: The mean doses received by blood volume ranged from 0.06 Gy to 5.41 Gy (average: 1.33 Gy), as estimated by 2-D method. For the 3-D method the mean doses for blood volume ranged from 0.06 Gy to 5.43 Gy (average: 1.36 Gy). No statistically significant difference in estimation of dose received by blood was seen for both methods applied.

Conclusions: Both methods applied for estimation of dose received give similar results. The highest estimated values of blood doses shown in the study suggest that in particular situations a dose for blood should be considered. It is a little known about its clinical relevance e.g. as a possible cause of lymphocytes depletion.

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EVALUATION OF DOSE DISTRIBUTION PARAMETERS IN HDR PROSTATE BRACHYTHERAPY- INFLUENCE OF DOSE DISTRIBUTION OPTIMIZATION ALGORITHMS

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Purpose/Objectif: The optimal prostate irradiation plan assumes a delivery of a prescribed dose to a prostate gland and maximal protection of organs at risk (urethra, rectum). The latter one is especially important in patients treated with external beam irradiation combined with brachytherapy. The aim of this paper is to compare selected dose distribution parameters of non-optimized and geometrically optimized prostate implants.

Materials/Methods: Ultrasound guided brachytherapy implants based on HDR stepping source were added as a boost for external beam irradiation. 215 prostate patients were treated between January 2001 and January 2005. We evaluated dose distribution parameters of 86 prostate implants performed for 56 consecutive patients. The mean number of needles in implant was 11.7 needles, the mean active length in implant was 2cm. For all implants two dose distribution plans were analyzed - non optimized plan (dwell times equal in all dwell positions) and geometrically optimized plan ("on volume" optimization algorithm). All patients were treated with optimized dose distribution plans.

PLATO (Nucletron) planning system was applied. Following dose distribution parameters were analyzed: reference volume V_{100} (volume inside 100% isodose), overdose volume V_{200}, overdose volume V_{150}, quality index (QI), uniformity index (UI), planned dose at urethra reference point and rectum wall reference point.

Results: Overdose volumes V_{150} and V_{200} were statistically significantly higher in non optimized implants versus geometrically optimized implants. V_{150} was 11% higher (16.2±7.5 cm^3 for non optimized and 14.5±6.2 cm^3 for optimized implants); V_{200} was 22% higher (6.1±2.9 cm^3 for non optimized and 4.8±1.7 cm^3 for optimized implants). The planned dose at urethra reference point and rectum wall reference point was respectively 7% and 6% higher in non optimized implants versus optimized implants. The mean of QI was 1.6±0.2 for optimized plans and 1.5±0.1 for non optimized plans.

Conclusions: The study demonstrates a beneficial impact of geometrical optimization on the analyzed dose distribution parameters. The effect of lowering the dose in the urethra and rectum is strong argument to use optimization algorithms in interstitial prostate implants.

625 poster

EXCELLENT LOCAL CONTROL BY HDR-BRACHYTHERAPY OF THE VAGINAL VAULT WITH THREE FRACTIONS OF 5-6.7GY IN 5MM DEPTHS IN POSTOPERATIVE EARLY STAGE ENDOMETRIAL CARCINOMA

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Purpose/Objectif: In endometrial carcinoma the optimal dosage and fractionation scheme for postoperative brachytherapy to the vaginal vault is still under debate. Therefore we analysed our institutional data from treatments with low total doses regarding the spectrum found in the literature.

Materials/Methods: From 1990 until 2002 142 patients with endometrial carcinoma underwent post-operative vaginal vault HDR-brachytherapy with Iridium-192 in curative intent as sole adjuvant treatment after hysterectomy +/- lymphonodectomy. For follow-up patients were contacted, interviewed on the phone and invited for re-examination along with thorough exploration of all available data from referring clinics, physicians, relatives and the tumor register Munich.

Results: Hospital charts and follow-up data were available in 139 patients (98%) who form the basis of the following evaluation. Median age at diagnosis was 64.7 yrs, range 37.2 - 88.8 yrs. Histopathological data was re-classified according to the 6th edition of TNM 2004, leading to 6 pts. with T1a (4%), 66 T1b (47.5%), 44 T1c (32%), 17 T2a-b (12%), 4 T3a (3%) and 2Tx. 1 patient presented with pelvic nodal involvement, all others were cN0 (44%) or pN0 (55%). Grading was G2 in 62% and classical endometrioid adenocarcinoma found in 84% of histologies. Institutional`s protocol for vaginal brachytherapy changed in 1998 from former 3x10Gy prescribed to the surface of the vaginal cylinder [94 of 97 pts.] to latter 3x5Gy at 5mm tissue depths [41 of 42 pts.] for the upper two thirds of the vaginal length, preferably in weekly fractions (range of total treatment time 6-21 days).After a median follow-up of 7.7yrs (8.9yrs for survivors, range 3.1-15.4yrs) 5- and 10yr-overall survival was 87% and 68%, with a disease-specific survival of 96% and 93%, respectively. Of 42 patients deceased, 8 were known to be endometrial cancer-related, 12 cardiovascular, 10 second primary, 7 others and 5 unknown. 10 patients had a recurrence of any sort, 7 with distant spread. Altogether 2 vaginal (including the pN1 patient) and 4 regional recurrences in the pelvis occurred. 10yr-actuarial local control was 98%, regional control 97% and metastasis-free survival 94%. De-escalation of

brachytherapy dosage did not lead to increase of recurrences. Treatment was well tolerated : apart from one GI-fistula not clearly related to radiotherapy, no other late toxicity > grade 2° RTOG was reported (toxicity data on 81 pts.).
Conclusions: In endometrial carcinoma postoperative vaginal brachytherapy with 3 x 5Gy in 5mm tissue depths can be recommended as it serves the ALARA principle with an excellent therapeutic ratio.

626 poster

FLATTERING FILTER DESIGN FOR HDR SURFACE APPLICATORS

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Purpose/Objectif: Small superficial malignancies are usually treated with megavoltage electron beams on linacs. An alternative treatment of these lesions is the use of Leipzig applicators as accessories to the microSelectron-HDR system. These cup-shaped applicators limit irradiation to the required area using tungsten-alloy shielding. One practical problem with these applicators is that the resulting isodoses are too rounded on depth, increasing dose heterogeneity laterally. The purpose of this work is to design a filter with the use of the Monte Carlo method, located at the end of the applicator, to equalize the dose laterally.
Materials/Methods: Monte Carlo GEANT4 code (version 4.7.0) has been used to obtain the dose-rate distributions in liquid water. The absorbed dose is approximated by kerma using the linear track-length kerma estimator evaluated in a 20x20 cm cylindrical water phantom scoring in 0.5x0.5 mm cylindrical voxels. Enough histories were simulated to obtain statistical uncertainties <1% (k=1). The Leipzig applicator geometry has been implemented according to manufacturer information. Dose distributions of the Leipzig applicators in liquid water have been obtained in a previous work (IJRBOP 62, 579-584, 2005) with an experimentally validated Monte Carlo code following the TG-43 U1 recommendations. The most important component to the dose rate distribution near of the Leipzig applicators is the primary dose. In order to obtain the required filter thickness, the primary dose component delivered by the Leipzig applicators without filter has been obtained. Assuming an exponential attenuation of the primary dose contribution due to the filter, exp(-mu*x) being mu the effective attenuation coefficient of the filter material and x the required filter thickness, the filter thickness in a first approximation has been obtained. A Monte Carlo simulation with the Leipzig applicator with filter has been done obtaining flatter isodoses. This new dose distribution is improved analytically again by using the factor exp(-mu*x) to calculate a second order correction to the filter thickness. This procedure has been repeated two times to improve the flattering of the isodose curves. Radiochromic film measurements have been performed over the final applicator plus filter to verify the Monte Carlo method and the manufacturing process.
Results: Monte Carlo GEANT4 and radiochromic results agree within their uncertainties. The filter has been designed for H-type and V-type 2 and 3 cm applicators. The average transmission resulting factor of the tungsten filter is about 40-50% in the central axis of the applicator.
Conclusions: With the added filter the dosimetric properties of the applicators have been improved, equalizing the dose laterally and obtaining flatter isodoses for all clinically useful depths. These developed filters have been integrated on the applicator with the name of applicators.

627 poster

HDR BRACHYTHERAPY FOR INOPERABLE ENDOMETRIAL CARCINOMA. COMPARISON OF TWO OPTIMIZATION TECHNIQUES.

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Purpose/Objectif: Purpose of this study is comparison of two optimization techniques for HDR brachytherapy patients, with inoperable endometrial carcinoma.
Materials/Methods: Thirteen patients with inoperable endometrial carcinoma were planned for HDR brachytherapy on three dimensional treatment planning system. Dose optimization was performed on images acquired on CT scanner, using two different optimization techniques. First optimization technique was using geometrical concept (points of normalization in myometrium with predefined coordinates) and second was volume optimization, according to three-dimensional target volume (uterus).
Results: In 3 (23%) patients we have noted sub dosage of target volume using optimization technique based on geometrical concept.
Conclusions: Volume based optimization technique is superior versus point based optimization technique and it could be useful in ¼ of the patients, treated with HDR brachytherapy as definitive treatment for endometrial carcinoma.

628 poster

HDR BRACHYTHERAPY IN CARCINOMA CERVIX: RECTAL REFRACTOR OF GAUZE PACKING?

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Purpose/Objectif: Intra-cavitary brachytherapy is an integral component of any radical radiotherapy regimen for carcinoma cervix. In recent times, high dose rate (HDR) brachytherapy with its inherent advantages has largely superseded the traditional low dose rate systems. One of the physical advantages of high dose rate has been the applicability of aggressive vaginal retraction and packing, enabling significant reduction in doses to the bladder and rectum. However, evidence regarding the superiority of rectal retractors over gauze packing during HDR brachytherapy is lacking. With an aim to directly compare the efficacy of the two commonly used techniques of retraction viz. gauze packing and rectal retractors in terms of rectal and bladder doses during fractionated HDR brachytherapy for carcinoma cervix we undertook this study.
Materials/Methods: Ten patients of carcinoma of the cervix stage IIB planned for fractionated HDR brachytherapy were included in this study. For each patient, the first of the five HDR applications was performed using gauze packing or rectal retractors by random assignment. Subsequently gauze packing and rectal retractors were used alternately for the remaining four fractions. Individual dosimetry was done for each application and the rectal and bladder doses were compared using the Wilcoxon signed rank test.
Results: A total of 48 HDR brachytherapy applications were performed. The maximum as well as mean rectal doses were significantly higher in applications where rectal retractors were used in

comparison to vaginal gauze packing (p=0.001 & 0.003 respectively). The maximum and mean bladder doses were also significantly higher (p=0.002 & 0.004 respectively) with retractors. This may have been partly due to the absence of anterior gauze packing when using retractors.
Conclusions: Gauze packing was the superior technique with rectal and bladder doses being significantly lower than with a rectal retractor during fractionated HDR brachytherapy for carcinoma cervix.

629 poster

HDR BRACHYTHERAPY PROSTATE AND BILATERAL HIP REPLACEMENTS

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Purpose/Objectif: Prostate cancer patients with bilateral hip replacements who are considered for HDR Brachytherapy (HDRBT) as a boost can present a challenge. Conventional CT scanning of these patients can be difficult - signal deficit and artefacts from the prostheses can obscure the prostate, implanted marker seeds and the implanted needle tips. At SCGH since 2004, six bilateral hip replacement patients were booked for HDRBT as a boost following external beam radiotherapy. The 1st patient was implanted with flexiguides and MRI imaging enabled successful treatment. For the 2nd patient MRI imaging was unsuccessful as a result of significant image distortion near the needle tips and the treatment was abandoned. Conventional treatment planning with external beam radiotherapy presents similar challenges and hence a solution using HDRBT for the boost was considered a high priority.
Materials/Methods: An agar gel prostate phantom was constructed that could accommodate various hip prostheses and needle implant models. The phantom was used to test different hip prosthesis combinations with MRI, single slice CT and the hospital's newly installed 64-slice CT scanner. A set of marker wires was constructed from retired Varisource "dummy wires" to closely mimic the displacement of the source wire within the flexiguides. For the next four patients, planning images 0.6mm thick and reconstructed in 2mm thickness, that included the modified marker wires, were obtained using the 64-slice CT scanner. MRI images were also obtained with 3mm slice thickness. In both modalities, scans were extended to include the HDRBT needle template. In all four patients, the CT set was used for planning and the imaged wire length was compared with the measured wire length (needle tip to template face).
Results: To date four patients with bilat- hip replacements were implanted with the flexiguides and imaged with 64-slice CT, and MRI, using the modified marker wires.
With 64-slice CT, the needle tip to template lengths agreed with the majority of the measured lengths (within +/- 1mm). In the MRI images many of the needle tips were still difficult to identify. This was particularly true of the posterior needles, where identification was complicated by the presence of blood vessels, which had a similar appearance in the images. In some cases, a difference of up to 15mm in needle length was observed between the MRI images and the actual measured lengths.
Conclusions: Planning images for the bilateral hip replacement prostate HDRBT patients using MRI is problematic, primarily due to prosthesis composition and the selection of scanning sequence used to date. The images obtained with 64-slice CT, in combination with modified marker wires and implanting only flexiguide needles, gave good results in terms of accuracy and confidence when identifying needle tips and prostate markers. Both modalities will be used in further investigations.

630 poster

HIGH DOSE RATE ENDOBRONCHIAL BRACHYTHERAPY DVH EVALUATION

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Purpose/Objectif: We describe High Dose Rate (HDR) endobronchial brachytherapy (EBT), with the total dose obtained by EBT and External Beam Radiotherapy (ERT), by dose volume histograms (DVH) evaluation.
Materials/Methods:
The HDR-EBT has an importante role in the treatment of bronchial carcinoma, with palliative and curative intent of haemoptysis and endobronchial obstruction.
EBT indications are: unic treatment, boost after or concomitant to ERT, re-irradiations, concomitant to chemotherapy; to reduce the total irradiation time. The tumour localization extrabronchial or invisible by bronchoscopy is a contraindication to EBT, the histology is no longuer one. Stas/Rocha chart use before each EBT allows risk evaluation. We never had any fatal or heavy complication.
Between 1/2000 and 12/2005, 40 patients were treated by EBT. One to three bronchial catheteres in each fraction are used, with bronchoscope locally placed on bronchial main bifurcation to have the same visually reference on X-Ray. A maximum treatment total dose of 40 Gy may be delivered in fractions of 5 Gy each, at least one week apart.
After all fractions, we reconstruct the aplications with X-Ray images from Nucletron's Integrated Brachitherapy Unit (IBU), duplicating the dwell positions and times, using bronchoscope image reference. Anatomical references are aleatories. The total dose is determined at the volume of interest.
Dose volume histograms are generated and evaluated. Later we calculate the volume total dose using data from EBT and ERT DVH's, to access a more accurate result.
Conclusions: This technique allows us to check the total doses and volumes irradiated, to escalate the total tumour dose and have better oncological results without complications.

631 poster

I125 MESH IMPLANT DOSE PENETRATION ASYMMETRY IN NON-PLANAR SCENARIOS

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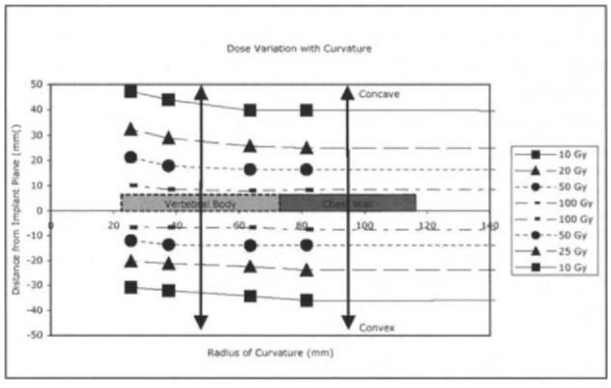
Purpose/Objectif: Conventionally dose estimates for I125 mesh implants assume a planar geometry. The implants are often placed against non-planar surfaces. This study examines the effect of curvature on dose distribution around an I125 planar implant for clinically relevant geometries.
Materials/Methods: Post-implant dosimetry CT scans of 10 patients who had undergone I125 mesh implants were analyzed to determine the mean curvature of the chest wall and vertebral body at the level of the carina. A representative planar implant (50x70 mm) was created using radio-opaque markers placed on a uniform grid of 1 cm spacing. CT scans (1 mm slice spacing) of the template on a flat surface and attached to objects of varying curvatures (25.5, 37.5, 63.5 and 81.5 mm radius) were acquired. The CT images were imported into Interplant version 2.0.4 (Burdette Medical Systems) seed localizer, the markers were located and dosimetry was performed for 0.5 mCi Oncura 6711 0.5 mCi seeds. For each curvature the distance to the 100 Gy, 50 Gy, 25 Gy and 10 Gy dose line in the center of the implant was measured on both the concave and convex side of the implant. The mean curvatures for the chest wall and vertebral body were related to the measured dose penetration.

Results: The mean radii of curvature for the chest wall and vertebral body at the level of the carina are 96mm (range [rg] 70-115mm) and 46mm (rg, 21-70mm) respectively. Isodoses on the concave side of the curvature are further in distance from the implant surface than isodoses on the convex side. (Figure1). The shaded boxes represent the range of the curvature measurements while the vertical arrows indicate the mean curvatures of the vertebral bodies and chest walls. Each curve is extrapolated to the distance of the implant for planar geometry (infinite radius of curvature).

Conclusions:

The asymmetry between the dose distribution on the concave and convex surfaces of a curvature increases with decreasing radii of curvature. These data will allow for better estimation of dose in clinical situations where the placement of the I125 mesh implant results in a curved geometry.



632 poster

IMPACT OF 3-DIMENSIONAL TREATMENT PLANNING ON LATE CRITICAL ORGAN TOXICTY IN THE INTERSTITIAL BRACHYTHERAPY FOR VAGINAL CANCER

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Purpose/Objectif: In patients with Vaginal cancer,interstitial brachytherapy delivers higher doses compared to incavitary technique. Because of precise localization of rectum & bladder on CT scan, the DVH analysis would be more accurate in CT based treatment planning rather than conventional planning.Investigate the utility and impact of interstitial implant quality parameters like Conformal index (CI), Uniformity index (UI), Natural dose ratio (NDR) , Peak dose (PD) and percentage of volume of critical organs(bladder & rectum) receiving mean prescribed dose, over late toxicity in vaginal cancer patients.

Materials/Methods: Study comprises of 22 vaginal cancer patients treated between 2003 and 2004 of which 18 were FIGO stage III and 4 were FIGO Stage II. All the patients were treated with concurrent chemoradiation using Inj.Cisplatin 40mg/m^2 weekly & a combination of 3 dimensional external megavoltage pelvic radiation to a dose of 5040cgy (with midline block at 3960cgy) followed by 2 applications of MUPIT interstitial radiation therapy, spaced 1 week apart, to a dose of 24-30gy. All patients underwent an fluoro-guided interstitial implant placement under epidural anesthesia followed by CT-based planning and were treated with 18 channel HDR brachytherapy remote afterloader (Microselectron, Nucletron). Triple Optimisation techniques (Geometric, Dose Point and graphical) are employed in the treatment planning. Natural DVH of 44 clinically executed implants were studied for this purpose. Dosimetry parameters for implant deduced from DVH included UI, CI, NDR, and PD. For critical organ dose analysis, the countured volumes is divided into 12.5%, 25%, 50% & 100% volumes. The mean dose delivered to respective volumes of the critical structures was calculated and the multinomial logistic regression model applied to check its relationship with manifested late toxicity.

Results: At a median follow-up of 18 months, 20 patients achieved clinical local control while 2 had progressive disease.In regular vaginal implants, mean QI, UI, CI for all the implants is 1.31, 1.23 & 1.14 respectively. 60% of patients had grade I, 34% had grade II and 6% had gr.III rectal toxicity. For rectal volumes V12.5%, V25%, V50% and V100% the mean doses delivered are 75%,65%,50% and 18% of the prescribed dose. While 70% of patients had no bladder toxicity, 20% developed grade 1 and 10% had grade 2 RTOG reactions. For bladder volumes V12.5%, V25%, V50% and V100% the mean doses delivered are 60%, 45%,35% & 10% of the prescribed dose. Multinomial Logistic regression analysis showed statistical significance for V12.5 &V25% for rectum ($p<0.052$) & Bladder ($p<0.063$). Compared to the non-optimized implants, optimization methods resulted in better protection for the bladder wall and rectum. Conformal dose distribution might result in increase of dose inhomogeneity within the target volume.

Conclusions: DVH based analysis of the dose distribution enables a clinically realistic evaluation of the brachytherapy application to be made. In view of precise delineation of the VOI & critical organs, CT-based optimized implant allows conformation of the dose distribution to the PTV while sparing normal tissue and organs at risk. A tradeoff between conformality and dose homogeneity results in an acceptable dose plan.

633 poster

IMPACT OF BIOLOGICAL EFFECTIVE DOSE (BED) ON THE SURVIVAL IN 261 PATIENTS TREATED FOR ADVANCED CERVICAL CARCINOMA.

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Purpose/Objectif: The purpose of this retrospective study is to analyze the effect of BED on global survival (SV_3) and disease free survival (DFS_3) in patients treated in our Institute for advanced cervical carcinoma.

Materials/Methods: We included in the analysis 261 patients with cervical carcinoma FIGO stages IIB-III, divided in two therapeutical groups: a first group of 107 patients received preoperative external beam radiotherapy (EBRT) of 46 Gy/ pelvis and 10 Gy/ point A medium dose rate brachytherapy (MDR-BT); after 4 to 6 weeks interval TAHBSO with bilateral pelvic lymphadenectomy was performed. A second group of 154 patients received definitive EBRT of 64 Gy/ pelvis + 14 Gy/ A/ 1-2 fractions MDR-BT. BED was calculated using an α/β ratio of 10 for tumour and 3 for late effects. The group has a median follow-up of 44.4 months (3.4-61.6).

Results: In the preoperative group the median BED_{10} value was 80 Gy, with a SV_3=98% when BED_{10}>80 Gy vs. 87% for BED_{10}< 80 Gy (p=0.08). We found a discriminative BED_{10} for SV_3 value of 76 Gy. The DFS_3 was 95% for BED_{10}>80 Gy vs. 84% when BED_{10}<80 Gy (p=0.05). In the definitive radiotherapy group the median BED_{10} value was 109 Gy, with a SV_3=70% when BED_{10}>109 Gy vs. 62% for BED_{10}<109 Gy (p=0.25). The DFS_3 was 66% in BED_{10}>109 Gy vs. 56 % if BED_{10}<109 Gy (p=0.24). When including the time factor we found the same difference for the first group: SV_3=98% for BED_{10tf}>69 Gy vs. 86% if BED_{10tf}<69 Gy (p=0.03). In the second group SV_3=75% for BED_{10tf}>93 Gy vs. 59% in BED_{10tf}<93 Gy (p=0.06).

Conclusions: For the patients treated with preoperative EBRT and MDR-BT a significant better SV_3 and DFS_3 was found when BED_{10}>80 Gy. In the definitive radiotherapy group we found same the same results for BED_{10}>109 Gy but without statistical significance.

634 poster

IMPACT OF DIFFERENCES IN ORGAN CONTOURING AND SEED LOCALISATION BY IMAGING MODALITY ON POST-IMPLANT DOSIMETRY PARAMETERS FOR PERMANENT PROSTATE IMPLANTS.

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Purpose/Objectif: Post-implant dosimetry is recommended for all patients undergoing permanent prostate brachytherapy as an integral part of QA. At present, CT-based post-implant analysis is the most commonly used method for quantitative dosimetric evaluations. However, MRI allows more accurate volumetric and anatomically relevant evaluation, which provides substantially more accurate dosimetric analysis of prostate implants. The MRI-derived source localisation is labour-intensive and needs to be done by an experienced physicist. CT-MRI fused images allow accurate determination of prostate size and seed position, making this an attractive option for post-implant analysis. In this study, we want to compare the outcome of three different image-based post-implant dosimetry methods (MR-T1 and MR-T2 fusion, CT, MR-T2 and CT fusion).

Materials/Methods: Twenty patients are included in this study. All patients are implanted with ^{125}Iodine seeds. MR-images are acquired using a T1-weighted gradient echo sequence, slice thickness 4.5 mm and a T2-weighted fast spin echo sequence, slice thickness 3 mm. CT-imaging is done on a Spiral CT with 3 mm slice thickness. CT-images are acquired after a median time of 37 days (30 to 42 days), MR-images after 42 days (35 to 93 days). Prostate contouring is performed both on CT and T2-weighted MR-images with 2 weeks in between jointly by a radiation oncologist and a radiologist. Registration between MR-T1 and MR-T2 and between MR-T2 and CT is done manually, based on both implanted seeds and anatomical repairs. Then the CT-MRI-based dosimetry is compared with the CT-based and with the MRI-based dosimetry using the DVH-related parameters recommended by the American Brachytherapy Society.

Results: To date, the results of the first five patients are available for analysis. Significant differences in prostate volume are found, depending on the image modality used. Average prostate volume contoured on CT is 24.1% higher than on MR-T2 (41.4 ± 12.3cc vs. 23.2 ± 10.1cc). QA DVH-related parameters strongly depend on the image modality: the mean D90 is 8.0% higher (1SD=9.1) and the mean V100 is 5.4% higher (1SD=5.9) for CT-MRI than for CT. When differences in D90 and V100 between CT-MRI and MRI are analyzed, large but unexpected differences are found between these imaging modalities in favour of CT-MRI.

Conclusions: Although earlier work (De Brabandere et al., 2006) indicated that the mean deviation of the reconstructed seed positions in a phantom was within acceptable limits for clinical evaluation of prostate implants by RX and MRI, these preliminary data may suggest that we cannot simply extrapolate these findings on a MRI compatible phantom to individual patients. The future of post-implant dosimetry probably lies in the fusion of CT and MRI to accurately determine prostate size based on MRI and seed position based on CT. To validate this hypothesis, the results on 20 patients will be reported at the time of the meeting.

635 poster

IMPORTANCE OF THE CT/MRI FUSION METHOD AS A LEARNING TOOL FOR CT-BASED POST IMPLANT DOSIMETRY IN PROSTATE BRACHYTHERAPY

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Purpose/Objectif: To compare the CT-based and CT/MRI fusion-based postimplant dosimetry after permanent prostate brachytherapy and to evaluate the improvement in CT-based dosimetry by radiologists with or without experience in using the CT/MRI fusion method.

Materials/Methods: Thirty-eight consecutive patients agreed to participate in a prospective study. All patients were treated with loose ^{125}I radioactive seeds using a Mick applicator. All patients underwent preoperative TRUS prostate volume studies 3-4 weeks before the implant. The Task Group 43 formalism and Variseed software package was used both for planning and calculating the final dosimetry. Post implant CT and MRI were obtained on the day after the procedure. CT was obtained using a CT scanner with 16 detector arrays. MR images were obtained with a five-channel sense cardiac coil under easy breathing with a slice thickness of 3 mm and no intersectional gap. The MR imaging sequence was contrast-enhanced T1-weighted spin-echo (repetition time [TR]/echo time [TE] in millisecond: 607/12) with 2 milliliter of gadopentetate dimeglumine administered per kilogram of body weight.The prostate contours from CT/MRI fusion are the gold standard for determining the prostate volume and dose volume histogram (DVH). CT-based postimplant dosimetries were performed by two physicians. Observer 1 was a radiologist who had never used CT/MRI fusion method for postimplant dosimetric analysis. Observer 2 was a radiation oncologist experienced in postimplant analysis using the CT/MRI fusion method. Both observers were unaware of the pre-planning TRUS results. therefore, although observer 2 had a little advantage of the knowledge of brachytherapy, the main different between the two observers was their experience in performing postimplant analysis using the CT-MRI fusion method. The prostate dosimetry was evaluated by prostate D90 and V100. The group comparisons for volumes and dosimetric parameters were performed using the t test.

Results: No significant difference was observed in the mean prostate volumes between the two observers and the CT/MRI fusion data. However, the correlation coefficient value for observer 2 (R^2=0.932) was greater than that for observer 1 (R^2=0.793). The D90 and V100 values as evaluated by the two observers were significantly underestimated in comparison to those evaluated using the CT/MRI fusion methods. The underestimation of the DVHs by observer 1 was thus greater than that by observer 2 (prostate D90: 99.56% for observer 1, 102.97% for observer 2, 109.37% for CT/MRI fusion. Prostate V100: 88.12% for observer 1, 90.14% for observer 2, 91.91% for CT/MRI fusion).

Conclusions: The difference in the mean value in D90 and V100 by observer 1 was significantly greater than that for observer 2. These findings suggest that the CT/MRI fusion method provides accurate feedback which thereby improves CT-based postimplant dosimetry for prostate brachytherapy.

636 poster

IMPROVING SEED MIGRATION RATE USING REAL-TIME NEEDLE NAVIGATION AND A ROBOTIC NEEDLE RETRACTION SYSTEM

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Purpose/Objectif: To demonstrate that seed migration rates for loose seed implantation techniques goes down with the use advance technology.

Materials/Methods: Our institution has an ongoing permanent

seed implant program since 1994. In February 2004, a systematic seed migration (SM) detection procedure was implemented in the clinic. It involved a highly sensitive NaI gamma counter detector. The detector is used to scan each patient, during the 1 months follow-up visit, from head to the umbilicus. A CT exam is conducted afterward for post-implant dose analysis. If the counter reads a positive signal of more than 1400 counts/minute, the patient received a chest X-ray and/or digital fluoroscopy for documentation purposes. A total of 367 patients were scanned to date. Of those, 107 were implanted using a pre-planning method for which the prostate volume is obtained a few weeks before the procedure (M1). All needles are loaded before the procedure, inserted based on the preplan. 177 were implanted using intra-operative volume acquisition and inverse planned dosimetry (SPOT PRO/IPSA, Nucletron). For these patients, the needles were built automatically on a table in the operating room and were inserted under 3D ultrasound guidance (M2). Finally, for 58 patients (M3) the intra-operative technique was modified so that M2 is supplemented by a robotic needle retraction system (seedSelectron, Nucletron). M1 and M2 correspond to technique where the physicians perform the needle retraction manually. The same treating physicians were involved for all the cases.

Results: SM was found to occur for 16.35% (60) patients. The NaI seed migration detector proved to be more efficient than either the chest X-ray or fluoroscopy. X-ray yields a false negative (FN) rate of 35 %, with only 39 patients detected out of the 60. Fluoroscopy gives a FN rate of 18.33% or 49 cases. The FN rates are due to fast moving seeds. The fraction of patients with SM went from 20.56% using M1 to 18.08% for M2 and 12.07% for M3. The use of the intra-operative volume and needle guidance allow a small decrease in the SM of 2.4%. However, replacing the manual retraction procedure of M1 and M2 by a robotic system improves the SM significantly, 6 to 8%. Thus manual retraction of the needles accounts for large fraction of detected SM cases. In term of migrated seeds, it corresponds to 70 seeds out of 19739 implanted seeds or 0.39%. Only 7 patients had multiple SM of 2 (4 cases) and 3 seeds (3 cases).

Conclusions: SM detectors save chest X-ray for almost 88% of our patients based on our actual implantation technique (M3). This corresponds to a reduction of unnecessary dose and use of resources. We have shown that advance technology such as intra-operative planning, needle navigation and robotic loading and retraction all have an impact on SM. The robotic retraction system was found to be the most effective loose seed implantation technique in terms of SM.

637 poster

INFLUENCE OF A COMMONLY USED STENT TYPE ON THE DOSE DISTRIBUTION IN ENDOVASCULAR BRACHYTHERAPY

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Purpose/Objectif: Endovascular Brachytherapy (EVBT) is a method to prevent restenosis after PTCA. The irradiation of the treatment site stops unwanted proliferation of tissue. Often EVBT is performed after a stent has been placed into the artery. As the stent is made of metal, it influences the dose distribution. The magnitude of this influence is still unknown. It is impossible to take this into account while planning the treatment. The stent could lead to serious underdosage and thus the treatment aim is missed.

Materials/Methods: A commonly used stent type was used for this investigation. The dose at different positions along the stent was determined.

Additionally the depth dose curves with and without stent were measured and compared. The comparison of the curve shapes gives indications about the change of the beta spectra with and without stent.

The dose distribution with and without stent was simulated with the Monte Carlo Code GEANT4.8.

Results: Measurements were performed at seven positions along the stent. The minimum value is 17% below the maximum value. At the position with the minimal response the detector was placed directly behind one strut of the stent.

A comparison of the percentage depth dose curves with and without stent shows good agreement. The shape of the two curves is comparable, that indicates that the stent does not change the beta spectrum signiﬁcantly.

The results of the simulation with GEANT4.8 show good agreement with the measurements.

Conclusions: For EVBT it is of vital importance to know the source parameters (dose rate, dose homogeneity) exactly. MOSFETs are a useful tool for QA in EVBT, as they allow easy handling and calibration without calibration sources. Additionally, their small size provides a better spatial resolution compared to other dosimeters That means that they are even capable of resolving the influence of very small structures like stents on the dose distribution.

The influence of stents on the dose distribution has two aspects. Firstly, a stent leads to inhomogeneity of the dose distribution along the source axis. The size of this inhomogeneity is ±8.5%. Due to the relatively large inhomogeneity of dose profiles behind the stent it is diffcult to give one value for the dose decrease. Depending on the position of measurement, the dose decrease can vary from hardly measurable to more than 10%.

The Monte Carlo simulation shows good agreement with this experimental results.

638 poster

INFLUENCE OF TISSUE COMPOSITIONS ON DOSE DISTRIBUTIONS FOR ^{125}I AND ^{103}PD SEEDS

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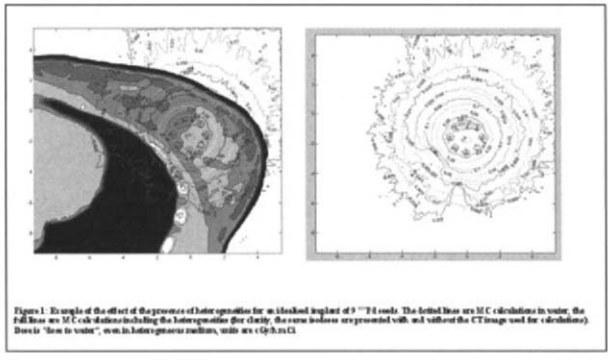
Purpose/Objectif: Low energy photon isotopes like ^{125}I or ^{103}Pd are widely used for brachytherapy (BT) applications, as in the treatment of prostate, eye or very recently breast. The mean energy is approximately 30 keV for ^{125}I and 20 keV for ^{103}Pd. In the vast majority of BT treatment planning the real compositions of the tissues, the presence of heterogeneities or the real shape of the body are not taken into account.

Materials/Methods: We used Monte Carlo (MC) techniques to estimate the impact of these approximations on the dose calculations. A first step was to calculate the radial dose functions for IBt seeds using MCNP4C in different situations and in different materials including body tissues. For these calculations, the MCNP4C default cross section library was modified to match EPDL972. In a second step, the effect of taking into account the real composition was further analysed for an idealised prostate and breast case by comparing the isodose distributions. The last step is to do these MC calculations for real prostate or breast patient cases

Results: The differences between radial dose functions calculated in muscle and in water can be as high as 15% at 5 cm for ^{103}Pd and 10% at 5 cm for ^{125}I. For breast tissue, with 50% adipose 50% gland, the comparison with water shows an underestimation of the radial dose function of up to 50% at 3 cm from a ^{103}Pd seed. Moreover due to photoelectric absorption, we show that the presence of even very limited amounts of high Z elements, such as Ca, has an effect on the radial dose function and so on the dose distribution around the seeds. This effect can be seen in the case Ca is present as a heterogeneity such as cortical bone or embedded in the tissue. It influences consequently the position of the isodoses calculated for implants in

a CT phantoms. An example for an idealised breast implant case is shown in figure 1. The effect of the tissue composition is particularly obvious due to the presence of the ribs and because of the inhomogeneity in the composition of the breast used in this example: in the upper left part, containing more adipose tissue, the difference between the isodoses calculated in water or in real tissue reaches several mm although the difference is much smaller in the denser lower right part of the breast.

Conclusions: The real composition of the body tissues, available through CT images, should not be neglected for LDR BT because of the large influence of high Z elements due to the high photoelectric cross section for low energy photons



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INTERSTITIAL HIGH DOSE RATE BRACHYTHERAPY FOR PARTIAL BREAST IRRADIATION: PRELIMINARY RESULTS OF A PHASE I-II PROSPECTIVE STUDY

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Purpose/Objectif: Preliminary results of a phase I-II prospective study evaluating feasibility and toxicity of accelerated partial breast irradiation (PBI) with interstitial high dose-rate brachytherapy in patients with early breast cancer with low risk for relapse are reported.

Materials/Methods: Study inclusion criteria are: written informed consensus, age ≥ 40 years, ECOG performance status 0-2, T dimensions ≤ 2.5 cm, negative surgical margins, negative axillary lymph nodes, no infiltrating lobular istology, absence of extensive intraductal component, multifocality and skin infiltration. Treatment schedule is 4 Gy twice a day for four days, up to a total dose of 32 Gy, with an interval between fractions of at least 6 hours. Therapy was delivered with a microSelectron HDR ^{192} Ir remote afterloading system (Nucletron, The Nederlands). From August 2003 to April 2006 52 patients aged 52-85 years (median 67.5) were enrolled. There were 42 infiltrating ductal (18 G1, 21 G2, 3 G3), 1 infiltrating tubular and 9 intraductal carcinoma, two of which with microinfiltration. In 46 cases tumors were biopatologically characterised; estrogen and progesterone receptors were positive in 39 and 27 cases respectively, Ki-67 was overexpressed (>25%) only in 6 cases, p53 was overexpressed (>20%) in 6 cases, c-ErbB2 immunohistochemistry was 2+ in 3 cases (FISH undetermined), negative in 41 and not determined in 12 cases. Implants were positioned using template guide during surgery in 13 patients and 6-8 weeks after surgery in 39 patients.

Results: A single-plan implant was constructed only in one case, a two plane in 8 and a three plane in 43, the median number of the catheters was 12 (range 4-15), the median V100 was 93.65 cm^3 (range 14.03-192), the median V150 was 24.1 cm^3 (range 5.70-50.25) and the median DHI was 0.75 (range 0.58 - 0.81). The median follow-up was 14 months (range 1-33). Incidence of perioperative and acute toxicity was low; haematoma was observed in 5 cases and cutaneous erithema in 5. Late toxicity was evaluated only in 42 patients with a follow-up longer than 6 months: in 3 patients grade 2 skin toxicity and in 1 case grade 1 was developed. Cosmesis was judged good to excellent in all cases. No relapses have so far occurred.

Conclusions: Our data show that accelerated PBI with interstitial ^{192}Ir multicatheter HDR brachytherapy is feasible and associated with very low acute and late toxicity and with good or excellent cosmesis. Lenght of follow-up does not permit relapse incidence evaluation.

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INTRA-OPERATIVE TREATMENT PLANNING: A WAY TO IMPROVE DOSIMETRY IN PROSTATE BRACHYTHERAPY

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Purpose/Objectif: To evaluate the advantage of intraoperative (IO) over pre-operative planning by analyzing the impact of patient's position on urethra and prostate dosimetry after I125 implant.

Materials/Methods: Real time dosimetry of a group of 15 patients treated with I125 permanent prostate implant was evaluated with changing leg and/or urethra's position. 3-D ultrasound was used to plan seed implantation. Scans were repeated after moving the patients urethra and legs downward. The initial IO clinical plans were applied to these new scans. The doses to urethra (D5, V150) and prostate (D90, V200) were compared for the different positions. Paired Student-T tests were performed.

Results: The mean value of prostate's D90 went from 194,2 Gy to 172,5 Gy after a urinary catheter displacement (p = 0,001) and to 170,2 Gy when legs were moved (p<0,001). The maximum variation observed was 40%, representing a decrease of 77,2 Gy. Two patients had a D90 below 140 Gy after a change of position. The maximum observed variation of the V200 to the prostate ranged from 3,7 to 12,4%, with a mean decrease of 7% for the 15 patients.The maximal urethra's D5 variation observed for each patient ranged from 4,2 to 70,7%, with a mean increase of 26,6%. A third of the patients (5/15) presented values of urethra's D5 beyond 300 Gy. A mean 17,7% variation of the urethra's V150 was observed for the 15 patients, going from an initial 8,1% to a value of 22,8% with a displacement of the urethra (p= 0,02) and to 28,7% when moving the legs (p= 0,001).
verage values of prostate's D90 and V200 and urethra's D5 and V150 before and after changes in position for the 15 patients

	Prostate's D90	Prostate's V200	Urethra's D5	Urethra's V150
Initial position	194,2 Gy	32,3 %	218,2 Gy	8,1%
Urethra down	172,5 Gy	26,5%	245,2 Gy	22,8%
p	0,001	<0,001	0,01	0,02
Legs down	170,2 Gy	26,5%	260,4 Gy	28,7%
p	<0,001	<0,001	0,002	0,001

Conclusions: Patient positioning has a strong impact on dosimetry. We observed a significant decrease of the prostate's D90 and V200 combined with a significant increase of urethra's D5 and V150 when moving patient's legs and even the urethra catheter. This translates in a clear dosimetric advantage of intraoperative dosimetry over preplanning. A direct correlation has been shown in previous publications between doses delivered to the urethra and morbidity and also between doses to the prostate and treatment efficacy. These results therefore suggest a clinical advantage of intraoperative over pre-operative treatment planning.

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INTRALUMINAL BRACHYTHERAPY FOR BILIARY TRACT MALIGNANCIES

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Purpose/Objectif: To evaluate the efficacy, safety and tolerability of intraluminal brachytherapy in patients with obstructive jaundice due to a biliary tract tumor.

Materials/Methods: During December 1993 and December 2005, 14 patients with obstructive jaundice due to a biliary tract tumor had received intraluminal brachytherapy for palliative intent. Brachytherapy catheter was placed via the metallic stent. Catheter position and the tumor localization was determined by AP and lateral orthogonal simulation films. Brachytherapy was delivered with microSelectron HDR-Ir 192. Median fractionation dose was 500 cGy (range 200-1000 cGy) prescribed to 1 cm from the catheter axis. Median total brachytherapy dose was 2000 cGy (range 1000-3500 cGy). Four patients also received external radiotherapy with 180 cGy daily fractions. The total external radiotherapy dose was 3960 cGy in two patients and 4500 cGy in two.

Results: Median age was 63 (range 35-76). Seven patients were male and 7 were female. Jaundice was the most common symptom in all of them. The other symptoms included nausea and vomiting and pruritus. Five patients were operated. Four patients already had liver metastasis at diagnosis. Median survival time was 9 months (range: 1-18 months). Palliation duration of 3 to 5 months was achieved in 6 patients.

Conclusions: Biliary tract malignancies are rare tumors with poor prognosis. Intraluminal brachytherapy has its place in the palliative treatment of these tumors being an easily applicable, safe and a tolerable treatment method.

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ION RECOMBINATION FOR THE PRIMARY STANDARD CAVITY CHAMBER OF THE IR-192 HIGH DOSE RATE REFERENCE AIR KERMA RATE STANDARD AT NPL

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Purpose/Objectif: Recombination in ionization chambers at therapy level dose rates is small but nevertheless significant for primary standard level dosimetry. NPL has recently developed a primary standard for the measurement of reference air kerma rate in high dose rate Ir-192 sources. The standard is based on a graphite cavity ionization chamber with a volume of about 102.5 cm^3.

Materials/Methods: The recombination correction was measured using the Niatel/Boutillon method, which applies to continuous radiation and allows separating of the contribution due to volume recombination from the combined contributions of initial recombination and diffusion losses. The measurements were performed using an x-ray set at a tube voltage of 50 kV, at a focal distance of 1 m and at various tube currents (0.25 mA, 0.5 mA, 1 mA, 2 mA, 3 mA and 5 mA). This range of tube currents was chosen such as to achieve the dose rates relevant for the primary standard. For each setting of the tube voltage and tube current, the ionization current in the cavity chamber was measured at the operating voltage V of 500 V and at the voltages V/n with n = 2, 2.5, 3 and 3.5.

Results: The recombination correction factor for the primary standard cavity chamber can be represented by the following the equation: $k_{ion} = (1.57 \pm 0.09) \cdot 10^7 I_v + (1.0025 \pm 0.0002)$ where I_v is the measured ionization current in A. For the typical currents measured at the time a new source is installed, this results in a recombination correction factor of $k_{ion} = 1.0028 \pm 0.0002$.

Conclusions: We conclude that an extensive set of measurements resulted in an accurate determination of the ion recombination correction for the primary standard cavity chamber of NPL's high dose rate reference air kerma rate standard for Ir-192. It was found that the correction is significant.

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IS INTRACAVITARY BRACHYTHERAPY REALLY OPTIMAL IN CERVICAL CANCER RADIOTHERAPY ?

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Purpose/Objectif: Brachytherapy (BT) is an essential part of radical radiotherapy of advanced cervical cancer. Intracavitary brachytherapy (ICBT) is a gold standard. The main limiting factor of ICBT is high radiation dose to critical organs i.e. bladder and rectum. To investigate whether an interstitial brachytherapy (ISBT) substantially reduce the dose to critical organs maintaining the same high dose to the tumor as ICBT.

Materials/Methods: From january to may 2005 75 patients with advanced cervical cancer (IIb- IIIb FIGO stage) treated with ICBT - 51 pts or ISBT -24 pts.

ICBT (120 procedures) was used as LDR Cs-137 source (42 pts) or HDR Ir- 192 (7 pts) source BT, while ISBT (96 procedures) was only HDR Ir - 192 treatment. In case of LDR BT 2 fractions of 22,5Gy during 14 days was used, in HDR treated group 4 fractions of 7,5Gy durig 21 days were applied. ICBT was performed using standard Fletcher type applicator. During ISBT intrauterine probe and 2-5 metal needles (according to the tumor size) inserted into the cervix were used. In every case dose was specified to point "A".

Results: No acute treatment related toxicity was observed. Substantial reduction of irradiated volume was detected in ISBT group in comparison with ICBT (mean volume difference 30 ccm, $p<0,001$, T-Test) . Similar reduction in median volume of irradiated bladder - mean ranks 35 vs 65 and rectum - mean ranks 50 vs 79 ($p<0,001$, Mann-Whitney Test) respectively was showed.

Conclusions: ISBT is superior to standard ICBT due to substantial reduction of irradiated volumes in critical organs.

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IS URETHRAL DOSIMETRY PREDICTIVE OF ACUTE URINARY MORBIDITY IN PATIENTS, WHO HAVE NO URINARY SYMPTOMS PRIOR TO PROSTATE BRACHYTHERAPY?

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Purpose/Objectif: To determine whether segmental urethral

dosimetry is predictive for the degree of acute urinary morbidity following prostate brachytherapy, in uniformly treated patients with no urinary symptoms prior to prostate brachytherapy.
Materials/Methods: Between May 2000 and November 2005, 1107 pts underwent Iodine 125 monotherapeutic brachytherapy with urethral sparing techniques. 165 patients fulfilled the selection criteria of pre treatment IPSS ≤ 5, no androgen deprivation therapy, no prior transurethral resection, with prostate volumes < 45 cc. The cohort thus represented a group of patients with no pre treatment risk factors for acute urinary morbidity. The median follow-up was 34 months (range 11.3-65.3 months). Prior to treatment and at each subsequent visit (6 weeks after implant and every 6 month afterwards), urinary symptoms were assessed using the IPSS. Acute urinary morbidity was defined by time to IPSS resolution (within 2 of baseline) and maximum increase in IPSS. For all patients the surrogate deviated urethra (as defined by Bucci et al) was contoured and doses calculated at the base, mid prostate, apex and urogenital diaphragm. Univariate and multivariate analysis were performed to evaluated overall urethral and segmental dosimetry (V200, V150, V100, V80, V60, D90, D50, D10), prostate (V200, V150, V100, D90), patient age, clinical stage, presenting PSA, Gleason score, ultrasound volume, number of needles, for their association with urinary morbidity. Models were generated to best predict acute urinary morbidity.
Results: Median baseline IPSS was 3. Median IPSS at 6 weeks, 6, 12, 24 and 60 months were 15,9,7,5 and 5 respectively. The mean and median time to IPSS resolution was 27.2 and 25.1 months respectively. Maximum increase in IPSS ranged from -1 to 30, with a median of 13. Univariate analysis showed urethral dosimetry at the base (D10, D50, V60, V80, V100, V150, V200) to be individually strongly predictive for maximum increase in IPSS (all p values <0.05). Pre implant volume and prostate V100 and D90 also predicted for maximum increase in IPSS. Urethral dosimetry at the base (V60, V80, V100, V200) strongly predicted for IPSS resolution. The multivariate model best predictive for maximum IPSS increase was urethral base V100 and pre implant prostate volume.
Conclusions: With the elimination of pre treatment factors predictive for increased urinary morbidity, radiation dose to the urethral base was strongly predictive of acute urinary morbidity.

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LIMITATIONS OF TM-170 FOR ITS USE IN HDR-PDR BRACHYTHERAPY

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Purpose/Objectif: The Tm-170 radionuclide is a promising radionuclide for use in brachytherapy because of the low mean-energy and the potential high specific activity. The purpose of this study is to determine the dosimetric characteristics of a hypothetical Tm-170 source.
Materials/Methods: The Monte Carlo method is used for this study. The feasibility of using the radionuclide as a possible source in brachytherapy is analyzed. The dose rate distributions for different source configurations have been obtained. Two different encapsulation materials have been studied.
Results: The specific geometric design of a Tm-170 source have played a very important role in the dose rate as a function of distance due to the relative high number of bremsstrahlung photons generated in the capsule and in the core source. Despite of the high activity of the Tm-170 source, it cannot be used for HDR or PDR brachytherapy due to its low dose rate.
Conclusions: The main conclusion obtained is that Tm-170 cannot be used for HDR or PDR brachytherapy using the dimensions and materials of present HDR and PDR sources due to its low dose rate.

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LOW INCIDENCE OF SEVERE EARLY TOXICITY IN PATIENTS WITH CERVICAL CANCER AFTER RADIOTHERAPY WITH PDR BRACHYTHERAPY BOOST IN HIGH DOSES PER PULSE OVER A SHORT TREATMENT TIME

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Purpose/Objectif: Curative radiotherapy of inoperable cervical cancer usually consists of a combination of external beam radiotherapy (EBRT) plus brachytherapy. Severe early toxicity (grade 3-4 within 3 months) is reported to be 5-15%. We assessed acute toxicity of a PDR brachytherapy boost given in high doses per pulse over a short treatment time.
Materials/Methods: From January 2004 to July 2005 36 patients with inoperable cervical cancer received EBRT to the pelvis (46/2.0 Gy) or pelvis plus para-aortal lymph nodes (50.4/1.8 Gy). Thereafter, a PDR brachytherapy boost with an intra-uterine tandem and two ovoids in the lateral vaginal fornices was given. The prescription dose was 24 Gy in 24 pulses of 100 cGy with a period time of 1 hour between the pulses. This dose is equivalent to a continuous LDR dose of 24 Gy at 100 cGy/h with a/b-ratio of 10 Gy and T1/2 of 1 hour. The dose was prescribed to the tumor volume as it was identified by clinical examination and CT-scan with respect to normal tissue tolerance dose. Patients with extra-cervical extension received an additional EBRT pelvic side-wall boost of 8-10 Gy. FIGO stage 1B-4A was treated with concurrent chemotherapy, hyperthermia or a combination of both. After treatment patients were seen every 3 months. Toxicity was assessed starting at date of brachytherapy by the CTC version 2 toxicity scoring system. All patients were followed at least 3 months.
Results: Mean point A dose, ICRU-bladder dose and ICRU-rectum dose were 93.2 cGy (53.1-130.3), 74.4 cGy (24.9-160.4), and 62.0 cGy (34.4-97.5) per pulse, respectively.
Twenty patients received concurrent chemotherapy, 2 patients had hyperthermia, and 6 patients received hyperthermia and chemotherapy. Eight patients received no concurrent treatment. Four patients have deceased. The median follow-up time for patients alive was 32.8 weeks (12.0-84.6).
Three grade 3 toxicities were seen (8.3% [95% CI 1.8 to 22.5]): Increased urinary frequency and urgency, vaginitis, and diarrhea. These severe toxicities were observed in 2 patients with a stage 1B-2A disease and 1 patient with a stage 3B disease. No grade 4 toxicity was observed.
Conclusions: Severe early toxicity after cervical brachytherapy with PDR in high doses per pulse over a short treatment time for cervix cancer is not increased compared to the incidence from the literature. This PDR schedule is thus feasible. The advantage of this PDR schedule is that in hospital treatment lasts only 24 hours, and that the number of applications can be limited to one.

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METHODS FOR DETERMINATION OF SHIELDING REQUIREMENTS IN HDR BRACHYTHERAPY BUNKERS

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Many facilities are acquiring high dose rate (HDR) remote afterloading units. The most common method for bunker shielding calculation which is suggested by NCRP Report No. 49 is using transmission data for primary calculation and also reflection coefficient for scatter calculations. In the other method absorbed dose rates in air by considering shield attenuation correction and build-up factors for different beam energies were derived for an HDR bunker. With the help of the Monte Carlo code (MCNP4C), Isodose kerma level and energy spectrum map of the bunker were obtained for Ir, Co and Cs sources. Flexishield software designed to calculate appropriate wall and door shield thickness. The Flexishield recommended thickness agrees to within 10% with that estimated by using the recently recommended method by IAEA.

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MODIFICATION OF A LARGE BORE CT SIMULATOR AND IMAGING ROOM FOR 3-D BRACHYTHERAPY

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Purpose/Objectif: In 2000 GEC-ESTRO established a working group to assess 3D imaging based treatment planning in gynecological brachytherapy. First recommendations for target volume delineation were published recently (Radiother. Oncol. 74 (2005) 235-245). Our old orthogonal x-ray imaging system for brachytherapy had to be renewed simultaneously with the purchase of a new CT simulator for external beam simulation. Decision was made to couple 3D imaging, treatment planning and delivery of gynecological HDR brachytherapy with the new CT simulator and an afterloader unit. The basis of this decision was the fact that the present big bore CT scanners are wide enough for patients in gynecological position.
Materials/Methods: When purchasing a new CT simulator, the demands from gynecological brachytherapy: compatibility to anesthesia, design and control of the CT gantry and various supporting devices for legs and pelvis were taken in consideration. Especially the design and extensions of the radiotherapy table top for the CT couch were not designed for BT. In addition, the shielding of the imaging room had to be rebuilt for Ir-192 source.
Results: We agree with GEC-ESTRO that 3D imaging will bring many benefits to gynecological brachytherapy. Assessment of doses to critical organs may better be evaluated while the dose to target volume is more conformal. On the other hand, this solution requires heavy shielding to the imaging room, designing a completely new CT-compatible leg support system and change of all applicators to CT-compatible ones. Our conclusion is that in the future CT scanner manufacturers should also take the demands of brachytherapy into consideration.

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MONTE CARLO CALCULATIONS OF RADIATION QUALITY CORRECTION FACTORS FOR RADIOCHROMIC FILM DOSIMETRY IN SURFACE AND OPHTHALMIC BRACHYTHERAPY

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Purpose/Objectif: High-dose-rate (HDR) beta-emitting sources are widely used in ophthalmic brachytherapy. Planar HDR beta sources can be also employed for brachytherapy surface irradiation of skin lesions. Radiochromic films (RCFs) are the most suitable detectors for source characterisation, quality assurance and treatment planning verification in brachytherapy applications. The aim of this work is to calculate the radiation quality correction factors of RCFs for beta absolute dosimetry in planar geometry, using Monte Carlo (MC) codes. Irradiations of MD-55-2 and HS RCF, with clinical beams and beta-emitting radioisotopes used in ophthalmic and surface brachytherapy (^{188}Re, ^{90}Y, ^{90}Sr/^{90}Y, ^{32}P), were simulated.
Materials/Methods: Denoting with Q and Q_0 the irradiation and calibration conditions of RCFs, the absorbed dose to water measured by RCF is **Eq 1**, where $R_{water,Q}$ is the RCF response, **Eq 2** is the ratio between the two film sensitivities and represents the radiation quality correction factor for the RCF response. F_{Q,Q_0} can be also expressed as **Eq 3**, $D_{film,Q}$ is the absorbed dose to film and $D_{water,Q}$ is the absorbed dose to water at the entrance of RCF, in the absence of detector. MD-55-2 and HS RCFs have been simulated with water as surrounding medium. The irradiations with clinical electron/photon beams have been simulated with the BEAMnrc code, the irradiations with radioisotopes with the MCNP4C code. The beta-emitters (^{188}Re, ^{90}Y, ^{32}P and ^{90}Sr/^{90}Y, the last filtered with 0.1 mm thick stainless steel or unfiltered), were simulated in a planar geometry, with 1 mm or 2 mm source-detector distance. The F_{Q,Q_0} values were calculated assuming four calibration conditions: 6 MV photon beam (named *CI*), 6 MeV electron beam (*CII*), filtered ^{90}Sr/^{90}Y at 1 mm or 2 mm distance (*CIII-CIV*).

$$D_{water,Q} = \frac{R_{water,Q}}{S_{water,Q_0} \cdot F_{Q,Q_0}} \qquad \text{Eq 1}$$

$$F_{Q,Q_0} = S_{water,Q} / S_{water,Q_0} \qquad \text{Eq 2}$$

$$F_{Q,Q_0} = \frac{\left(\frac{D_{film,Q}}{D_{water,Q}}\right)}{\left(\frac{D_{film,Q_0}}{D_{med,Q_0}}\right)} \qquad \text{Eq 3}$$

Results: F_{Q,Q_0} are reported in the **Table**. The combined statistical uncertainty ($2f\tilde{a}$) was always within 2%. For each source, the mean energy calculated by the fluence spectrum at 1 and 2 mm water depth are also reported. The results evidenced that absolute dose measurements with both RCF types calibrated by clinical photon/electron beams (*CI-CII*) would be affected by underestimations from 5 to 12%. Otherwise, for the calibration with filtered ^{90}Sr/^{90}Y (CIII-CIV): the MD-55-2 would yield a dose underestimation between 3-5% for ^{32}P and discrepancies within ±2% for ^{188}Re and ^{90}Y; the HS would yield a dose underestimations that can reach 4% for ^{188}Re and 6% for ^{32}P.

			CI	CII	CIII	CIV
MD-55-2 radiochromic film	^{188}Re	d = 1 mm, E_m=634 keV	0.910	0.931	0.982	1.000
		d = 2 mm, E_m=565 keV	0.914	0.935	0.986	1.004
	^{90}Y	d = 1 mm, E_m=758 keV	0.927	0.948	1.000	1.018
		d = 2 mm, E_m=677 keV	0.922	0.944	0.995	1.013
	^{32}P	d = 1 mm, E_m=588 keV	0.886	0.907	0.956	0.973
		d = 2 mm, E_m=460 keV	0.879	0.900	0.948	0.966
	$^{90}Sr/^{90}Y$	d = 1 mm, E_m=748 keV	0.901	0.922	0.972	0.990
		d = 2 mm, E_m=682 keV	0.913	0.935	0.986	1.003
	$^{90}Sr/^{90}Y$ filtered	d = 1 mm, E_m=758 keV	0.927	0.948	---	1.018
		d = 2 mm, E_m=677 keV	0.910	0.932	0.982	---
HS radiochromic film	^{188}Re	d = 1 mm, E_m=634 keV	0.919	0.907	0.960	0.975
		d = 2 mm, E_m=565 keV	0.929	0.917	0.970	0.985
	^{90}Y	d = 1 mm, E_m=758 keV	0.941	0.929	0.983	0.999
		d = 2 mm, E_m=677 keV	0.942	0.929	0.983	0.999
	^{32}P	d = 1 mm, E_m=588 keV	0.914	0.902	0.955	0.970
		d = 2 mm, E_m=460 keV	0.901	0.889	0.941	0.956
	$^{90}Sr/^{90}Y$	d = 1 mm, E_m=748 keV	0.926	0.914	0.967	0.982
		d = 2 mm, E_m=682 keV	0.938	0.926	0.980	0.996
	$^{90}Sr/^{90}Y$ filtered	d = 1 mm, E_m=758 keV	0.958	0.945	---	1.016
		d = 2 mm, E_m=677 keV	0.943	0.930	0.985	---

Conclusions: The MC codes are the most accurate theoretical tool to calculate the correction factor value whatever the RCF structure and the source detector geometry. For absolute beta dosimetry, a correction factor dependent on the radiation quality is needed. The extent of dosimetric discrepancies, connected to the RCF calibration conditions and the source-detector geometry, could affect the clinical outcomes in some brachytherapy applications.

650 poster

MONTE CARLO DOSIMETRY STUDY OF THE FLEXISOURCE IR-192 HDR SOURCE

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Purpose/Objectif: Brachytherapy with high dose rate (HDR) sources of ^{192}Ir is a usual practice in clinical brachytherapy today. The TG43 U1 update report recommends that accurate dose distribution data of the brachytherapy source in use should be obtained experimentally or by Monte Carlo (MC), to be used as input in the HDR Treatment Planning System (TPS). The purpose of this study is to obtain the dose rate distribution in liquid water media for the Flexisource HDR ^{192}Ir source (Isodose Control GmbH, Germany) using the Monte Carlo method to obtain the TG43 U1 parameters and the 2-D rectangular dose rate table.

Materials/Methods: The MC code GEANT4 (7.1 version) was used to estimate dose rate in water and air-kerma strength around the Flexisource Ir-192 source following the TG43 U1 recommendations. All the details about the design an material of the Flexisource have been included in the simulation.

Results: A complete dosimetric dataset for the Flexisource is presented. TG43 dosimetric functions and parameters have been obtained as well as a 2-D rectangular dose rate table, consistent with the TG43 dose calculation formalism.

Conclusions: The dosimetric parameters and functions obtained for the Flexisource have been compared with that obtained in the literature for others HDR sources, showing that the use of specific datasets for this new source is justified. This dataset can be used as input in the TPS and to validate its calculations. As policy of BRAPHYQS-ESTRO task group, this dataset will be incorporated to the website: http://www.uv.es/braphyqs available to users in excel format.

651 poster

MOSFET DOSIMETERS: A DOSIMETRIC STUDY FOR HDR BRACHYTHERAPY AND ELECTRON BEAM THERAPY

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Purpose/Objectif: High Dose Rate (HDR) brachytherapy offers an alternative radiotherapy modality to electrons for the treatment of skin lesions. In the present work dose at the skin was evaluated using micro mosfet dosimeters. For each techniques the mosfet reproducibility and linearity were discussed.

Materials/Methods: HDR brachytherapy consists of placing high intensity radioactive sources very close to or in contact with the target tissue. To realize this treatment a remote afterloading device was used. This system consists of a motor driver source transport device for transferring radioactive source between a shielded safe and each treatment applicator. In our Medical Physics department of the A.O. S. Giovanni di Dio e Ruggi d'Aragona in Salerno, a HDR brachytherapy is realized (Micro Selectron HDR Nucletron) with a remote controlled afterloading system and using Leipzig applicators. These consist of six tungsten bell-shaped applicators with an inner diameter of 10, 20, 30mm with a protective plastic cap 1 mm thick. An Ir-192 radioactive source (gamma factor of 0.466 $R'm^2'h^{-1}'Ci^{-1}$, half life of 74.02 days, average energy of 397 KeV and total reference air kerma of 0.16 cGy at 1m) travels parallel and perpendicular to the contact surface.

For external beam radiotherapy an Elekta Treatment System SL20 was used. With this accelerator is possible to produce electrons of 4, 6, 9, 12, 15, 18, 20 MeV. In this work 6 MeV electrons and a 10'10 cm^2 field were used.

The dosimeters system is composed by the reading device TN-RD50, produced by the Thomson&Nielsen Electronics, five dosimeters and a bias supply (+9V). The mosfets are not invasive dosimeters and have extremely reduced dimensions (2mm).

For brachytherapy, the dosimeters were calibrated using an Ir-192 source and circular applicator with a 30mm diameter. Calibration factors ($mV'cGy^{-1}$) were calculated using an equivalent water phantom with 200 cGy.

For the external beam the dosimeters were calibrated using 6 MeV electron beams. Calibration factors were calculated using an equivalent water phantom, 1 cm of build-up, with 200 cGy.

Results: The reproducibility for the external beam therapy is <2%, for the brachytherapy is <3% in agreement with the manufacturer specifications. For the linearity the correlation factor is <0.999 for both techniques.

Conclusions: The results show that the mosfet dosimeters can be used for different treatment modality and they are useful during in vivo dosimetry procedure also for special techniques as the brachytherapy.

652 poster

MRI CONTRAST MEDIA FOR IMAGE GUIDED BRACHYTHERAPY IN CANCER OF THE UTERINE CERVIX

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Purpose/Objectif: To demonstrate negative MRI contrast using paramagnetic manganese for image guided brachytherapy

Materials/Methods: A standard UK vaginal packing protocol for CT planned brachytherapy was assessed for CT and MRI discrimination (CT-Somatom, MRI-GEC). Ribbon gauze was soaked in iothalamate meglumine (Conray) and Proflavine cream 1% (Proflavine 1% BPC). The iodine contrast gives x-ray contrast on simulators and CT scans, but its water base gives high T2 MRI signal. This can obscure the GTV of tumour in the cervix. We added serial dilutions of manganese (Manganese Amino Acid Chelate, Nature's Best) until the excess T2 signal was suppressed.

Results: At manganese concentrations between 10 and 20mg/10ml, optimal contrast is produced on both CT and MRI.

Conclusions: Negative MRI contrast agents include chemicals such as magnetite albumin microspheres, superparamagnetic iron oxide and Perfluorochemicals. The advantage of negative MRI contrast materials is the lack of signal in the vaginal packing. This removes a source of ghosting artifacts from spin echo sequences that may be present with positive agents that can obscure the cancer in the cervix (which will usually show high T2 signal). The disadvantages of conventional negative contrast materials include their high cost and lack of general availability. Manganese will also suppress MRI signal, and is available at low cost in nutritional preparations. Combined with x-ray contrast and antiseptic in vaginal packing, both CT and MRI planning can be performed with discrimination of organs at risk and tumour GTV.

653 poster

MRI IN POST- PLANNING PROCEDURES AFTER PERMANENT SEED IMPLANTS

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Purpose/Objectif: Treatment post-planning has become an integral step in the process of prostate brachytherapy. The aim of this study is to prove the quality of MRI based post-planning after image fusion or with MRI alone. Different dosimetry parameters as the D90 (dose received by 90% of the target) and V100 (volume of prostate receiving 100% of prescribed dose) were considered.

Materials/Methods: Since October 2005 and after establishment of MRI in post-planning procedures in 17 consecutive patients with permanent seed implants, the post-planning was performed with MRI alone. The seed implants were done with J-125 Seeds of 0,618mCi (+0,09mCi), stranded Seeds (RAPID STRAND® / ISOcord® and the planning system VARISEED 7.1®. The median prostate size was 39,7ccm +10ccm; 54 +9,3 seeds were implanted.The seed detection was realized by manual seed recognition and the redundancy module integrated in the software. The MRI image fusion was managed by the software module. The matching of similar structures like pairs of seeds as a method of matched pair fusion. Eight pairs per patient were performed. The transfusion error (RMS; root mean square error), the homogeneity index (NDR; natural dose ratio), V100 and D90 as parameters was calculated. With the BEBIG S017 seed a fusion was not necessary. The seeds were clearly marked due to the halo effect on the T2 weighted TSE sequence (Image. 1). For other seeds the fusion with a T2 weighted FFE sequence was performed.

Results: MRI based post-planning results revealed a D90 of 159,8Gy (+13,6Gy). The parameters V100, RMS and NDR resulted in 93,2% (+2,7%), 0,65mm (+0,3mm) and 1.38 (+0,3). With the BEBIG S017 seed only one transversal sequence is necessary for the post-planning procedure. With other seeds a second data set for seed recognition is needed. If a image fusion was performed with two transversal MRI data sets the transformation error was below 1mm (0,69mm + 0,3mm).

Conclusions:MRI in terms of seed implant post-planning methods leads to optimized quality results and high precision. In MRI images shape and size of the prostate are marked excellent, which is an advantage in comparison to CT based post-planning. You can achieve very good image fusion results with a deviation fault less than 1 mm (0,65mm + 0,3mm; RMS). Results have to be further evaluated in a larger series.

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OPTIMIZATION OF THE LOCATION OF THE IODINE 125 SEEDS PER SCANNER FOR A TREATMENT OF PROSTATE BRACHYTHERAPY

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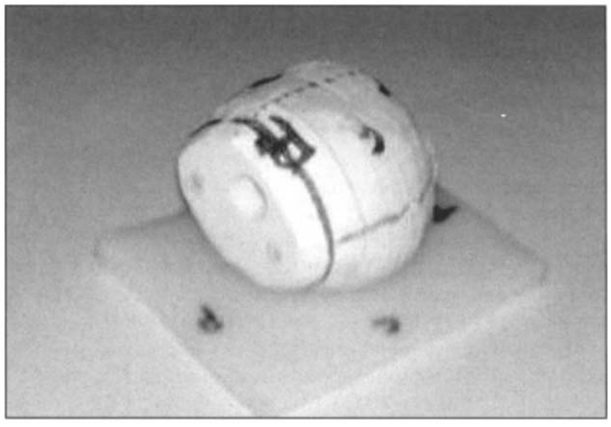
Purpose/Objectif: All the centers practising the prostate brachytherapy in France were contacted by phone, in order to know their scanner prtocols, the type of Iodine seeds and the software used. A data base, which gathers these various methods of procedure was created.Using a prostatic phantom, four softwares are evaluated according to the various types of existing seeds. The study scanner seeks the couples resolution-contrast which make it possible to get an optimal image. The physicist will able to re-use these data to obtain a better placement of the seeds in the prostate by the software and to improve their detection with the aim of optimizing his dosimetric study.

Materials/Methods: The plate of PMMA used to carry out this phantom is 5mm thick and has a density of 3 (density identical to that of water). The phantom is composed of eight cuts of different size ressemble at prostatic volume. In each section, holes of 0,8mm of diameter spaced of 1mm, 2mm, 4mm, 5mm and 1cm are drilled, in a right plan as well as in an oblique plan. About thirty Iodine 125 seeds are inserted in the latter.

For each type of seeds, the study on phantom is carried out under the same conditions as the center user. With preoccupations of reproductibility, the phantom must always remain in the same position at the time of its passage to the scanner. The space location of the seeds is carried out on a score of sequences for which, the parameters mA, KiloV, thickness and the number of revolutions are modified. The interpretation of the results evaluates the detection of these seeds according to the software of planimetry used.

Results: In scanner spiral mode, the images have many artefacts. The rebuilding adds seeds. The software recognizes them but places them randomly. We can then conclude that this mode is not an adequate technique whatever the other parameters used. In sequential mode, the thickness of cut and the step are identical. Under the same conditions as the centers called (thickness of 3,75mm, 5mm), for any kV or mA used, the software does not correctly count the 30 established seeds.

Conclusions: After analysis of the scanner images, we determine a trio (Kv, mA, thickness) for which the resolution is of the order of the millimetre. The results, in term of the type of seed and software of planimetry, will be communicated at the time of the congress.



655 poster

ORGAN – SPARING THERAPY IN PATIENTS WITH CANCER OF THE PENIS:A PILOT STUDY EVALUATING EARLY RESULTS AND TOXICITY AFTER PULSED-DOSE-RATE (PDR) - INTERSTITIAL BRACHYTHERAPY.

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Purpose/Objectif: To evaluate the efficacy and side effects of organ - sparing approach using PDR-interstitial brachytherapy (iBT) in patients with cancer of the penis.

Materials/Methods: From 8/2002 to 3/2006 we treated in our department 5 patients with cancer of the penis (cT1 - cT3) with PDR-iBT alone (3 patients) or in combination with external beam radiation (2 patients). The pulses 0, 50 - 0, 54 Gy were delivered 24 hours a day with a time interval of 1 hour between two pulses. In one patents we applied 12 Gy to the penis as boost and in 4 cases we applied a median dose 60, 98 Gy (range 60 - 64 Gy) as iBT alone. The dose prescription was done in all cases according the Paris system. We implanted 3 - 15 tubes or needles and the implant volume was in median by 18 cm^3. In 2 of 5 cases the patients received supplementing external beam radiation: one patient 46.8 Gy to the penis and one patients 50,4 Gy to the separate target volume of regional inguinal and iliac lymph nodes. 3/5 patients were also treated with simultaneous cisplatin-based chemotherapy either during the time of the iBT or the external beam irradiation. A follow-up of all patients was done closely to analyse local control, acute and delayed toxicity. The analysis was performed after median follow-up of 2 - 45 months (median 6 months).

Results: No patient received recurrence in the treated area. Only one patient presented a second tumour by the date of analysis. Now the tumour was located in the left corpus cavernosum with no connection to the first localisation (glans penis). No intra or post operative complications like penis infection or haematoma were recorded. Acute toxicity was registered as mucositis grade 2 in all patients. No serious late toxicity was observed. In all patients no erectile dysfunction was reported.

Conclusions: The results of this prospective pilot study confirm the previous results of LDR-brachytherapy and suggest that also the interstitial pulsed-dose-rate brachytherapy with or without chemotherapy for patients with cancer of penis is an effective organ - sparing therapy with minimal toxicity.

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PALLIATIVE COMBINED TREATMENT BY HIGH-DOSE-RATE BRACHYTHERAPY (HDR-BT) AND STENTS IN PATIENTS WITH ESOPHAGEAL CANCER.

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Purpose/Objectif: HDR brachytherapy (HDR-BT) in treatment of esophageal cancer most often has a palliative character. When esophageal cancer is great enough to make using of intraluminal brachytherapy impossible it is still chance to help patients by insertion of a metal stent into the lumen of esophagus. Stents have proved to be a reliable way to alleviate dyphagia, which, without treatment, leads to a poor quality of life and rapid weight loss. The prognosis for such patients is still not satisfactory, even though combination of HDR brachytherapy and metal stent using seems to be the best palliative treatment in such kind of cancer. The aim of this work was to analyze the results of palliative HDR-BT connected with stent insertion in patients with advanced esophageal cancer.

Materials/Methods: Fifty patients with unresectable, advanced esophageal cancer were treated palliatively with intraluminal HDR-BT from June 2001 to December 2005 at the Greatpoland Cancer Center in Poznan . All patients enrolled in this study were also treated by metal self-expanding stents because of the obturation of the lumen. The mean age was 59.3 years (ranged: 44-79 years). 82% of treated patients were men. The mid-third of the esophagus was involved in 30 patients (60%) and 40 patients (80%) had length of tumor <10 cm. 40 patients (80%) received brachytherapy alone, whereas the remaining 10 patients (20%) received additionally external beam radiotherapy (EBRT) and chemotherapy. 36 patients received 3 fractions (one fraction per week) of 7.5 Gy up to total dose 22.5 Gy, 14 patients 2 fractions of 7.5 Gy. EBRT consisted total dose 20 Gy given in 5 fractions. 2 patients had distant metastases (liver and brain), 4 patients had secondary malignant tumor in different localization in the past.

Results: Median observation time for this group of patients was 5.4 months. A longer median observation time was observed when tumor size was less than 5 cm (6.1 months), than in a group with tumor longer than 10 cm (4.9 months). Overall improvement in swallowing status was seen in 33 patients (partial and complete remission - 66%) in 4 weeks after the end of treatment. Overall early complication rate was 22% with ulceration seen in 1 patients (2%), bleeding in 1 patients (2%) and tracheo-esophageal fistula in 9 patients (18%). We have not observed any significant correlations between previous external radiation treatment and higher complication rate. Apart from that, median overall survival was shorter (3.5 months) for the group with tracheo-esophageal fistula.

Conclusions

1. Insertion of stent allowed in many cases use of HDR-BT. 2. High-dose-rate brachytherapy connected with placement of self-expanding stents has a good, but a short- term palliative effect of diminishing dysphagia in patients with malignant esophageal strictures. 3. These two modalities of treatment achieves good palliation with acceptable rate of complications which is similar to those observed after single radiotherapeutic treatment.

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PERIOPERATIVE HIGH DOSE RATE (HDR) BRACHYTHERAPY IN MULTIMODALITY TREATMENT OF PAEDIATRIC MALIGNANT TUMOURS - A FEASIBILITY REPORT

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Purpose/Objectif: In an effort to minimize toxicity from normal tis-

sues such as growth retardation or second primary tumours brachytherapy (BT) has recently been used for six children with malignant tumours at the Karolinska University Hospital, Stockholm . An intraoperative approach was used with the advantage of a more precise mapping of areas at risk for malignant clonogen dissemination, i.e. definition of the clinical target volume CTV. Compared to external beam therapy (EBRT) brachytherapy avoids safety margins for set-up uncertainties and provides a rapid fall-off of dose from the target volume.

Materials/Methods: Between June 2004 and April 2006 6 children (4 girls and 2 boys) have been treated with brachytherapy at Radiumhemmet. Their age at treatment was 10-37 months. BT was for the children used as part of a multimodality program with cytoreductive chemotherapy, EBRT when indicated (Table) and conservative surgery including the BT procedure.

The CTV was covered with parallel interstitial catheters placed in a single plane, at intervals of 1.0-1.5 cm with a margin of 0.5-1.0 cm in all directions. For one child a mould was used. Catheters were attached at the skin with plastic buttons and silk sutures, the latter obligatory when catheters with blind ends were used. Once the implant was performed, the surgeon proceeded with closure of the surgical defect.

While still anaesthetised the child was then taken for a CT examination. The CT slices were imported into our dose planning system (Plato 14.2.10, Nucletron, the). An individual 3D dose plan was made and exported to the treatment machine (HDR micro-Selectron, Nucletron, the). All treatments were performed twice daily with HDR brachytherapy. The dose per fraction was 3.0-3.3 Gy and the total dose was 18 - 36 Gy. Most treatments were performed under mild sedation.

Results: After a follow-up of 2 - 20 months all are alive with no evidence of local recurrence except in one child who had a local recurrence in the margins of the volume treated by EBRT.

Conclusions:

Brachytherapy remains an elegant way of selectively delivering a high dose to a small volume also in children. Compared with external beam therapy brachytherapy could induce less long-term sequelae.

Case nr	Diagnosis	Target	Nr of cath-eters	EBRT Dose Gy	BT HDR Gy	BED α/β=3	BED α/	Out-
1	rhab-domysar-coma	bladder	5	18 pre BT	17.7	36	23	DFS
2	rhab-domysar-coma	orbit	4		18	36	23	DFS
3	teratoma	presacral	5	18 post BT	18	36	23	LC after sal-vage
4	rhab-domysar-coma	parap-harynx	1		29.7	62	39	DFS
5	retinoblas-toma	orbit	4		26.4	55	35	DFS
6	squamous cell ca	auditory meatus	3		36	72	46	DFS

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PRACTICAL RECONSTRUCTION METHOD FOR 3D CT-BASED BRACHYTHERAPY WITH SHIELDED COLPOSTATS

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Purpose/Objectif: The most extended worldwide HDR and PDR afterloading machines are from Nucletron, using the Plato Treatment Planning System (TPS) to perform the clinical dosimetry. The Fletcher-Williamson (FW) vaginal colpostat applicators are widely used with these machines, they are made of a very dense material (densimet-17) which allows shielding up to 50% of the dose. Almost all the TPS have incorporated the CT-Based Brachytherapy (BT), in which the CT catheters and applicators reconstruction is based on contiguous CT transverse slices where the user points the catheter position. The problem with these applicators is the production of artefacts that makes the reconstruction impracticable. CT Orthogonal Scout Views or scanograms (OSV) to reconstruct sources in Brachytherapy, have been well described (Meli 1995, Yue 1999). The purpose of this work is to incorporate the OSV reconstruction method to the PLATO TPS.

Materials/Methods: We have taken profit of the fact that the TPS keeps the CT coordinates. A spread sheet has been developed to reconstruct the FW from OSV. The advantage of this method is that the obtained catheter coordinates are referred to the CT coordinates. The obtained OSV points are introduced on TPS as markers in the contouring routine because the TPS does not allow direct catheter coordinate input. Even in the catheter reconstruction routine it is easy to follow the markers to recognize the catheter within the FW. Some phantoms have been built with pellets to check the procedure accuracy.

Results: The global OSV accuracy obtained with the phantom tests is estimated to be within 1 mm. Significant step by step examples will be shown.

Conclusions: The method is easy and feasible for Plato TPS users, and not only for shielded colpostats but also for implants quasi parallel to the CT slices as breast implant.

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PROSTRATE BRACHYTHERAPY USING I-125 IMPLANTS: RESULTS IN 120 PATIENTS

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Purpose/Objectif: The planning target volume (PTV) for early prostate cancer should be the prostate gland. Therefore, brachytherapy is one of treatments of choice.

Materials/Methods: December 1999 to January 2006, 120 pts with early prostate cancer underwent transperineal I-125 implants. The brachytherapy was done in two separate stages: prostate volume study and the implant, usually with a two week interval. Both were done in the operating theater, with epidural anesthesia and in Lithotomic position. A CT scan for dosimetry was done, one month later.

Patient's characteristics: Median age 68.5, 62 pts - T1C, 52 - T2A and 5 T2B, Gleason 5 (2+3) - 10 pts, 6 (3+3) - 104 pts and 7 (3+4) - 6 pts, median serum PSA 6.6, median prostate volume before implant 30ml (range 14 -57), median IPSS 6. 57 pts received hormonal therapy,2 injections of LHRHAA, before the implant for reducing prostate volume.

Treatment: The prescription dose for PLV was 140Gy. Median number of seeds per implant was 84 (range 58-117).

Results: Median serum PSA at 3, 6, 9, 15, 30, 24 and 36 months post-implants was: 0.7, 0.7, 0.5, 0.6, 0.6, 0.6, 0.6ng/ml, respectively. 8 pts received hormonal treatment because of increase in serum PSA. No

patient suffered from clinical relapse. All pts suffered from acute uretheritis and 14 developed temporary acute urinary retention which was resolved by conservative treatment, except one who needs TUR-P. One patient suffered from proctitis.
Conclusions: I-125 implant is an effective and tolerated treatment for patients with early prostate cancer.

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PULSE-DOSE-RATE (PDR) BRACHYTHERAPY AS MONOTHERAPY FOR LOCALIZED PROSTATE CANCER. FIRST EXPERIENCES REGARDING FEASIBILITY, TOXICITY AND OUTCOME.

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Purpose/Objectif: Low-dose-rate brachytherapy using permantent implants of ^{125}I or ^{103}Pd seeds is known to be an effective treatment of localized prostate cancer. There is only few data using temporary implants with high-dose-rate or pulse-dose-rate brachytherapy as monotherapy for localized prostate cancer. We report from our first experience using pulse-dose-rate brachytherapy as monotherapy for localized prostate cancer.
Materials/Methods: Patients were eligible for treatment with PDR-brachytherapy with stage T1 - T2b tumors. Transperineal ultrasound guided implantation was performed under general or spinal anesthesia following PDR-brachytherapy with a single pulse dose of 0.65 Gy/h, 24 pulses a day up to a dose of 32.5 Gy. The procedure was repeated after two weeks up to a total dose of 65.0 Gy.
Results: From 8/2003 till 4/2006 we treated 26 Patients with localized prostate cancer (T1a 6 %, T1c 29 %, T2a 53 %, T2b 12 %) with PDR-brachytherapy. Treatment was performed as planned in all patients, no severe complications occurred during the brachytherapy procedure. Grade 3/4 proctitis or severe urinary symptoms did not appear. After a median follow up of 10 months we have noticed no biochemical relapse.
Conclusions: PDR-brachytherapy as monotherapy is a feasible treatment for localized prostate cancer associated with minimal acute toxicity. Longer follow-up is needed to evaluate late toxicity and biochemical control.

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PULSED DOSE RATE BRACHYTHERAPY IN THE TREATMENT OF UNRESECTABLE BILE DUCT CANCER

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Purpose/Objectif: To assess the feasibility of intraluminal Pulsed Dose Rate (PDR) brachytherapy in the treatment of locally advanced bile duct cancer. Early results and a new trans-hepatic technique are reported.
Materials/Methods: Seventeen patients with advanced bile duct cancer were treated using trans-hepatic technique between May 2003 and December 2005 in Greatpoland Cancer Center . Four patients was treated with combined treatment: brachytherapy and external beam therapy, 13 exclusively with brachytherapy. Percutaneous trans-hepatic technique was used to implant catheter into bile duct. Brachytherapy was started in the same day after insertion of intraductal catheter. A French 5 catheters (Nucletron®) were used. Patients received in all cases 25 pulses of 0.8 Gy hourly, total dose for one treatment phase was 20 Gy. In 13 cases they received one phase, in 4 cases - two phases of 20 Gy. Target Volume encompassed tumour visualized at cholangiography and a 1 or 2 cm margin taken proximally and distally. Dose was prescribed at 10 mm from the source axis. In second phase of combined treatment - external beam therapy 15 MV photons were used. Four patients received 40 Gy in 20 fractions of 2 Gy daily.
Results: Longest overall survival time (OS) and Disease Free Survival Time (DFS) was 36 months, shorter - 2 months. It has been established, that the use of Pulsed Dose Rate brachytherapy was feasible and had a low early complication rate. A new percutaneous transhepatic technique allowed to perform whole treatment (insertion of catheter, PDR brachytherapy) in one day.

662 poster

QUALITY ASSESSMENT OF BRACHYTHERAPY TREATMENTS PLANS - TWO YEARS EXPERIENCE

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Purpose/Objectif: Images from CT, US or MRI are nowadays the definitive support of most brachytherapy techniques. They allow the guidance and the reconstruction of catheters and applicators, as well as the delineation of the target and organs at risk. The treatment plan evaluation is based on calculated dose distributions, dose-volume histograms and dose volume indexes. The purpose of this work is to present the results of two years experience (2004-2006) concerning the quality assessment of brachytherapy treatment plans based on dose-volume indexes in three pathologies: gynaecology and breast (HDR) and prostate (LDR).
Materials/Methods: For HDR treatments, a microSelectron-TCS unit and Plato BPS, version 14.2.4. both from Nucletron, were used. Regarding breast treatments the Comfort (Nucletron) catheter system was used. For LDR prostate implants two different techniques have been used: intra-operative treatment planning using VariSeed (Varian) version 7.1 with RapidStrand 6711 Amersham seeds, from January 2004 until February 2006, and real time planning using FIRST (Nucletron) system with Isotron loose seeds, since March 2006. Treatment reporting is done according to international recommendations. In what concerns the treatment plan acceptance, a set of criteria have been defined by the clinicians regarding the values of selected dose-volume indexes for each pathology.
Results: In what concerns the prostate treatments, considering the intra-operative planning, the clinical acceptance criteria were fully respected. Dose-volume indexes evaluation at the time of the post implant dosimetry (day 30) showed some discrepancies (D_{90}) with the intra-operative values. The cause is directly related with the difference in prostate volumes (US_implant vs CT_post implant). Those discrepancies are also related with the development of a normal learning curve and are consistent with other published results. Regarding breast treatments, with the methodology followed, we have been able to fulfil the clinical acceptance criteria for the treatment plans, including conformity indexes above 0.6. For the gynaecologic pathology, the dose delivered to points AA is still the main factor determining the clinical acceptance of the treatment plans. The target volume is not yet delineated. The dose delivered to the organs at risk has been reported in order to assess the correlation between radiation dose and normal tissues effects.
Conclusions: The locally adopted methodologies accomplish the international recommendations for modern brachytherapy techniques. The calculation and the report of dose-volume indexes, allowing the assessment of treatment plans quality, lead the changing of practices with confidence. Also, the correlation with treatment outcome has been reinforced allowing the further implementation of new brachytherapy techniques and a more consistent follow-up of patients.

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QUANTIFICATION OF INTEROBSERVER VARIATION IN DELINEATION OF TARGET VOLUMES USING THE GEC –ESTRO RECOMMENDATIONS FOR MRI BASED BRACHYTHERAPY OF THE CERVIX.

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Purpose/Objectif: This work describes an interobserver study designed to assess and quantify variability in target definition based on the recently published recommendations of the GEC-ESTRO Gyn 3D Network for MRI based brachytherapy of the cervix uteri.

Materials/Methods: 30 participants from 10 countries and 12 centres gathered in Dublin in December 2005. Following a series of lectures under the direction of the University of Vienna the participants were divided into 8 groups. Each group was asked to delineate GTV_{BT}, HRCTV and IRCTV on three patients chosen to represent typical clinical situations. All cases had full pelvic MRI while one case had CT and MRI. The data was subsequently analysed in terms of volume analysis and 3D spatial variation. Finally an attempt was made to quantify the extent of systematic uncertainty introduced by calculating an isotropic margin to grow the HRCTV to a HRPTV using the Dose Population Histogram method of van Herk.

Result: GTV_{BT} demonstrated the largest variation in volumes with a coefficient of variance (COV, s/m) ranging from 0.4-0.6. HRCTV and IRCTV results were similar (0.35-0.15). The 3D shift of geometric centre was calculated for HRCTV and found to range between 1.8 and 6.2 mm. For HRCTV the standard deviation between centres was greatest in the right and left lateral (1 std dev; 5-15 mm) and the cranial direction (1 std dev; 6-10 mm). The ratio of common to encompassing volume ranged form 0.15 to 0.31 for HRCTV and IRCTV. Margins of 8 mm in the Ant/Post directions 16mm in the lateral directions and 17 mm in the crano/caudal directions were calculated.

Conclusions: The study reveals large variation between groups for all volumes. It illustrates the need for significant training in the use of MRI scans for the identification of gynaecological structures and the importance of radiological support. The application of margins remains a point of controversy between the authors. The results serve however as a comprehensive benchmark from which further improvement in technique can be assessed.

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RADIOACTIVE GOLD GRAIN IMPLANTATION FOR PATIENTS WITH CARCINOMA OF THE ORAL TONGUE

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Purpose/Objectif: To review our experience of radioactive gold grain implantation alone or in combination with external-beam irradiation (EBRT) for superficial or exophytic carcinoma of the oral tongue.

Materials/Methods: Between June 2000 and September 2003, 20 patients with non-metastatic squamous cell carcinoma of the oral tongue were treated by gold grain implantation. Of 20 patients, 1 patient had bilateral lesions. 10 lesions were T1 and 11 were T2. 14 patients with superficial lesion were treated by gold grain implantation alone and 7 patients with exophytic lesion were treated by gold grain implantation in combination with EBRT (20-30 Gy/10-15 fractions). The average permanent implant dose (total decay) in the primary lesion by brachytherapy (BT) was 79.2 Gy (80.1 Gy for patients receiving BT alone and 77.4 Gy for those receiving combined BT and EBRT).

Results: At a median follow-up 44 months (range 21-61 months), 4 patients had failure locally. The 3-year local control rate was 81 %. Of 4 patients, 2 patients received re-irradiation (gold grain implantation), 1 patient received partial resection and the remaining received no further treatment. The 3-year local control rate was ultimately 95 %. 4 patients developed neck lymph-node metastasis. The 3-year cause-specific survival rate was 90 %.

Conclusions: Radioactive gold grain implantation alone or in combination with EBRT was found to be efficacious for superficial or exophytic carcinoma of the oral tongue.

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REIMPLANTATION FOR SUBOPTIMAL PROSTATE IMPLANT. FEASIBILITY STUDY.

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Purpose/Objectif: To demonstrate the feasibility of reimplantation in case of focal underdosage after I125 prostate implant in 4 patients.

Materials/Methods: 300 patients presenting low-risk prostate cancer were treated with brachytherapy from 7/2000 to 12/2005 with I125 loose seeds and real-time dosimetry. The prescribed dose was 160 Gy. Dosimetric evaluation was performed for every patient 30 days later. The median D90 was 158 Gy (range 97-222), the median dose to 30% of the urethra 210 Gy (122-395), and the median rectal volume receiving 160 Gy 0.28cc (range 0-3.9). 4/300 (1.3%) had a D90 less than 120Gy and were found focally underdosed.

A reimplantation of the underdosed region was planned. The reimplant was preplanned on the first post-implant CT image to deliver 160 Gy. The positions of needles and seeds were superimposed on the TRUS images of the first implant, which allowed to define the positions according to the grid. The seed's strength was determined according to the volume of the underdosed region.

The second implant was performed with TRUS, using XR views to verify the position of the needles according to the initial implant. A second CT scan was realized 30 days later to evaluate the final dosimetry.

Results: The dosimetric results after reimplantation available for 3 patients at the moment were as follows: D90 161, 177 and 141 Gy, dosimetric values after the first implant being respectively 119, 116, 102 Gy ; dose to 30% of the urethra 195, 375 and 242 Gy, first implant values being 163, 275,184 Gy ; rectal volume receiving 160 Gy 1.25, 1.4, 0.05 cc, first implant values being 0.87, 0.79, 0.01cc.

This represented a mean increase of 47Gy to the D90, 63Gy to 30% of urethra, and 0.36cc of rectum receiving 160Gy.

The final D90 values were superior to 140 Gy in every case, while doses remaining acceptable for organs at risk, except for patient number 2 for whom the urethral dose became higher than usually tolerated.

Acute toxicity was moderate. IPSS score slightly increased (7 points) in 2 patients, one month following the second implant, and returned to the anterior value within 3 months. No patient complained of a change in sexual activity or presented signs of rectal injury.

Conclusions: Reimplantation after prostate brachytherapy is feasible in case of sub-optimal implant, when a focal underdosage is obvious.

Dosimetric results after the second implant appear satisfactory, but

great care has to be taken to limit the dose to the urethra.
Acute toxicity is acceptable, with return to baseline in all cases.
The impact of this second implant on the biochemical disease-free survival remains to be evaluated.

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RELATED TOXICITIES AND RESULTS IN POSTOPERATIVE LOW-DOSE-RATE (LDR) AND HIGH-DOSE-RATE (HDR) BRACHYTHERAPY (BRT) IN STAGE I-II ENDOMETRIAL CANCER PATIENTS (PTS)

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Purpose/Objectif: To compare toxicity and results of adjuvant LDR and HDR BRT in stage I-II occult endometrial cancer.
Materials/Methods: Between October 1989 and December 2005, 207 stage I-II endometrial cancer patients (pts) underwent postoperative vaginal cuff BRT. LDR BRT was administered to 126 pts; from October 2002, 82 pts had HDR BRT. Median age was 61 years (range 40-81) for LDR and 62 (range 42-82) for HDR group. For all, surgery consisted of total abdominal hysterectomy and bilateral salpingo-phorectomy; lymph node sampling or dissection was done on 36 (28,6%) LDR pts and on 35 (42,7%) HDR pts. All nodes resulted negative. The principle histology was endometrioid adenocarcinoma in both groups. Stages were: 9 IA, 72 IB, 33 IC, 4 IIA for LDR; 3 IA, 48 IB, 29 IC, 2 IIA for HDR. LDR BRT was administered through two Cesium 137 sources charged on personalized endovaginal moulds; dose was 50 Gy at 5 mm depth. HDR was administered utilising an Iridium 192 source, charged on standard applicators, the dose was 21 Gy at 5 mm depth, administered in 3 fractions weekly.
Results: Median follow-up was 94 months (range 38-213) for LDR group and 23 (range 6-45) for HDR group. RTOG/EORTC scale was used to evaluate toxicity. G1-G2 acute toxicity was observed in 16 pts (12.7%) in LDR group and in 17 (20.7%) in HDR group (p= 0,0371). Generally, toxicity consisted of diarrhea and cystitis in LDR group, 4.8% and 4.8% respectively; in HDR group cystitis and vaginal mucositis were 13.4% and 12.2% respectively. Late toxicity G1-G2 was observed in 8 pts (7.4%) in the LDR group and in 18 pts (21.9%) in the HDR group (p= 0,8711). Mostly, late toxicity consisted of slight-moderate atrophy and dryness of vagina and mucous teleangiectasia both in LDR and in HDR pts. Two LDR pts had chronic G4 toxicity: 1 had a recto-vaginal fistula and 1 a rectal necrosis. There was no observed G3-G4 toxicity in HDR group.
In the LDR group 3 pts had nodal relapses, 5 distant metastasis and 3 nodal and distant relapses. No pts had local or distant relapse in the HDR group.
Overall survival and disease-free survival at 3 years were 81,5% ± 3,5 and 89,6% ± 2,9 for LDR and 96,9% ± 2,2 and 98,4% ± 1,6 for HDR, respectively. A statistical significant difference between the two groups was observed (p= <0,0001) favouring the HDR group.
Conclusions: Acute G1-G2 toxicity in HDR pts was superior to LDR pts; this could be due to better follow-up information that was recorded in the HDR group. Late toxicity was similar in both groups. No local or distant relapses in HDR group have been seen and overall survival and disease free-survival has been better in this group, however a longer follow-up is needed. This difference could be due to better imaging and surgical staging done in the latter pts accrued. Vaginal BRT is a safe and effective adjuvant treatment for intermediate-high risk endometrial cancer pts, particularly when optimal staging is performed.

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TECHNICAL FAILURES OF PDR BRACHYTHERAPY AFTERLOADER

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Purpose/Objectif: The aim of this work is to analyze technical failures of the Nucletron's microSeletron PDR brachytherapy afterloader, during the first 150 breast tumour treatments.
Materials/Methods: In June 2005 our instituition starts the pulsed dose rate (PDR) technique for breast intersticials implants, and since then 150 patients were treated, 146 as boost and 4 as complete treatment. The ^{192}Ir source has a maximum activity of 0.5 Ci, and treatment dose rate were between 80 to 100 cGy/h, with 1 hour pulse period.
The microselectron PDR system consists of several components, in a network: treatment plan station, treatment control station, treatment control panel, emergency system, nurse station display, treatment light system, radiation monitor and door control. The system has three types of alert: infos, errors and warnings.
In this study all patients were implanted with rigid needles, with an average number of 6 (in a range of 4 to 9) and an average number of pulses of 19 (in a range of 16 to 46).
In this evaluation, we will quantify the number of treatements that ended successfully and all interruptions that happened, and we will quantify the interruptions that were made by human errors (obstruction of check-cable and source because of bad patient positioning or connection) and by software and hardware problems.
Results:
The next table shows the results, based in the level alerts, being the statistics of communication errors averaged with number of patients treated (150), and the physical errors (obstructions and fricctions of check-cable and source) averaged with the number of times that the source came out (17.400), for the same number of patients.

Level of alert	Kind of failures	N	%
Info	Obstructions detected for check-cableLost of communication	464	0.32.7
Error	Fails of transmissionLost of communication	89	6.05.3
Warning	Failure of source controlObstruction detected for source	55	3.30.0

The level of success treatments was 99.3% (only one patient in 150 has not concluded treatment successfully), 51.3% ended with one or more fails and 48.7% have finished without any failure alert. When we do not take into account human errors, we find that 17.3% of the treatments ended with one fail and 82.7% have finished without any failure alert.
Conclusions: The main conclusion is that this version of microSelectron PDR has high levels of success, and the main number of failures have easy solution. We also concluded that the human action rizes the number of failures, leading to a high level of quality control protocol.

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THE ADVANTAGES OF LDR BRACHYTHERAPY IN MODERN MULTIMODAL TREATMENT OF BREAST AND UROGENITAL CANCER.

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Purpose/Objectif: The appearance of new generations of brachytherapeutic equipment and technologies based on using of new radioactive sources with high and middle dose rates, made us to eval-

uate the significance of LDR brachytherapy in modern conditions of treatment when we can choose the variant of brachytherapy.
Materials/Methods: 157 patients, 32-84 y.o., were included, 73 of them - with breast cancer T1-2No-1Mo, 70 - with gynecological tumors (38 primary untreated patients with vulva cancer T1-3N0-1Mo, 32 patients have recurrent gynecological tumors in vagina or vulva), 14 pts. with T1-3N0-1Mo cancer of penis.
Results: In 73 patients with breast cancer segmental mastectomy, axillarian lymphadenectomy with interstitial brachytherapy (LDR Microselectron afterloading equipment, Cs-137) as boost, was fulfilled. Dose rate 60-90 sGyh, during 15-17 hours, total dose of 10Gy (80% isodose). On the 12-15-th day we began whole-breast RT, axillarian lymph nodes area included, total dose (TD) of 50Gy. In patients with axillary node involvement supra-subclavicularian lymph nodes area was treated, TD of 44-46Gy. The duration of observation 44,3+1,3mnth., 3-5-year DFS 95,1+3,2%, 90,1+5,9%. In 70 patients with gynecological tumors and 14 pts with penis cancer simple afterloading technique (Co-60 LDR needles with increased activity at the ends) were used. Dose rate 58-80sGyh, during 36-58 hours, TD of brachytherapy 25-40Gy. In 38 patients with vulvar cancer LDR brachytherapy was the last step in multymodal programme of treatment included: local or intravenous chemotherapy, external RT 3Gy fraction, TD 39-42Gy(45-50Gy equivalent). In 32 patients with recurrent gynecological tumors in vagina or vulva LDR interstitial brachytherapy had been combined with HDR vaginal brachytherapy (HDR AGAT-VU, Co-60), 3-5Gyfraction, TD 21-30Gy andor external RT, 2-3Gyfraction, TD 39-42Gy. The minimal size of needles (active length 1,0sm, diameter 0,3sm) and individually prepared fixative plates gave an opportunity to treat solitaire or several tumors 0,5-2sm^3 with complex geometrical configuration, located in different parts of vagina and vulva, near urethra, rectum, where it was impossible to use remote afterloading techniques Co60 HDR. Full regression was registrated in 6 (18,7%), partial regression - in 14 (43,7%), disease free interval (DFI) 4-46 mnth. 14 pts with penis cancer received organ-conservative treatment where external beam RT of penis and ileo-inguinalis LN area, 2-3Gyfraction, TD 20Gy) had followed by Co-60 LDR brachytherapy (60-80sGyh, TD 40Gy). The duration of observation 12-120mnth., no local recurrence, urolgenital disorders, erectil disfunction had been registrated.
Conclusions: LDR interstitial brachytherapy occupies its own important place in modern multimodal treatment of breast and urogenital cancer, insures adequate medical and economical results of organ-conserving treatment and DFI with low rate of complications and high level of life quality.

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THE CORRELATION BETWEEN VAGINAL CUFF DOSES AND VAGINAL VAULT COMPLICATIONS IN PATIENTS WITH CANCER OF THE UTERINE CERVIX, TREATED WITH HIGH DOSE RATE (HDR) BRACHYTHERAPY (BT)

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Purpose/Objectif: While a correlation between vaginal cuff doses and vaginal vault radiation induced complications has been documented for LDR BT, there is a lack of data concerning the definition of vaginal dose and correlation with vaginal cuff tolerance in HDR BT. The purpose of this analysis is to correlate the vaginal cuff doses with vaginal vault complications in patients treated by EBRT and HDR BT for cervical cancer.
Materials/Methods: A cohort of 50 consecutive patients with carcinoma of the uterine cervix who were treated between May 1998 and May 2002 with a combination of external beam radiotherapy, concomitant weekly cisplatin for 5 cycles and HDR BT, form the basis of this analysis. Average age was 59.6 years (38-93). Average time from completion of the treatment to assessment 50,7 ±19.8mo. All patients were FIGO stage IB2-IIIB. HDR BT was performed using a "Fletcher Suit"-like applicator. Doses to the vaginal mucosa were assessed using 2 sets of points for each ovoid. (The dosimetric method has been described in a previous publication). Total doses for the whole EBRT and brachytherapy at the vaginal points were calculated for each patient. Patients were examined every 4 months during the first two years and then biannually. During each visit, patients were asked to report all details concerning bowel, urinary and sexual function.Toxicity was assessed at 2 years and at 4 years following completion of treatment, using the EORTC - RTOG toxicity score.
Results: Average dose to the vault was 10275 cGy ± 1143 cGy (range: 7928 - 14251 cGy). Grade 0-1 toxicity to vaginal vault was observed in 37 patients, grade 2 in 5 patients and grade 3 in only one patient. Toxicity could not be assessed in 7 patients due to early recurrence or surgical interventions. With these dose levels, a correlation between vaginal vault doses and toxicity was not found.
Conclusions: As has been shown for LDR BT, in the absence of severe toxicity at the vaginal vault using HDR-BT, it is suggested that doses in excess of 14251 cGy to the vaginal vault can be delivered when indicated. The maximal doses should be assessed by further studies.

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THE CUMULATIVE TRANSIT DOSE COMPONENT IN PULSE DOSE RATE BRACHYTHERAPY: MEASUREMENTS AND RESULTS FROM THE INSTITUTE OF ONCOLOGY, LJUBLJANA, SLOVENIA

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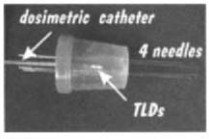
Purpose/Objectif: Current brachytherapy treatment planning systems do not account for the transit doses but calculate dose only from the source dwell positions. We measured the cumulative transit dose of Ir-192 PDR of nominal activity 1Ci (37 GBq), using the calibrated TLD micro rods. The cumulative transit dose was measured at distance 1 cm from the needle.
Materials/Methods: The phantom filled with meat was holding the needles and the dosimetric catheter. The two TLD LiF-100 micro rods (f=1mm, length=4 mm) were used for the transition dose measurements. The TLDs were calibrated with the dose 100 cGy. At the cumulative transit dose measurements four 20 cm long needles were placed in the phantom 1 cm away from the centrally positioned dosimeters. The only dwell positions of the source were at the tips of the needles and were as short as possible. Ten (10) irradiation pulses were performed. Under those conditions the dose measured with TLDs corresponded to the transit dose delivered with the treatment of 40 pulses at the distance 1 cm away from the needle. The activity of the source at the day of the measurement was 0.75 Ci (27.8 GBq) ie 1.33 times lower than the nominal activity.
Results: The cumulative transit dose of forty pulses delivered with the Ir-192 source of the activity 1.33 times lower than nominal, was **10 cGy** measured at the distance 1 cm away from the needle.
In PDR treatments with Ir-192 the fresh sources are of nominal activity and they are replaced no longer as the activity drops 3.3 times. The cumulative transit doses of 40 pulses at the distance 1 cm away from the needle are the highest with the fresh source of nominal activity 13.3 cGy and the lowest is just before the source replacement 4.4 cGy.
Conclusions: To calculate the transit dose at other than measuring positions the Sievert integral was applied. We established that already 2 mm from the needle the transit dose can be expressed as a reciprocal function of distance within 5% accuracy. In reciprocal approximation the transit dose as a function of the distance from the needle is: Dt (d) =a n/d f

Dt.. transit dose; a..measured transit dose per pulse = 0,332 cGy; n...number of pulses; d...distance from the needle; f...factor of the source decay (1 to 3.3);
The transit doses in PDR brachytherapy are not completely negligible as for example at treatment with 40 pulses with the source of activity 1.33 times lower than nominal, the transit dose in the tissue 2 mm away from the needle would be more than 0.5 Gy and 5mm from the needle would be more than 20 cGy.



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THE INFLUENCE OF APPLICATOR ANGLE ON 3D DOSIMETRY IN VAGINAL VAULT BRACHYTHERAPY FOR ENDOMETRIAL CANCER

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Purpose/Objectif: Does the angle of insertion of the vaginal applicator for vaginal vault HDR brachytherapy impact on the bladder and rectal doses when they are reported according to the new GEC-ESTRO guidelines for image guided brachytherapy?
Materials/Methods: We looked at 30 consecutive patients undergoing vaginal vault HDR-brachytherapy as adjuvant treatment for endometrial cancer. For their first insertion, patients were catheterised, and examined internally to determine a suitable vaginal cylinder size. The cylinder was inserted and clamped in place so that it lay at its natural angle. Patients then underwent CT scan, in the treatment position (lying supine with legs down). Using the Brachyvision planning software, the angle of the cylinder was measured in relation to the couch top. OARs (rectum and bladder) were outlined on each CT slice. DVHs were produced and we have reported the dose to $D_{0.1cc}$, D_{1cc} and D_{2cc} for rectum and bladder.
Results: The cylinder size used ranged from 2.3 to 3.5 cm. The angle of the cylinder ranged from -17.1° to +13.8° (negative prefix indicates an applicator angled posteriorly positive prefix indicates one angled anteriorly), with a mean angle of -2.99°. The difference in mean rectal dose between the most posterior and the most anterior cylinders was less than 5%. The difference between the mean bladder doses was almost 17%, although the actual values were 23.5% and 40. 3% for the most posterior and anterior cylinders respectively.
Conclusions: From our limited study, there does not seem to be any evidence to recommend that the vaginal applicator needs to be held in a horizontal position. We would advocate allowing the cylinder to lie in the natural position, which may well be the most comfortable position for the patient. There may also be a benefit in that it may decrease the likelihood of the mucosa being pulled away from the applicator surface and causing underdoses. This becomes particularly important when we consider that the target volume is less than 5mm from the applicator surface.

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THE THERASIGHT TRIAL: A FEASIBILITY AND SAFETY STUDY OF THE THERASIGHT R OCULAR BRACHYTHERAPY SYSTEM FOR TREATMENT OF AGE RELATED MACULAR DEGENERATION

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Background: Age-related macular degeneration (AMD) is the leading cause of blindness in people 65 years if age or older. The use of brachytherapy as a treatment was previously tested in a randomized trial using a Strontium applicator by Jaakolla et al. This study showed a benefit on visual functionat 6 months that was lost by 12 months of follow-up. The premimse for building the TheraSight® device and initiating the TheraSight trial was that treatment to a larger area with a high dose using a more penetrating isotope (^{103}Pd) may result in sustained benefit from treatment.
Materials/Methods: This trial was approved by the FDA and by the Human Investigation Committees and Radiation Safety Committees of the participating institutions. In this study patients were randomly assigned to doses of 12, 14 and 16 Gy at 2 mm from the source. Major eligibility criteria included age >50 years and active primary or recurrent subfoveal choroidal neovascularization secondary to AMD with a minimally classic or occult appearance.
Results: 16 patients were enrolled on the study from 5 of the 6 participating institutions (9 females and 7 males). The average patient age at time of treatment was 79 years (range 63-94). Median visual acuity in the affected eye was 20/125 (range 20/80 to 20/640). Treatment was delivered successfully to all enrolled patients. (5-12 Gy; 6-14 Gy; 5-16 Gy). The average treatment time was 9 minutes and 26 seconds (range 5:50 to 16:10). With a median follow-up of >180 days 6 serious adverse events were reported with none judged to be related to treatment. At latest follow-up 3 of 16 patients had progression (> 3 Snellen line loss); 3 were improved and 10 were stable. No radiation retinopathy has been observed.
Conclusions: Enrollment to this trial was terminated prematurely based on promising results of intravitreal injection of anti-angiogenic drugs. Evaluation of the benefit of the TheraSight device would require a randomized trial. Preliminary analysis showed that this treatment could be safely delivered with the majority of patients being stable to improved at 6 month follow-up.

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THE VARIABILITY OF APPLICATOR POSITION AMONG HIGH DOSE RATE (HDR) INTRACAVITARY BRACHYTHERAPY APPLICATIONS IN CERVICAL CANCER PATIENTS TREATED WITH RING & TANDEM APPLICATORS

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Purpose/Objectif: The interindividual and intraindividual applicator position variability was evaluated retrospectively in HDR intracavitary brachytherapy (ICBT) applications performed in cervical cancer treatment using ring and tandem (R&T) applicators.
Materials/Methods: Eight patients with cervical cancer formed the study population who had been treated in Dokuz Eylül University Department of Radiation Oncology between the years 2000 and 2005 with HDR brachytherapy using R&T applicators. Patients were treated with 45 Gy external radiotherapy (RT) using pelvic box technique and then they were given ICBT in 3 fractions of 8 Gy (to point A). The 3-D geometrical variation of applicator center in craniocaudal (CC), mediolateral (ML) and anteroposterior (AP) directions was determined on the basis of bony reference points in 24 pairs of orthogonal films. Then the following evaluations were performed: (1) The applicator position variability in all applications (interindividual variability), (2) The applicator position variability of other two applications relative to the 1st application in a single patient (intraindividual variability relative to the 1st application), (3) The applicator position variability of 3 applications relative to the mean of 3 applications in a single patient (intraindividual variability relative to the mean of 3 applications). In the lateral simulation films, the distances between applicator center and bladder and rectum reference points

were also measured. Among the potential factors that could influence the reproducibility of R&T applications, age, stage, the period between external RT and brachytherapy were evaluated with univariate analysis.

Results: The range of R&T applicator center's position was 13,1 mm, 1,7 mm, and 15 mm in CC, ML and AP directions, respectively. Standard deviation (SD) of interindividual applicator variability was 3,8 mm in CC, 0,4 mm in ML and 2,9 mm in AP directions. SD of intraindividual variability relative to 1st application was 1,9 mm in CC, 0,4 mm in ML, and 4,3 mm in AP directions. And SD of intraindividual variability relative to the mean of 3 applications was 0,95 mm in CC, 1,9 mm in ML, and 1,2 mm in AP directions. The lateral angulation of R&T applicator (α) was 10° to the right and 0° to the left while AP angulation (β) was 30° to the anterior direction and 0° to the posterior direction. SD of the distance between applicator center and bladder and rectum reference points was 1,19 mm and 0,5 mm, respectively. In the univariate analysis, there was no factor influencing applicator position variability.

Conclusions: According to the results of this study, the applicator position variability in R&T applications was relatively less compared to other studies in the literature. In order to extract definitive conclusions about factors affecting positional reproducibility of R&T applicators, studies are needed that evaluate more parameters and that include higher number of patients.

674 poster

VALIDATION OF THE METHOD BASED ON THE DELINEATION OF THE EXTERNAL CONTOUR OF THE ORGANS AT RISK IN 3D TREATMENT PLANNING BRACHYTHERAPY FOR CERVICAL CARCINOMA

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Purpose/Objectif: 1) To compare dose values from cumulative dose-volume histograms (DVHs) based on organ contour and organ wall delineation for organs at risk 2) To analyse the correlation between dose values from DVHs based on organ wall delineation, and doses calculated in the ICRU reference points.

Materials/Methods: CT scan based treatment planning of 46 consecutive patients treated with brachytherapy for cervix carcinoma were reviewed. Bladder, rectum and sigmoid were delineated slice by slice by the same observer using 2 methods: delineation of external contour of the organ (ext) and delineation of the organ wall (w). The whole bladder was delineated whereas rectum was delineated from the anus to the rectosigmoid flexure. Bladder and rectum reference points (B and R points respectively) were localized in CT scan slices according to ICRU 38 recommendations. The absorbed dose at this points (D_B point and D_R point) and the minimum dose value of 0.1 cc, 2 cc, 3 cc, 5 cc and 10 cc of organ and wall volumes receiving the highest dose (computed from DVHs) were recorded (D0.1, D2, D3, D5, D10, respectively).

Results: 1) For volumes of 0.1 cc and 2 cc, dose values computed from DVHs based on external contour and organ wall were very similar. Indeed, the mean of ratio $D0.1_{ext}/D0.1_w$ was 1.00 +/- 0.01 for bladder, rectum and sigmoid; the mean of ratio $D2_{ext}/D2_w$ was 1.07 +/- 0.06 for bladder, 1.15 +/- 0.10 for rectum and 1.28 +/- 0.19 for sigmoid. For larger volumes, the difference between dose values computed from DVHs based on external contour and organ wall became larger. The mean of ratio D_{ext}/D_w was higher than 1.30 for volumes over 2 cc for sigmoid, 3 cc for rectum and 5 cc for bladder.

2) D_B point was not correlated with D0.1 and D2 of bladder wall. D_B point was inferior to D0.1 and D2 of bladder wall in 100% and 41% of patients respectively. D_B point underestimated D0.1 and D2 of bladder wall from an average of 39% and 15% respectively. D_R point was correlated with D0.1 and D2 of rectum wall (coefficient of correlation of 0.86 and 0.83, respectively; $p<0.0001$). D_R point was inferior to D0.1 of rectum wall in 94% of patients and superior to D2 of rectum wall in 80% of patients. D_R point underestimated D0.1 of rectum wall from an average of 20% and overestimated D2 of rectum wall from an average of 20%.

Conclusions: In this cohort, the dose absorbed by 0.1 cc and 2 cc of bladder, rectum and sigmoid wall, was evaluated with reliability with DVHs based on the delineation of the external contour of organs. D_R point was correlated with doses computed from DVHs, and overestimated D2 of rectum wall in 80% of the cases; there was no correlation between D_B point and doses computed from DVHs.

This favors the routine use of 3D planning for uterovaginal brachytherapy. Evaluation of dosimetric data through DVHs in large cohorts of patients is mandatory to establish a correlation between D0.1 and D2 of the organs at risk and grade 3 toxicies.

Posters Breast Cancer

675 poster

ACUTE NORMAL TISSUE REACTION (MOIST DESQUAMATION) IN PATIENTS WITH EARLY BREAST CANCER TREATED WITH 30GY IN 6 FRACTIONS OVER 15 DAYS: RESULTS OF A PILOT STUDY.

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Purpose/Objectif: If the high fractionation sensitivity of breast cancer is confirmed by the NCRI Standardisation of Radiotherapy (START) trial, the implication is that larger fraction sizes have no disadvantages, and may have significant advantages, for women with early breast cancer. A single arm pilot study was designed to examine the effect of delivering large fraction size over a shorter treatment time on acute normal tissue reaction.

Materials/Methods: 30 Patients suitable for whole breast radiotherapy (no boost) after local excision of early breast cancer (Age ^{3} 50, pT2 <3.0cm, pN-, LV-, negative margins), were entered into this single arm study. Radiotherapy was delivered via tangential fields to the whole breast and cardiac shielding. The dosimetry fulfilled ICRU 50 guidelines; IMRT was used where required. Follow-up forms recording severity of skin reaction: erythema and moist desquamation (Grade 0 = None, 1 = Mild, 2 = Moderate, 3 = Severe) were completed weekly in the outpatient department for 7 weeks from the start of treatment. The primary end point was moist desquamation, a secondary endpoint being photographic breast appearance at year 2.

Results: Grade and Duration of Moist Desquamation Cases (4 / 30) after start of radiotherapy

Case	0	1	2	3	4	5	6	7
1	0	0	0	0	0	0	1	0
2	0	-	0	0	1	0	0	0
3	0	0	0	1	2	2	1	0
4	0	0	0	0	0	1	0	1

Grade 1 or 2 moist desquamation was recorded in 4 patients out of 30 (13.3%). In cases 2 and 3 this was limited to the infra-mammary fold. In case 3 'Sweets Syndrome' was also diagnosed. Erythema for

each of these cases had a maximum grade of 2 and was otherwise unremarkable for the rest of the test group, only one patient graded with a maximum of 3. All reactions were easily managed by the patients.

Conclusions: This pilot study found that 30Gy in 5 fractions over 15 days did not result in a higher incidence of moist desquamation or severity of eyrthema for patients than might be expected after 50Gy in 25 fractions over 35 days. Depending on the outcome (late adverse effects) of the current NCRN FAST trial (testing 30Gy in 5 fractions over 29 days), there appears to be scope for evaluating a 15-day schedule and possibly a 5-day schedule of a 5 fraction regime, if 2-year photographic and clinical assessments are satisfactory.

676 poster

ADJUVANT ACCELERATED RADIOTHERAPY (ART) FOR ELDERLY BREAST CANCER (EBC) PATIENTS: LONG TERM RESULTS

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Purpose/Objectif: ART can overcome logistical barriers of time and travel created by the conventional 6-weeks course of RT and can be more suitable for elderly women. It can also improve local control by reducing tumor proliferation despite the risk of a worse toxicity profile than standard regimens. The purpose of this study is to value local control, disease free survival, overall survival, acute and late toxicity, patient's compliance and cosmetic results.

Materials/Methods: Elegibility criteria included: age ≥65 yrs; histological proven breast cancer (including DCIS and LCIS); stage pTis,T1-2,N0-1a-1bi-bii,M0-1(life expectation >6 months); conservative surgery with negative margins (≥ 2mm);written informed consent. Tangential RT was delivered at the daily fractionation of 1.8 Gy twice a day, 6 hour apart, for a total dose of 36 Gy, usually completed within 10 days (2 weeks) and should be considered equivalent to the standard dose calculated assuming an α/β value of 4Gy for late responding tissues and 10 Gy for acute responding, according linear quadratic model. Toxicity was evaluated according RTOG/EORTC score systems. Survival curves were plotted using the Kaplan-Meier methods.

Results: Between January 1998 and December 2001, 76 patients were treated with ART after conservative surgery. The mean age was 74.4 years (66-89). 57% had a T1c tumor, 13% a T1b and 24% a small T2 tumor; only 6% pts were classified T4 for skin infiltration by tumors <2cm. G2 ductal carcinoma was diagnosed in 75% of cases and lobular carcinoma in 20%. There were 2 DCIS. 25% of pts were treated with telecobalt therapy and 75% by LINAC 6MV. Acute skin toxicity was modest limited mainly to G1-2 erythema showed by 19% of pts. 60% of pts did not show skin toxicity. Acute skin toxicity was more common in those who had been treated with telecobalt therapy. With a mean follow up of 66 months a pt showed late skin toxicity. No pts showed local recurrence. 3 patients showed metastases. Overall survival was 92.9% at 5 yrs.

Conclusions

This data suggest that the accelerated treatment of breast cancer was well tolerated with only mild acute side effects, reduced the time of treatment allowing including also elderly patient with an optimal compliance. The results in local control and survival were not different from those of standard radiotherapy.

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ADVANTAGES IN EVALUATING THE RADIATION DERMATITIS BY PHOTOGRAPHS IN PATIENTS WITH BREAST CANCER UNDERGOING BREAST CONSERVATION THERAPY WITH A SHORT FRACTIONATION.

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Purpose/Objectif: The aim of this study is to clarify the efficacy in estimating the radiation dermatitis by using photographs in patients with breast cancer treated with breast conservation therapy (BCT).

Materials/Methods: From December 2003 to July 2005, 78 patients underwent radiation therapy with a short fractionation as a part of BCT. The mean age was 54.3 y.o. ranging from 33 y.o. to 84 y.o. All the patients were delivered 44 Gy with 16 fractions in 22 days with tangential portals, and 38 patients with a positive margin underwent the boost irradiation (3 Gy x 3) to the tumor bed. The photographs of the irradiated breast and axilla were taken every one week from the start of the radiation therapy to 7-10 days after the completion of the radiation therapy. The radiation dermatitis was graded by using the photographs and the grades were compared with those evaluated by medial observation at the outclinic. Grading of the radiation dermatitis was determined according to CTCAE v.3.0.Two forms of assessment were used: A batch evaluation method; Evaluators A, B (the photos were lined up and viewed side by side in each patient), and a successive evaluation method; Evaluators C, D (the photos were viewed sequentially, as if on successive pages). Each method employed two radiation oncologists and overall assessments were carried out

Results: The Grade 3 or less radiation dermatitis was found in all the patients. The numbers of the patients in Grade 0 and Grade 1-3 were 15/33/25/15/12 (medical observer/ Evaluator (E)-A/ E-B/ E-C/ E-D),and 63/45/53/63/66, respectively. The p-value between the medical observer and the evaluator A, B, C, and D was 0.0018/0.0667/1.0000/0.5255, respectively. Likewise, the p-value regarding the axilla was 0.0001/0.0035 for evaluators A/B. The batch evaluation method had a significant difference in evaluating the toxicity of the breasts and axilla when compared to the medical observation. We could distinguish the redness related to the radiation therapy from that related to the changes caused by lumpectomy prior to the radiation therapy by using the batch evaluation method. However, the successive evaluation method could not distinguish the two types of the redness. The grading of the toxicity by the successive evaluation method was similar to that by the medical observation. It is probably because one cannot assess the sequential changes over time when evaluating at the time of the medical observation.

Conclusions: The batch evaluation method can estimate the radiation dermatitis more accurately than the successive evaluation method or the medical observation at the outclinic.

678 poster

ANALYSIS OF RELATIONSHIP BETWEEN DYNAMIC MRI PARAMETERS WITH PROGNOSTIC FACTORS AND SURVIVAL IN BREAST CANCER PATIENTS

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Purpose/Objectif: To assess the value of preoperative dynamic contrast enhancement magnetic resonance imaging (DCE-MRI) semiquantitative parameters in predicting the disease-free and overall survival in breast cancer patients treated in a single institution.

Materials/Methods: Forty patients with diagnosis of breast carcinoma were evaluated with 1.0 T MR scanner as a part of their preoperative diagnostic work-up. Dynamic studies were performed in using fast low angle shot (FLASH) sequence. Maximal relative en-

hancement within first minute (E1), maximal relative enhancement within second minute (E2), maximal relative enhancement (Emax), time-signal intensity (TSI) curves and steepest slope of the enhancement curve were used as dynamic contrasting semiquantitative parameters. The association of image analysis with other clinicopathologic factors was assessed using the Kruskal-Wallis test. Survival curves were calculated using the Kaplan-Meier method. Statistical differences between survival curves were calculated by means of the log-rank test.

Results: Significant associations were observed between histologic grade and E2, Emax, steepest slope, TSI curve, and types of qualitative contrast parameters (p=0.009, 0.019, 0.008, 0.05, 0.001, respectively), between nuclear grade and E1 and types of qualitative contrast parameters (p=0.027 and 0.001), vascular invasion and E1, E2, Emax, steepest slope and TSI curve type (p= 0.046, 0.01, 0.031, 0.05 and 0.04, respectively), between lymphatic invasion and Emax (p=0.031), between presence of axillary lymphadenopathy and TSI curve type (p=0.037). After a 53-month median follow-up of the patients, the overall five years probability of overall and disease-free survival was 63.4% and 76%, respectively. Although the 5 year disease-free and overall survivals were lower in the group with high dynamic contrast parameters, it was not found to be statistically significant. The relationship between disease-free and overall survivals and lymphovascular invasion (p=0.007 and p=0.025, respectively) and stage (p<0.0005 and p=0.005, respectively) were found to be statistically significant.

Conclusions: Although we detected a statistically significant relationship between DCE-MRI semiquantitative parameters and prognostic factors, there was no statistically significant association between survival. In our opinion, this situation needs further clarification through studies with larger patient populations and a longer follow up period.

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ANALYSIS OF THE CONSERVATIVE TREATMENT IN DUCTAL CARCINOMA IN SITU OF THE BREAST. EXPERIENCE OF HOSPITAL UNIVERSITARIO "12 DE OCTUBRE"

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Purpose/Objectif: The widespread use of screening mammography has resulted in a significant increased in the rate of detection of DCIS. In the past, routinely DCIS was cured with mastectomy but with the acceptance for breast conserving therapy for the invasive carcinoma the use of conservative treatment is widely used in patients with localised DCIS

Materials/Methods: Between January 1981 until Dec 2004 we analyse 164 patients diagnosed of DCIS treated with breast conserving therapy followed of radiotherapy to the whole breast in the University hospital "12 de Octubre". The most common presentation in 82% of the patients was an abnormal mammography. In 13,4% the clinical presentation was a palpable mass and in 3,7% referred a pathologic nipple discharge. The median age was 54 (range 29-77). Histopathologic examination revealed a diagnosis In 34 patients of comedocarcinoma, in 24 patients was a cribiform pattern and in 53,7% was a DCIS without specification. The median tumour size was 0,9 mm (range 0,2 -6 cm) and in 27 patients the tumour size was unknown. In 47,6% of our series the margin status was negative, less that 5mm in 34,1%. The margins were positive in 4,9% and unknown in 13,4%. All the patients received radiotherapy treatment to the whole breast through two opposing tangential fields giving a dose of 50 and in 72,6% of the patients received a boost in the tumoral bed. Tamoxifen was administered in 55% of the patients. The median follow up was 64 months (range 11-296m

Results: 97,6% of the patients were free of local and distance failure and any patient had death cause by progression of DCIS. We have no case of cardiac or pulmonary toxicity. In this work we analyse the risk factors for local recurrence and disease free survival

Conclusions: In localised DCIS, the breast conservative treatment followed of radiotherapy is an effective treatment with an excellent local control and overall survival. In our serie with an adequate dosimetric planning, the risk of cardiac or pulmonary toxicity is null. We need more prospective trial to define the subgroup of patients that can be avoided of radiotherapy treatment with this excellent local control

680 poster

APPROACHES TO POSTMASTECTOMY RADIOTHERAPY (PMRT) IN THE INTERGROUP EXEMESTANE STUDY (IES)

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4 - For the IES

Purpose/Objectif: Within IES, we have previously shown that the threshold for mastectomy use varies greatly between countries (EJC Suppl. 2004; 2: 163). Whereas tumor excision (TE) in early breast cancer is typically followed by RT, indications to RT after mastectomy (M) are still debatable. IES allows us to describe factors affecting PMRT use according to geographical region.

Materials/Methods: In the IES (NEJM 2004; 350: 1081), postmenopausal patients (pts) with operable breast cancer who had received tamoxifen for 2-3 years were randomized to continue tamoxifen or switch to exemestane to complete a total of 5 years adjuvant endocrine therapy. Eligibility criteria included positive or unknown steroid receptor status and adequate local treatment (M or TE followed by radiotherapy). PMRT was administered according to local center policy.

Results: Of the 4664 pts enrolled who received adequate local therapy, 2226 (48%) underwent TE followed by RT and 2438 (52%) underwent M. Overall, PMRT was administered in 858 pts (18%); 10% in N0, 23% in 1-3+ lymph nodes (LN) and 45% in 4+ LN. Within patients undergoing M, use of PMRT was independently related to nodal status (OR 2.11 [95% CI 1.70-2.61] and 5.31 [4.10-6.89] for 1-3+ and 4+ LN, respectively), tumor size (OR 1.31 [1.07-1.61] and 2.32 [1.63-3.30] for 2-5 cm and >5 cm, respectively), and adjuvant chemotherapy (OR 1.38 [1.13-1.68]). Additionally, there were large differences in PMRT use between countries; e.g in LN+ M pts: France 96%, UK 66% Netherlands 62%, USA 30%, Denmark 26%, Poland 18%, Italy 18%. Due to different thresholds for undertaking M, M pts in and Central Europe were approximately 5 and 3 times more likely, respectively, to receive RT than M pts in the USA.

Conclusions: The use of M and subsequent PMRT in breast cancer pts vary between countries. Simple comparison of PMRT rates internationally is confounded by differing use of M vs TE.

681 poster

ASSEMENT OF THE ACCURACY OF TREATMENT FIELDS WITH ELECTRONIC PORTAL IMAGING DEVICE (EPID) IN A BREAST IRRADIATION

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Purpose/Objectif: the aim of this study was to evaluate the accuracy of treatment fields and set-up errors by the use of EPID images in a 3-D tangential breast irradiation.
Materials/Methods: Electronic portal images were acquired using a video-based imaging system. After contrast enhancement, these images were compared to portal images for on-line verification. Fiveteen patients who referred to our instutions for breast irradiation were included in this study. Radiotherapy was applied to the whole breast (50 Gy) in 2 Gy per fraction and five times a week with 6 MV photon beams produced by Siemens® Primus. An additional boost was given to the tumour bed by an external bem technique (electrons). Two hundered twenty six EPID images for each of the tangential fields were obtained in 15 consecutive patients. In a digitally recontracted radiography (DRR) and EPÝD images ; central lung distance (CLD), central irradiated width (CIW) and cranio-caudal distance (CCD) were measured. Centers of fields were determined by placing a lead marker into the centers of the tangential fields in a set-up position and the distances were measured over the central axis in a millimeters. Measurements which were obtained from EPID and DRR images were compared separately for each patient. The discrepancies measured for each set of images were analysed statistically by One -sample T test, and standart error of mean was calculated.
Results: In avarage, 15 EPIDs (8-20) were obtained from each patient during 5 weeks of total treatment. Mean differences in CLD, CIW and CCD measurements were 0.34 ± 0.6 mm, -0.6 ±0.7 mm and -1.4 ± 0.9 mm, respectively. Mean standard errors were 2.4 ± 0.1 (0.7-4.9) mm, 3 ± 0.2 (1.2-7.4) mm and 1.9 ± 0.1 (0.6-4.1), respectively. For these measurements, 95% of the geometrical uncertainties in standard deviation values were less than 5 mm.
Conclusions: The evaluation of EPID images with DRRs showed that average errors in a set-up position during treatment were less than 1.5 mm for each of the three parameters. This study shows that our set-up technique for breast irradiation is accurate and reprodicible.

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BOOST IN BREAST CANCER AS INFIELD BOOST - A PRACTICABLE POSSIBILITY

KJ. Buth[1]

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Purpose/Objectif: Radiation treatment of breast after limited surgery of cancer is obligate. Total dose (TD) of 50,0 Gy (50,4 Gy) is treated with 2,0 Gy (1,8 Gy) per fraction, with an consecutive boost to the primary size with an TD 10,0 Gy (16,0 Gy), with 2,0 Gy per fraction. A higher biological effectiveness from boost treatment is possible by higher dose per fraction, but with a higher risk of side effects for lung, skin and heart. If the boost is integrated in the basic radiation, a dose not higher then 2,15 Gy per fraction is necessary for 60,40 Gy TD in the tumor volume.
Materials/Methods: For the integration of the boost treatment in the basic radiation series at the application of COMART (Conformal-MLC-arc), will be two fields more used then the standard radiation fields of COMART. The radiation treatment with sliding window doesn't need more fields. Both methods show dose distributions with 50,4 Gy for breast with 1,8 Gy per fraction and 60,2 Gy for tumor (boost volume) with 2,15 Gy per fraction. It will be shown examples for each technique.
Results: The biological effectiveness for tumor volume is higher because the dose will be given in 28 fractions instead of 33 fractions and the risk of side effects for lung, skin and heart is the same as the basic radiation with connected boost radiation. This will be shown in dose distribution of the radiation techniques. Consequently are unfavorable late reactions not to be expected.
Conclusions: Integration of the boost treatment in basic radiation series can improves the biological effectiveness for tumor volume. At the same time the side effects for organ at risk are the same as for the connected radiation. Cosmetically results will be prospectally note in our institution. But unfavorable late reactions are not to expect, because of the only low higher dose per fraction.

683 poster

BREAST CANCER FOLLOWING TREATMENT OF HODGKIN S DISEASE. CLINICAL FEATURES AND THERAPEUTIC APPROACH: THE ISTITUTO NAZIONALE PER LO STUDIO E LA CURA DEI TUMORI EXPERIENCE

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Purpose/Objectif: Second malignancies are an important late event in Hodgkin's lymphoma (HD) long-term survivors and one of the leading causes of mortality. We reviewed a single institution series to investigate clinical features and treatment modalities of breast cancer (BC) developed in HD survivors.
Materials/Methods: 54 patients (pts) with BC were collected among 2300 HD pts treated at Istituto Nazionale per lo Studio e la Cura dei Tumori (INT) from 1963 to 2004. Main pts characteristics were as follow: median age at diagnosis:26 (range 11-66) yrs; stage: early in 35 pts and advanced in 19; NS histology:37. Treatment consisted of subtotal nodal radiotherapy (RT) as a single modality (17) or in combination with chemotherapy (CT) (19), extended fields -/+ CT (6 and 1), involved fields -/+ CT (2 and 5), bulky disease RT + CT (3), RT alone (1).
Mantle field RT was performed in 43 pts.
Median dose to involved sites was 40 Gy, to uninvolved sites 36 Gy both in adults and in children. 8 pts recurred and all achieved a second CR after second line treatment. Alkylating CT was administered in 19 pts, ABVD in 8, Velbe in 1. Median fup was 25 yrs.
Results: 70 BC were diagnosed. The median age at diagnosis was 41 (range 27-76) yrs and the median interval from HD was 17.5 (range 1-36) yrs. Laterality was equally divided, and 55% of the tumours were located in the upper outer quadrant (UOQ). In mantle fields treated pts, 28 tumours were observed in UOQ. 3 pts developed synchronous bilateral tumours and 13 bilateral metachronous tumours. 44 pts were subjected to quadrantectomy, 20 to radical mastectomy, 5 to tumorectomy. Surgery was not performed in 1 case because of metastatic disease at diagnosis. 44 pts had axillary dissection, 12 sentinel node biopsy, 13 no dissection, 1 case unknown. Ductal infiltrating carcinoma was documented in 52 cases (in 6 cases associated to DCIS), 16 tumours were multifocal. 32 node positive pts. Adjuvant chemotherapy was given in 35 pts, endocrine therapy in 33 pts.
37 pts had breast or chest wall RT, in 7 cases RT was not feasible for dosimetric reason. in 26 pts RT was not performed.
6 MV photons were used in 11 cases, Cobalt in 10; median dose with tangential fields was 50 Gy/2 Gy x fraction; boost to tumour bed was used only in 8 cases median dose 10 Gy/2 Gy x fraction. Chest wall irradiation was performed with 40 Gy/1,8 Gy x fraction. No G2/G3 side effects after RT were observed. Cosmetic results are good or mild.
No HD related death were observed. 13 pts died of BC progression/relapse (median fup 4 years). 1 pt died of cardiac failure.
During fup period 5 other malignancies were observed.

Conclusions: As the risk of BC is high, regular and prolonged follow-up are mandatory in pts treated for HD. Particular attention to breast cancer prevention is needed. In selected cases secondary BC may be treated with conservative approach.

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BREAST CANCER IN PATIENTS CARRYING A GERM-LINE CHEK2 MUTATION: OUTCOME AFTER BREAST CONSERVING SURGERY AND ADJUVANT RADIOTHERAPY

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Purpose/Objectif: Cell-cycle checkpoint kinase 2 (CHEK2) is a central mediator of cellular responses to DNA damage. It could be demonstrated that women with mutations in the CHEK2 gene are at an increased breast cancer risk. Data about outcome and prognosis for these patients after standard multimodality treatment are scarce at present.

Materials/Methods: Between 1995 and 2002 genomic DNA samples had been collected from a large unselected hospital-based series of more than 1000 breast cancer patients which had been irradiated postoperatively after breast conservative surgery at a single institution. A mutation in the CHEK2 gene could be detected in 35 patients; of these, ten patients with locally advanced tumours or distant metastases at the time of diagnosis were excluded. 125 patients without a CHEK2 gene mutation (non-carriers) served as a comparison group and were derived from a subcollective of the above mentioned series of breast cancer patients that had previously been analysed for the prevalence of ATM gene mutations. Postoperative radiotherapy was delivered with 6 MV linac photons with whole breast dose ranging from 45 to 54 Gy (median: 53 Gy, single: 1,8 Gy). Relevant prognostic factors between carriers and non-carriers were well balanced.

Results: 25 patients with early-stage breast cancer were identified being heterozygous for one of three CHEK2 gene mutations (I157T, n=13; 1100delC, n=10; IVS2+1G>A, n=2). During a median follow-up of 87 months, local recurrences occurred in 13 patients (carriers, 3; non-carriers, 10), distant metastases in 27 patients (carriers, 8; non-carriers, 19) and 25 patients had deceased (carriers, 8; non-carriers, 17). Actuarial 7-year local relapse-free survival was 86 % in carriers versus 90 % in non-carriers (p = 0,475). Actuarial metastasis-free and overall survival at 7 years were 64 % vs. 84 % (p = 0,045) and 69 % vs. 87 % (p = 0,097), respectively. In a multivariate step-wise Cox regression analysis presence of a CHEK2 mutation (p = 0,048) remained next to T-stage (p = 0,001) a borderline statistically significant discriminator for metastasis-free survival.

Conclusions: Our results indicate that variants in the CHEK2 gene may be associated with an increased risk of distant failure with the CHEK2 status representing an adverse prognostic factor. If confirmed in larger studies these data may serve as a basis for future treatment strategies and intensified follow-up taking into account individual germline mutational status.

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BREAST PATIENT SET-UP VERIFICATION: COMPARISON BETWEEN EPI AND CONE BEAM CT MATCHING RESULTS

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Purpose/Objectif: With the introduction of cone-beam CT (CBCT) systems in our clinic, verification protocols based on setup data obtained with electronic portal images (EPI) have gradually been replaced by CBCT based verification protocols for several patient groups. The purpose of this study is to determine the effect of such an approach for breast cancer patients and to determine the accuracy of CBCT based setup errors compared to EPI for this patient group.

Materials/Methods: CBCT scans of 16 patients (7-8 scans per patient) were acquired during the same treatment fractions as EPI acquisition. The EPI match data were used in a shrinking action level (SAL) setup correction protocol (9 mm, 3 fractions). EPI were acquired from the opposing oblique treatment beams, after which the ribs were registered to the DRRs. By assuming the setup error in the direction of the central beam axes to be zero, the 2D registration result (U, V) could be converted into a 3D couch shift (x,y,z). The U direction is roughly perpendicular to the patient surface, whereas V is parallel to it. Prior to imaging, patients were shifted according to the SAL protocol. CBCT scans were retrospectively analyzed by grey value registration of the bony anatomy (ribs) to the planning CT scan. Registration results of both imaging modalities were compared in the 2D EPI-coordinate system U, V, after computing a $(U, V)_{CBCT}$ pair from the CBCT registration result $(x, y, z)_{CBCT}$.

Results: The match results in the (U, V) plane were calculated as systematic errors (Σ), random errors (Σ) and group mean. The correlation for the U direction is fair (0.7), for the V direction poor (0.4). The difference (last column) expresses the mean difference in the mean patient position, as established by EPI and CBCT. For both directions there was a significant difference between the two methods: for the U direction this was 1.1 mm (p=0.007), for the V direction it was larger: 2.4 mm (p=0.001). The group mean for left-sided patients differed from right-sided patients, for EPID +2.2 mm (left) vs. -1.5 mm (right) (p=0.002), for CB +0.4 mm vs. -1.2 mm (p=0.1).

Conclusions: The setup errors found by EPID and CB differed significantly. CB verification found considerable residual errors during treatment while using the EPID setup verification protocol, indicating that either CBCT overestimates these errors or EPI underestimates them. The matching structures (ribs) are much less well defined in EPIs than in CBCT scans. We conclude therefore, that set-up verification with CBCT is considered to be more accurate than EPID verification for breast cancer patients.

Table 1.

	EPID (mm)			CBCT (mm)			Correlation means		Difference (mm)			
	mean	Σ	σ	mean	Σ	σ	R2	p	mean	Σ	SEM+	p*
U	1.0	2.5	2.3	-0.1	1.9	1.7	0.67	<0.001	1.1	1.4	0.4	0.007
V	-0.7	1.9	2.2	-3.1	2.9	2.3	0.38	0.01	2.4	2.3	0.6	0.001

* paired t-test, + SEM = standard error of mean

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CHANGES OF THE RADIOTHERAPY BOOST VOLUME IN BREAST CONSERVING THERAPY: COMPARING THE INITIAL PLANNING-CT WITH A SECOND SCAN PERFORMED A WEEK BEFORE COMMENCEMENT OF THE BOOST.

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Purpose/Objectif: To examine the influence of time dependent changes in the post-surgical tumour bed on clinical target volume (CTV) delineation of the boost, using a second pre-boost treatment planning CT.

Materials/Methods: Treatment planning CT-scans of 12 consecutive patients undergoing BCT were repeated in the week preceding the breast boost. In patients with surgical clips, the maximal three-dimensional (3-D) distances (Z= cranio-caudal, X= medio-lateral, Y= dorso-ventral) between the clips were measured on both scans. In patients with apparent post-surgical changes due to seroma or haematoma, maximal 3-D distances of these changes were separately

measured on both scans.
Results: Eight of 12 patients presented with more than 3 surgical clips. Mean maximal distances between surgical clips on the initial scan were: Z: 34 mm, X: 31 mm and Y: 22 mm. The mean changes of the maximal 3-D distances between clips were: Z: 3.8 mm (range 0-12), X: 3.3 mm (range 1-6) and Y: 3.3 mm (range 0-9). The largest differences were noted in 3 patients with a seroma or haematoma. Four of 12 patients presented with apparent post-surgical changes: mean maximal distance on the initial scan was: Z: 41 mm, X: 38 mm and Y: 30 mm. The mean changes of the maximal 3-D distances were: Z: 18 mm (range 6-30), X: 17 mm (range 6-30) and Y: 13.3 mm (range 3-26). In three patients considerable changes of more than 15 mm in 3-D distances were noted.
Conclusions: We confirm that 3-D changes in maximal surgical clip distances are minimal (less than 4 mm), with the largest changes noted in patients with seroma or haematoma. In patients presenting with apparent post-surgical seroma or haematoma, the 3-D changes were of clinical importance (13.3 - 18 mm). Therefore, we recommend a second pre-boost treatment planning-CT in patients presenting with apparent seroma or haematoma.

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COMPARING ULTRASOUND (US) WITH COMPUTERIZED TOMOGRAPHY (CT) IMAGES TO CHOOSE ELECTRON ENERGY FOR BOOST FIELD IN BREAST CANCER PATIENTS WITH BREAST CONSERVING SURGERY (BCS)

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Purpose/Objectif: To compare US with CT to choose electron energy for radiotherapy (RT) boost field in patient with BCS.
Materials/Methods: Thirty seven women who threated between January 2003 and June 2005 was evaluated in this trial. Median age was 49 (32-82). According to the Dokuz Eylul Breast Tumour Group Protocol, in patients with BCS, RT was performed 5000 cGy to the breast (+/- lymphatic area) and boost with electron energy to the primary tumour bed [1000 cGy if surgical margin is (-), or 1600 cGy if surgical margin is (+)]. Before January 2003, "skin-the deepest point of tumour bed (STD), skin-clips (SCD), skin-fascia (SFD)" distances were measured with US to choose electron energy in boost field. After then, CT simulation images were used for this purpose. These two imaging systems were compared in this trial. Electron energy was selected after measurement of the deepest metalic clips in CT simulation images (82%) or measurement of the STD if there was no clips (18%).
Results: Median measurements with US and CT were as follows: STD: US 12 (4-35) mm, CT 28 (2-54) mm; SFD: US 25 (6-57) mm, CT 31 (2-93) mm; SCD: US 14 (7-26) mm, CT 29 (2-68) mm. The median electron energy was 9 (6-12) MeV é for US and 12 (6-21) MeV é for CT. Accordance in US and CT measurements were 27%.
Conclusions: To choose electron energy with CT could be more reliable than US because of cutaneous and subcutaneous alterations due to RT and radiologist experience.

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COMPARISON OF FOUR TECHNIQUES OF WHOLE BREAST IRRADIATION (WBI) AND BOOST DELIVERY AFTER BREAST CONSERVING SURGERY IN EARLY BREAST CANCER.

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Purpose/Objectif: Breast conserving treatment (BCT) is accepted as a standard therapeutic option in a majority of patients with early breast cancer. This method is expected to combine high local control, safety, satisfactory cosmetic effect and acceptable cost-efficacy. An important aspect of BCT is an optimal delivery of radiotherapy, which is administered in virtually all patients after tumor removal. Aim of the study: To compare target coverage, target dose uniformity and normal tissue complication probability for the heart, left anterior descending coronary artery (LADCA), ipsi- and contralateral lung, and contralateral breast with four techniques: (1) standard whole breast irradiation (WBI) using wedged pair tangential field (50 Gy/25 fractions), followed by electron boost (16 Gy/8 fractions); (2) the same WBI followed by photon boost; (3) tangential fields with simultaneous integrated boost with the use of electronic compensator (60 Gy/25 fractions); and (4) intensity modulated radiotherapy (IMRT) with simultaneous integrated boost (60 Gy/25 fractions).
Materials/Methods: Computed tomography (CT) scans from 10 retrospectively selected patients with early, left-sided breast cancer were used to generate and then compare the above techniques. The average breast equivalent uniform dose, ipsilateral and contralateral lung dose (lung V_{20}), contralateral breast dose, heart dose (V_5) and LADCA dose were compared.
Results: IMRT plan produced significantly better target coverage and target dose uniformity, as well as reduced dose to the contralateral breast and reduced hot spots to the ipsilateral lung compared to electronically compensated tangents and standard wedged pair tangents with either electron or photon boost. Also the median LADCA dose was lower, however this parameter was influenced by the patients' anatomy and the breathing motion. In contrast, IMRT was associated with higher mean contralateral lung dose.
Conclusions: IMRT with simultaneous integrated boost seems to offer more uniform target dose coverage and better sparing of the heart and lung, however at the expense of higher mean contralateral lung dose.

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COMPARISON OF THE DOSE-MASS-HISTOGRAM (DMH) AND DOSE-VOLUME HISTOGRAM (DVH) CONCEPTS IN PREDICTING RADIATION INDUCED PNEUMONITIS FROM BREAST CANCER RADIOTHERAPY

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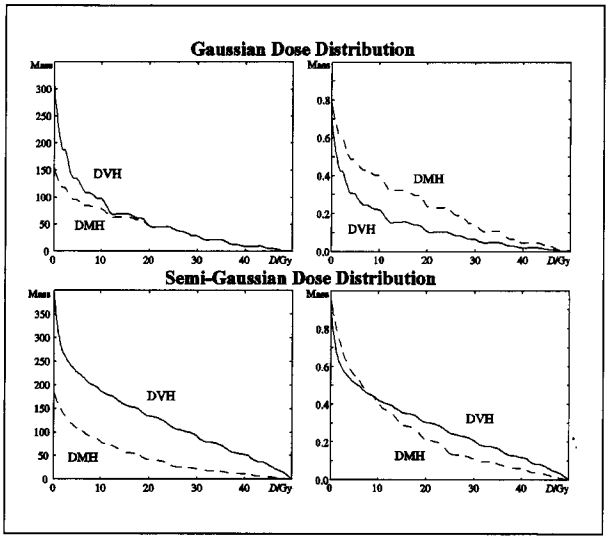
Purpose/Objectif: In radiotherapy for breast cancer, lung is often partly within the irradiated volume even though it is a sensitive organ at risk. Consequently, it is very important to accurately estimate the expected treatment complications. In this study, it is examined whether the Dose Mass Histogram (DMH) concept can be better associated with the expected lung complications than the widely used Dose Volume Histogram (DVH) concept.
Materials/Methods: The problem was investigated theoretically by applying two hypothetical dose distributions (Gaussian and Semi-Gaussian shaped) on two lungs of uniform and varying densities. DMHs were generated based on computing the mass in the vicinity of each dose calculation point by multiplying the volume by the local lung density. Furthermore, a group of 10 breast cancer patients was used to clinically quantify the difference between DVHs and

DMHs. These patients had negative node involvement and were treated with resection and irradiation with two tangential fields. The influence of the deviation between DVHs and DMHs on the clinical outcome is estimated by using the Relative Seriality and LKB models using the Gagliardi et al 2000 and Seppenwoolde et al 2003 parameter sets, respectively. Radiation pneumonitis was used as the clinical endpoint for lung complications. Furthermore, the biological equivalent of the corresponding difference in their mean dose was estimated by the Biologically Effective Uniform Dose (BEUD) and Equivalent Uniform Dose (EUD) concepts, respectively.

Results: It is shown that the relation of the DVHs and DMHs varies depending on the underlying cell density distribution and the applied dose distribution. However, the range of their deviation in terms of expected clinical outcome was proven to be very large both for the theoretical and the clinical studies. For the group of patients, according to the DVH, lung receives 9.82 Gy, whereas according to the DMH it receives 8.06 Gy (a difference of 1.76 Gy). In order to interpret these figures in terms of tissue response it has to be said that DVH gives 0.30% probability for lung complications compared to 0.10% given by DMH for the Relative Seriality model. Similarly, for the LKB model the corresponding values are 2.62% and 1.85%, respectively.

Conclusions: The impact of the deviation between the mean DVH and DMH of the patient group is significantly larger than the impact of the DVH variation when the patient positioning (setup) and breathing uncertainties were taken into account. Concluding, the expected lung complications appear to be overestimated when using the DVH concept whereas the effectiveness of the dose distribution delivered to the patients is closer related to the radiation effects when using the DMH concept.



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CONCURRENT CYCLOPHOSPHAMIDE, METHOTREXATE, AND 5-FLUOROURACIL CHEMOTHERAPY (CMF) AND RADIOTHERAPY FOR BREAST CARCINOMA

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Purpose/Objectif: The current study was conducted to assess the toxicity of concurrent adjuvant CMF chemotherapy and radiotherapy (RT) for early breast carcinoma.

Materials/Methods: In the current analysis, the authors reviewed the records of 563 consecutive breast carcinoma patients who received adjuvant CMF in concomitance with RT and 603 consecutive breast carcinoma patients who received only adjuvant RT at the University of Florence between 1981-2002. All patients underwent breast conserving surgery. The CMF schedule was 1;8;28. RT was delivered using photon beam with tangential fields. The mean dose delivered was 50 Gy, 2Gy daily fraction (range 46-52). The tumour bed boost was delivered by electrons. At the discretion of the radiation oncologist the total boost dose (2Gy daily fraction) ranged between 6 and 10 Gy for patients with negative surgical margins and between 14 and 16 Gy for patients with close margins. Adverse effects of RT were graded retrospectively using the Radiation Therapy Oncology Group (RTOG)/European Organization for Research and Treatment of Cancer (EORTC) system.

Results: The median age of the patients who received CMF+RT was 49.1±9.1 years and 52.1±7.4 in patients who received only RT. Patients characteristics are equally distributed in both groups.

In RT+CHT group radiotherapy was interrupted due to side effects in 8.3% of patients, within in RT group in 7% (p=0.26). The incidence of Grade 3 or Grade 2 RT toxicity in RT+CMF group was 1.1% and 21.1% respectively, and 1.6% and 18% for the RT groups (p = 0.57). Cosmetic results was similar for both group.

Conclusions: The results of the study demonstrated that the concurrent administration of CMF and RT is associated with a low risk of serious toxicity and is an acceptable adjuvant regimen for patients with breast carcinoma.

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CORRELATION BETWEEN ACUTE SKIN TOXICITY AND FATIGUE IN BREAST CANCER PATIENTS RECEIVING ADJUVANT POSTOPERATIVE RADIOTHERAPY

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Purpose/Objectif: Radiotherapy is associated with several side effects. Skin-reaction and fatigue are one of them. They adversely affect the quality of life during and after treatment. The aim of the study was to evaluate the level of subjective feeling of fatigue and radiation induced skin reaction receiving adjuvant postoperative radiotherapy in breast cancer patients after breast-conserving surgery.

Materials/Methods: 50 patients (age 33-76 years, mean 57 years) with early breast cancer were recruited between May and October 2004 and followed longitudinally from onset of treatment to 3 moths post treatment. The subjective feeling of fatigue intensity was measured according to 10-score visual analog scale. RTOG Acute Radiation Morbidity Scoring Criteria (0-4) were used for an estimation of acute skin reaction in 4 areas (by patients, physicians and nurses).

Results: Fatigue intensity increased gradually during radiotherapy. Fatigue level in the last day of treatment was 2.42 in fatigue-VAS scale (mean fatigue-VAS before treatment was 1.18). On the last day of radiotherapy patients estimated radiation-induced skin side effects according to RTOG scale on mean 2.72 (median 3), nurses on mean 2.47 (median 2), physicians on mean 2.34 (median 1.5). There were correlation between fatigue level and the intensity of skin-reaction for radiotherapy. If patients estimated skin-reaction on 1 or less, mean fatigue-VAS was 1.14 (identical like before treatment). Patients that estimated a skin-reaction more than 3, experienced fatigue on a higher level (mean fatigue-VAS 3.13). 3 months after radiotherapy fatigue intensity was lower than the pretreatment (mean fatigue-VAS 0.62). However, in the case of 6 patients who defined their skin-reaction on more than 1, fatigue level was still high three months after radiotherapy had ended (mean fatigue-VAS 2.5). Patients estimate their radiation-induced skin side effects on higher level compared to nurses and physicians.

Conclusions: Patients estimate their radiation-induced skin side effects on higher level compared to nurses and physicians. A positive correlation between the level of fatigue and the intensity of skin-reaction was found, for breast cancer patients receiving adjuvant postoperative radiotherapy.

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DEVELOPING A SIMULTANEOUS INTEGRATED BOOST (SIB) TECHNIQUE FOR TREATMENT OF BREAST CANCER

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Purpose/Objectif: Recently, the "Young Boost trial" has started looking at the advantages of a higher boost dose of 26 Gy compared to the traditional given 16 Gy, preferably given as a SIB. The purpose of this work is to compare a sequential and a simultaneous planning approach to implement a SIB technique.

Materials/Methods: The treatment planning was performed in Pinnacle version 7.6c using the inverse planning algorithm DMPO. The boost volume is the original tumor plus a rim of tissue of 1.5 cmr. For both approaches we use IMRT for the regular beams existing of 2 large open tangential beams delivering at least 80% of the dose, combined with 2 IMRT tangential beams for the remainder of the dose and the dose homogenization. In the simultaneous approach ('SIB-plan') the dose due to the regular and the boost fields are planned in the same optimization. A non-tangential IMRT beam contributed to both the boost and the regular dose. Due to the direction of the non-tangential beams, excess dose was delivered to heart and lung. Therefore, we fixed the non-tangential beams as segments conformal to the boost PTV. During the optimization, the weight of these segments was optimized together with the inverse planning of the tangential beams. In the sequential approach ('SEQ-plan') the boost fields are first planned using optimum gantry and collimator rotation and wedges. Planning objective for these beams was the additional boost dose. Subsequently, an IMRT optimization for the whole breast was performed, as a superposition to the dose already planned for the boost fields.

Results: The breast tissue close to the medial and lateral border were slightly under dosed if the SIB-plan was used. This was less pronounced for boost PTV's located at the medial or lateral border, as in these cases the IMRT segments covering the boost accidentally also contributed to the homogenization of the dose in the breast tissue. The breast volume receiving a dose of 95% or higher was slightly improved from 97.7% to 99.8% for a central tumor, and from 99.0% to 99.8% for a lateral tumor. The boost PTV dose was indifferent to the approach applied. As compared to the SIB-plan, the SEQ-plan optimization process turned out to be more robust to tumor localization.

Conclusions: For SIB techniques, a sequential approach has clear advantages in dose distribution over the simultaneous approach. Although intuitively a simultaneous optimization may be more attractive, the limitations of the algorithm combined with the restrictions on the IMRT beams let the sequential approach prevail.

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HEART AND CORONARY ARTERY DOSES FROM BREAST RADIOTHERAPY

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Purpose/Objectif: Long-term follow-up of women irradiated for breast cancer has revealed that past breast radiotherapy regimens have increased the risk of death from heart disease. Assessment of the relationship between this risk and radiation dose to the heart requires detailed dosimetry.

Materials/Methods: A large database of international breast radiotherapy regimens used since the 1950s has been compiled using trial publications and protocols, textbooks and information from practising and retired radiotherapists. Sufficient information was obtained in order to allow accurate reconstruction of each regimen. A technique based upon virtual simulation and CT-based 3-dimensional treatment planning has been used in order to reconstruct these regimens on a representative patient. Dose distributions were performed by the treatment planning system, Helax TMS version 6.1B, Nucletron Ltd. In addition, dose distributions for a number of 250 keV breast radiotherapy regimens and iridium wire implants were derived using manual planning techniques. For each treatment plan, dose volume histograms were generated. Estimations of dose to the whole heart, left anterior descending coronary artery, right coronary artery and circumflex coronary artery were performed. Several sources of variability associated with these methods were assessed. For comparison with contemporary breast radiotherapy, heart and coronary artery doses were assessed for fifty five patients who received adjuvant left tangential breast or chest wall irradiation in 2006. Dose calculations were performed using Theraplan Plus, Nucletron UK Ltd.

Results: Radiation fields that were used to treat the internal mammary lymph nodes resulted in the highest heart doses, particularly for left-sided photon irradiation which delivered between 13 and 17 Gy mean dose to the heart. Of the cardiac structures considered, the left anterior descending coronary artery generally received the highest doses for all regimens.

Comparison of previous and contemporary left tangential pair radiotherapy revealed that radiation dose to the heart has reduced considerably over the past 40 years: the typical mean heart dose for this technique was 13 Gy in the 1970s and 2 Gy in 2006.

Conclusions: Virtual simulation and CT planning enable the measurement of detailed, accurate estimates of radiation dose to the heart and coronary arteries. We plan to combine these dose estimates with studies investigating subsequent heart disease in order to evaluate existing dose-response relationships and to predict the likely cardiac risk of current and future breast radiotherapy regimens.

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IMPACT OF YOUNG AGE ON OUTCOME IN PATIENTS WITH DUCTAL CARCINOMA IN SITU OF THE BREAST TREATED WITH CONSERVATIVE SURGERY AND RADIOTHERAPY: A MULTI-INSTITUTIONAL ITALIAN RETROSPECTIVE STUDY

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Purpose/Objectif: To evaluate the influence of young age on the outcome of ductal carcinoma in situ (DCIS) treated with conservative surgery (CS) and postoperative radiotherapy (XRT).

Materials/Methods: We retrospectively evaluated a consecutive series of 474 cases treated between February 1985 and March 2000 at the Department of Radiation Oncology of 8 Italian Institutions. The

median age was 54 years (range 29-84). All patients (pts) underwent CS followed by breast XRT. Among these pts. 28 out of 477 (5.9 %) were 40 years old or younger. Table 1 shows the patient and treatment characteristics.

Results: After a median follow-up of 88 months (range 23-227 months), 42/474 pts (8.9%) experienced a breast recurrence: 7/28 (25%) in pts 40 years old or younger compared with 35/446 (7.8%) in the older pts ($p<0.01$). In the former group, 4 local relapses were invasive and 3 non invasive; in the latter, 22 were invasive and 13 non invasive; recurrence location was at the initial quadrant or in close proximity in 5 cases in the former group and in 22 in the latter one. Elsewhere failures were observed in 9 cases; 23 pts developed a contralateral breast cancer (invasive in 17 cases) and 17 a second primary tumou in a different organ. The 8-year actuarial local recurrence-free survival was 91.1% for all the cases; all but 8 pts were salvaged with mastectomy.

Conclusions: The influence of age on the outcome of breast conserving therapy in pts with DCIS has not been extensively studied. However larger trials seem to suggest a significant difference based on age. The results of this study confirm an increased risk of local failure which is statistically significant. Succesful treatment of younger pts with DCIS with CS and XRT requires careful attention to clinical and radiological evaluation and selection of the pts and to surgical techniques: only at these conditions, age at diagnosis should not be a contraindication to breast conserving therapy.

	Age < 40	Age > 40
Patients	28	446
Quadrantectomy	21	370
Wide excision	5	38
Tumorectomy	2	38
Axillary dissection	14	206
No axillary dissection	14	240
Node positive	0	1
Median dose irradiation (Gy)	50 (46-50.4)	50 (30-60)
Boost	12	247

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IMPROVED DOSE CALCULATION WITH MONTE CARLO FOR INTERNAL MAMMARY NODAL IRRADIATION FOR BREAST CANCER.

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Purpose/Objectif: Loco-regional radiation is used frequently as part of high risk breast cancer treatment. The inclusion of internal mammary nodes (IMNs) is felt to be an important component of the treatment by many radiation oncologists. However the IMNs can be difficult to treat adequately without causing excess dose the heart and/or lung, and this is one of the reasons why IMN treatment is controversial. Significant discrepancies have been reported between dose distributions calculated by commercial treatment planning systems (TPS) and Monte Carlo (MC) in targets adjacent to inhomogeneities, particularly lung. These differences have been attributed to the inability of conventional inhomogeneity algorithms to model electronic disequilibrium.

Materials/Methods: One published technique used to treat the IMNs employs a mixed electron (80%) and 6 MV photon (20%) beam which is junctioned to the medial tangent photon field. We retrospectively compared dose distributions of patients treated with this technique. Comparisons between MC and TPS were made for the IMN's, lung and heart, and at the junction with the medial tangent photon field.

Results: We found that the TPS overestimated the mean and median doses to the heart and ipsilateral lung by approximately 15%, as compared to MC. The doses to the IMN's did not significantly differ between the two methods. A detailed quantitative analysis on a group of 15 patients will be presented.

Conclusions: The improved heart and lung dose accuracy achieved with MC is important in optimizing the treatment of the internal mammary nodes.

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IMPROVEMENTS IN DOSE HOMOGENEITY IN TREATMENT OF BREAST CANCER OVER TIME WITHOUT IMRT

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Purpose/Objectif: IMRT is increasingly used in breast irradiation to 1) reduce radiation dose to uninvolved tissues and 2) to improve dose homogeneity within the breast. IMRT increases the cost of radiation therapy and its true benefit in breast cancer treatment has yet to be proven. Over the past 2 decades there has been improvement in dosimetry due to increased utilization of CT scans in planning. Wedge selection as compensators and use of segments have appeared to improve dose homogeneity within the breast without IMRT. The records of patients with documented minimum and maximum dose within the target (the breast) were reviewed to assess improvements in dose homogeneity with technical changes over time.

Materials/Methods: From 1993 through 2006, 811 patients with breast cancer treated with lumpectomy and breast irradiation were assessed. Between 1992 and 2004, 91 patients were planned on a fluoroscopic simulator without CT scanning and with 3 contours - at the center plane, 5 cm above, and 5 cm below. Between 1988 and 1995, 178 patients were planned with a non-dedicated CT scan. 5 cuts were obtained and images transferred to the planning computer. Lung inhomogeneity was used. Between 1988 and 1995, most patients were treated with 4 MV photons and external wedges from 15 to 60 degrees. From 1995-2006, most patients were planned with a dedicated CT scanner using lung inhomogeneity and internal wedges. Most patients were treated with 6 MV photons. In later years, high energy beams were increasingly used for a portion of treatment for large breasts. Dose was prescribed to the isodose line that covered the breast target. The maximum dose point was determined to calculate dose inhomogeneity.

Results: Table 1 shows continued improvement in dose homogeneity over time using 3D planning, lung inhomogeneity, segments, and use of higher energies for a portion of treatment.

Year	Planning method	# pts	Inhomogeneity	Range	Median	
1992 -2004	-Non CT	-3 contours	-No lung inhomogeneity	-4 or 6 MV (10 MV*)	91	110%
1988 -1995	-Non -dedicated CT	-5 contours	-Lung inhomogeneity	-4 MV (18 MV*)	178	107-137%
1995 -2000						118%

Conclusions: IMRT may not be necessary in the treatment of breast cancer if its goal is to improve dose homogeneity. CT based treatment planning has provided the tools necessary to optimize dose distribution without the expense of IMRT.

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IMRT IN BREAST IRRADIATION: CLINICAL ASPECTS AND ACUTE TOXICITY

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Purpose/Objectif: To present our clinical experience using IMRT in patients with breast cancer treated with breast conservative or mastectomy surgery and to evaluate the acute toxicity.
Materials/Methods: Forty-five women were treated with 6-MV photons and IMRT technique from May 2002 to April 2006. For fourteen patients the regional lymph nodes (axilla, internal mammary chain, sopraclavicular) were included in the target. For thirty-one patients the IMRT was choosen to cover a complex -target as the chest wall anatomy. The dose prescription ranged from 48.6 Gy and 50 Gy to the whole breast ,or chest wall, 1.8 - 2 Gy per fraction, and a boost of 12 or 16 Gy. The acute toxicity was evaluated with common terminology criteria (CTC) until six weeks after the end of radiotherapy.
Results: The target volume (PTV) ranged from 194 to 2713 cm^3. For all patients a Dose Volume Histogram analysis has been conducted on omolateral and controlateral lung, heart, controlateral breast and PTV. To evaluate the acute toxicity the median follow-up of 3 months (range:1-44 months) was considered adequate. Only 1 patient had pulmonary toxicity, after 1 months from the end of RT, and quickly recovered. No cardiac complications were observed. The acute skin toxicity was observed in thirty-eight patients (84%): G1 in 20 pts., G2 in 16 pts., G3 in 2 pts. (5.2%), 1 pts. developed a cutaneous fistula in the irradiated volume. Both these two patients, with G3 cutaneous toxicity , were treated with Herceptin^R concomitant to radiotherapy. The PTV of these patients was 2713 and 1614 cm^3.
Conclusions: Postoperative breast irradiation with IMRT technique is feasible and indicated for cases with complex anatomy of the chest wall and/or to include regional lymph nodes in the PTV. The incidence of severe acute toxicity is very low comparable with conventional technique. The concomitant use of HerceptinR with RT should be investigated with attention for the observed higher rate of severe cutaneous toxicity above all in case with extended PTV.

698 poster

INDIVIDUAL PATIENT POSITIONING FOR ADJUVANT BREAST IRRADIATION

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Purpose/Objectif: Adjuvant radiotherapy is an important component of the curative treatment in early breast cancer. The occurrence of early and late radiogenic sequelae depend on the volume of and the dose to the irradiated healthy tissues. Since the anatomy of the target volume and the organs at risk vary individually, more favorouble radiation treatment plan might be generated after having positioned the patients individually.
Materials/Methods: We aimed at comparing the radiation treatment plans of early breast cancer patients who 40 patients were included in the analysis. The patients were positioned on the supine and prone breast modules of the AIO (All in One) Solution™ (ORFIT) system. For the radiotherapy of the first 20 patients thermoplastic mask fixation was applied on both breasts in the supine position, while no such fixation was used in the prone position. In the second series of patients, thermoplastic mask fixation was used in both positions, but in the supine position, the irradiated breast was not covered with the mask because of its bolus effect. The target volume and the organs at risk were contoured on the CT slices acquired every 1.0 cm throughout the entire planning volume, in the XIO™ (CMS) treatment planning system. Analyses of the dose distribution in the planning target volume and the radiation exposition of the organs at risk by assessing the volume of the ipsilateral lung receiving 20 Gy (V_{20Gy}), the mean lung dose (MLD), the central lung distance (CLD), the maximum heart distance (MHD), the mean dose to the heart, the volume of the heart receiving (V_{20Gy}) and the mean dose to the contralateral breast were performed.
Results: No significant differences were found in the target volume coverage or the dose homogeneity of the PTVs comparing the radiation treatment plans in the supine or the prone position. The irradiated volume of and the dose to the ipsilateral lung by means of all the parameters registered, were decreased in the prone position by two thirds ($p<10^{-8}$) compared to that in the supine position. Likewise, in the left sided cases, the width of the heart included in the radiation field (MHD) was lower ($p=0.03$) in the prone position, but the differences in the mean dose to the heart and the V_{20Gy} did not reach statistical significance.
Conclusions: The use of the thermoplastic mask improved patient repositioning and limited organ motion in either positions. The prone position for radiotherapy after breast conserving surgery is advantegeous especially when the risks of radiogenic heart or lung sequaelae would be high in the supine position. The application of mask-fixation for better accuracy is recommended in both positions.

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INFUSION THERAPY OF PAMIDRONATE IN COMBINATION WITH RADIATION THERAPY IN CANCER PATIENTS WITH ADVANCED, PAINFUL, METASTATIC BONE LESIONS

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Purpose/Objectif: Palliative radiation therapy is successful in the treatment of painful bone metastases; however, complete pain relief can be achieved only in about half of the patients and almost every fourth patient is refractory to such therapy. Pamidronate (Aredia®), a bisphosphonate, has shown substantial analgesia in patients with preceding radiation therapy and therefore is a promising candidate for a combination with radiation therapy.
Materials/Methods: In a prospective, randomized, double-blind, placebo-controlled, multicenter parallel group design, cancer patients with solitary or multiple painful, metastatic osteolytic bone lesions in the region of femur, humerus, pelvis or spine were treated with palliative radiation therapy (2 Gy/day for 18 to 23 days depending on type of tumor) and one of the following: placebo, 90 mg pamidronate on day 1, 15 and 29 (2-weekly) or on day 1 and 29 (4-weekly interval). Patients were followed up until month 12 after start of therapy. Response to treatment was defined by an at least 50% decrease of intensity of bone pain over at least four weeks as measured on item 3 (worst pain during the past 24 hours) of the Brief Pain Inventory:
Results: N=76 patients were treated (55% females, median age: 66 years) in nine radio-oncological centers in Germany. Half of the patients (48.0%) in the placebo group responded to radiation therapy

alone; under combined pamidronate therapy, responder rate was higher after 2-weekly (73.1%) than after 4-weekly (56.0%) application. Sample size was too low to confirm a superior efficacy of the 2-weekly pamidronate therapy over placebo (p=0.10, one-sided exact Fisher test). Pain relief by 50% of the baseline value was achieved after 28, 32 and 34 days under pamidronate therapy in 2-weekly and 4-weekly intervals or under placebo. In contrast to the placebo group, no clear advantage of the 2-weekly compared to the 4-weekly interval could be detected in further outcome measures (pain scores, Karnofsky-Index, quality of life, analgesics consumption).
Conclusions: The results of this study appear to support the claim that radiation therapy combined with pamidronate 90mg infusion therapy is superior to radiation therapy alone in reducing the pain in progressive painful metastatic bone lesions. There is no advantage of the 2-week application schedule if the two modes of application are compared. There were no new findings regarding the toxicity of the test drug such as vomiting or anemia.

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INTERSTITIAL HIGH DOSE RATE (HDR) BRACHYTHERAPY FOR EARLY STAGE BREAST CANCER

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Purpose/Objectif: External Beam Radiation Therapy (EBRT) has been the standard of care for breast conservation radiation therapy. Recent data indicates that Interstitial Implant and High Dose Rate (HDR) radiation afterloading compares very favorably to EBRT in selected patients.
Materials/Methods: Patients with Tis, T1, and T2 tumors measuring < 3 cm, negative surgical margins, and negative axillary lymph nodes were judged to be candidates for Interstitial Implant. Subsequently, patients who had, or were scheduled to receive anthracycine based Chemotherapy were excluded.
Results: Between 2000 and 2006, 117 patients underwent Interstitial HDR Implant under Stereotactic Mammographic guidance with conscious sedation and local anesthesia. Conscious sedation consisted of Morphine and Versed. Local anesthesia was given with a mixture of 1% Lidocaine, 0.25% Marcaine, 1:100,000 Epinephrine, and 4% Sodium Bicarbonate neutralizing solution. The implants were placed using the Anderson-Nair Template using from 3 to 6 planes, and 8 to 43 needles. Catheters were subsequently threaded thru the needles, and the needles removed. Catheter spacing was 1.0 to 1.5 cm. Radiation Treatment planning was performed using CT Scanning and the Plato System. Treatment volumes ranged from 25 cm^3 to 359 cm^3. HDR treatment was given using the Nucletron afterloading system. The breast implant volume received 3400 cGy in 10 fractions prescribed to the Planning Target Volume, given BID over 5 days. The procedure was well tolerated. No patient required hospital admission. With a median follow-up 40 months (range 6-68 months), local recurrence occurred in 3.4% (4/117). Cosmetic results were good to excellent in 86.3% (101/117) of the patients. Wound healing complications developed in 6.8% (8/117). Three of these patients had received anthracycline based Chemotherapy. The other five had large (> 200 cm^3) implant volumes and catheter spacing of 1.5 cm. Two patients healed after 6 months of conservative treatment. Surgery was required in six patients who developed fat necrosis.
Conclusions: With median 40 month follow-up, Breast Conservation radiation therapy utilizing Interstitial HDR Implant has yielded local recurrence rates and cosmetic results which compare favorably to EBRT in selected patients. Longer follow-up is needed. Treatment with anthracycline based Chemotherapy and large (> 200 cm^3) implant volumes appear to be relative contraindications to Interstitial HDR Implant. Finally, catheter spacing of 1 cm yielded optimal dosimetry and minimized complications.

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IONIZING RADIATION AND TOBACCO USE INCREASES THE RISK OF A SUBSEQUENT LUNG CARCINOMA IN WOMEN WITH BREAST CANCER: CASE-ONLY DESIGN

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Purpose/Objectif: To analyze the risk of lung cancer in women treated with radiotherapy for breast cancer. We accessed the lung dose in relation to different radiotherapy techniques, provided excess relative risk (ERR) estimate for radiation associated lung cancer, and evaluated the influence of tobacco use.
Materials/Methods: The Swedish Cancer Registry (SCR) was used to identify 182 women diagnosed with breast and subsequent lung cancers in Stockholm County during 1958-2000. Radiotherapy was given to 116 patients. Radiation dose was estimated from the original treatment charts and information on smoking history was searched for in case records and among relatives. The risk of lung cancer was assessed in a case-only approach where each woman contributed a pair of lungs.
Results:
The average mean lung dose to the ipsilateral lung was 17.2 Gy (range 7.1-32.0). A significantly increased relative risk (RR) of a subsequent ipsilateral lung cancer (2.04, 95% confidence interval [CI]=1.24-3.36), was seen ≥10 years of follow up. Squamous cell carcinoma (RR=4.00; 95% CI: 1.50-10.66) was the histopathological subgroup most closely related to ionizing radiation. The effect of radiotherapy was restricted to smokers only (RR=3.17; 95% CI: 1.66-6.06). The ERR/Gy for women with latency ≥10 years since exposure was 0.11 (95% CI: 0.02-0.44).
Conclusions: Radiotherapy for breast cancer significantly increases the risk of lung carcinoma more than 10 years after exposure in women that smoked at time of breast cancer.

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IS THERE AN ASSOCIATION BETWEEN LATE NORMAL TISSUE RESPONSE AND TUMOUR CONTROL AFTER LOCAL TUMOUR EXCISION AND RADIOTHERAPY FOR EARLY BREAST CANCER?

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Purpose/Objectif: To test for an association between the risk of late adverse effects and local tumour control.
Materials/Methods: Between 1986 and 1998, 1410 patients were enrolled in a randomised controlled trial testing non-standard frac-

tionation to the whole breast after breast conservation surgery for early breast cancer. Patients were randomised to 50 Gy in 25 fractions (control) versus 2 dose levels of an experimental schedule delivering 13 fractions of 3.0 Gy or 3.3 Gy. Electron boost allocation (10 Gy in 5 fractions) was determined independently of this randomisation. Frontal photographs were taken after surgery and repeated annually to 5 years and then at 10 years. Change in photographic breast appearance was scored at each time point as none, mild or marked in comparison with the baseline. Changes that occurred after 5 years were ignored for the purposes of this analysis, since they were thought unlikely to identify radioresponsive individuals. Cox proportional hazards regression was used to model time to local relapse (or date last seen), taking into account the time at which change in breast appearance occurred, and adjusting for factors associated with relapse and adverse effects (fractionation schedule, boost, axillary treatment, tamoxifen, breast size and age). Breast size was fitted as a proxy for dose inhomogeneity.

Results: Of the 1202 patients with a baseline and at least one follow-up photographic assessment, 267 had mild change in breast appearance within 5 years of radiotherapy, 53 had marked change within 5 years and 125 had an ipsilateral breast relapse. Compared with no change in breast appearance, the adjusted hazard ratio for local relapse associated with mild change was 0.59 (95% confidence interval 0.29-1.18), and for marked change it was 0.64 (0.15-2.77) (trend test p=0.16).

Conclusions: Statistical power is low, but the results suggest that there may be an association between reduced risk of local tumour relapse and change in breast appearance after primary tumour excision and whole breast radiotherapy for early breast cancer. If confirmed by independent studies that effectively control for dose inhomogeneity, it would support the need for a strategy of predictive testing to identify patients in whom the severity of late adverse effects could be reduced by modest dose reductions while retaining acceptable rates of tumour control.

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LONG-TERM OUTCOME OF BREAST-CONSERVING THERAPY IN EARLY BREAST CANCER: ANALYSIS OF FACTORS AFFECTING RECURRENCE AND EVALUATION OF RADIOTHERAPY VOLUME

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Purpose/Objectif: We present a retrospective analysis of long-term results for patients receiving breast-conserving therapy with early breast cancer to evaluate the factors affecting recurrence and patterns of recurrence, and to estimate compatibility of radiotherapy volumes.

Materials/Methods: From 1991 to 1995, 362 patients with AJCC stage I and II breast cancer (42% stage I, 38% stage IIa, 19% stage IIb) who received breast conserving therapy were evaluated retrospectively. The median patient age was 44 years (range 23-80). All the patients received breast conserving surgery (wide excision to quadrantectomy) and axillary lymph node dissection (except 2 patients) followed by radiotherapy. The radiation dose to the whole breast was median 50.4 Gy (range 45-55.8) and with boost doses of 10 Gy (range 0-20). The radiation volume was the involved breast alone in the patients with less than 4 positive axillary lymph nodes, and breast and supraclavicular fossa in patients with 4 or more positive axillary lymph nodes. Adjuvant chemotherapy was performed in 168 patients before or after radiotherapy. The median follow-up period was 123 months (range 3-169).

Results: The 10-year overall survival, disease-free survival, local recurrence-free survival, regional recurrence-free survival, and distant recurrence-free survival rates were 89.7%, 87.6%, 97.3%, 95.4%, and 91.9%, respectively. Local recurrence, regional recurrence, and distant recurrence occurred in 14 (3.9%), 17 (4.7%), and 40 (11.0%), respectively. By univariate analysis, factors affecting disease recurrence were age (<35), T stage, N stage, tumor location, and AJCC stage. Age and N stage were statistically significant factors affecting disease recurrence in multivariate analysis. Among 310 patients receiving radiotherapy on breast alone, 15 patients (4.8%) had regional recurrence and especially patients with inner quadrant lesion had high regional recurrence rate (11/98, 11%) ($p < 0.001$).

Conclusions: These low local recurrence rate may explain that current technique of radiotherapy was relevant. But, in case of inner quadrant lesion, although involved lymph nodes did not exist, there were many regional recurrences. Therefore, it may suggest a potential role of irradiation on regional lymph nodes in this group.

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POSSIBILITY OF REPLACEMENT OF WHOLE BREAST RADIOTHERAPY WITH ACCELERATED PARTIAL BREAST IRRADIATION FOR TREATMENT OF EARLY STAGE BREAST CANCER

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Purpose/Objectif: Radiotherapy is standard part of modern breast saving therapy for early stage breast cancer. At present only whole breast postoperative irradiation is performed in Latvia. For selected group of patients this treatment can be substituted with accelerated partial breast irradiation in order to shorten overall treatment time and potentially to reduce acute reactions and/or late toxicity, maintaining the same tumor control.Aim of this work is to show, that during whole breast irradiation dose maximum and tissue volume which receives doses more than 105% from prescribed dose, is linked with size of treated volume (treated volume - tissue volume receiving > 95% from prescribed dose), which is strictly linked with breast volume. Because of this for large breast volumes there will be higher complication probability performing whole breast irradiation, and it seems to be meaningful to use accelerated partial breast irradiation for selected patients from this group.

Materials/Methods: 50 patients receiving whole breast irradiation after breast salvaging surgery in Latvian Oncology Center during 2005 were analyzed. 3D treatment planning with individual dose optimization was performed for all patients. In all cases tangential photon fields (4 - 6 MV) with wedges and MLC were used. Parameters to be analyzed: dose maximum (Dmax, % from prescribed dose), treated volume (TV, cm^3), volume which is receiving more than 105% from prescribed dose (V105, cm^3), and V105 and TV ratio (V105/TV, %).

Results: Dmax was between 105.6 and 120%, TV - from 392.8 to 3648.3 cm^3, V105 - from 0.2 to 1167.5 cm^3 and V105/TV - from 0.1% to 36.0%, respectively. Dmax, V105 and V105/TV is rising with rising of TV ($p < 0.0001$, $p < 0.0001$ un $p = 0.001$ respectively). Dmax is also higher for higher V105/TV ($p = 0.001$). For TV 711.0 cm^3 Dmax and V105/TV were 107.0% and 2.1% and for TV 3245.9 cm^3 - 115.0% and 36.0% respectively.For large breast volumes dose distribution was worse, which can be attributed to technical limitations of whole breast irradiation, even using modern treatment planning and dose delivery methods.

Conclusions: For large volumes to be treated, dose maximum and volume of dose maximum are rising unavoidable. Even using modern external beam techniques for whole breast irradiation, for patients with large breast volume it is not possible to maintain appropriate dose coverage of breast during postoperative radiotherapy without formation of unwanted dose maximum in treated volume. For selected group of patients Accelerated Partial Breast Irradiation may not only shorten overall treatment time, but also have poten-

tial to reduce late toxicity associated with dose maximums in breast tissue.

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PROGNOSTIC FACTORS FOR CHEST WALL RECURRENCES AFTER TOTAL MASTECTOMY FOR BREAST CANCER.

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Purpose/Objectif: To investigate the age factor for local recurrence after mastectomy for breast adenocarcinoma.

Materials/Methods: Between 1973 and 2004, 2106 patients were treated with total mastectomy and axillary lymph node (LN) dissection for invasive breast adenocarcinoma. Chest wall irradiation (RT) was given to 48.5 % of patients, regional LN RT to 47.1 % and chemotherapy to 35.1 %. The median follow-up was 118 months (172 months in censored patients). Chest wall local recurrence (LR) was assessed with the actuarial method and the influence of prognostic factors was studied using tho Logrank test.

Results: LR was observed in 140 patients. The 5-year and 10-year actuarial LR rate was 2.7 % and 5.5 %. Despite a higher frequency of radiotherapy being given to patients 35 or less (78 % vs 55 % in older patients, $p < 0.0001$), they experienced significantly higher LR rates: 13.7 % at 10 years, versus 4.1 % for those 35 - 50, 7.3 % for 50 - 65, and 4.5 % for patients older than 65 ($p = 0.0063$). Hormone receptors also affected LR ($p = 0.0009$). Concerning the LN status, the most significant prognostic parameter was the percent positive LN after axillary dissection ($p < 0.0001$), with a relative risk of 1.4 % per percent positive LN. Patients less than 35 had significantly more positive LN ($p < 0.0001$) and less positive HR ($p = 0.038$). Yet, upon multivariate analysis, all 3 factors retained their significance in the Cox model. Age was not related to either tumour size or histological grade.

Conclusions: As for LR after conservative surgery, patients less than 35 years are at a significantly high risk of chest wall LR after total mastectomy, despite being given radiotherapy more often than older patients. In addition to the presence of a high percentage of positive LN and negative HR, other factors should be looked for to explain the high LR rates in these young patients.

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PULMONARY TOXICITY IN WOMEN WHO UNDERWENT BREAST IRRADIATION AFTER BREAST CONSERVATIVE OPERATION: DOSE VOLUME HISTOGRAM AND DOSE RESPONSE FUNCTION

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Purpose/Objectif: To study radiologic pulmonary toxicity in women with early stage breast cancer who underwent irradiation after breast conserving operation in relation to dosimetric factors

Materials/Methods: CT scans of the lung were performed before and four months after radiotherapy in 456 breast cancer patients treated with three different radiotherapy techniques in three different hospitals. Mean age was 55 years old, and 63 patients were treated by the djuvant tamoxifen. There were no patients who were treated by the adjuvant chemotherapy. Two hundred and nineteen patients were irradiated with parallel opposed beams of 4MW X-ray (Tc-1), 169 patients were irradiated with tangential opposed beams of 4MV X-ray (Tc-2), and 68 patients were irradiated with tangential opposed beams of 6MV X-rays (Tc-3). All patients underwentthree-dimensional dose planning and dose volume histograms (DVHS) of the ipsilateral lung were calculated. A prescribed dose as 50 Gy / 25 fractions / 5 weeks. The local fields were planned to contain the ipsilateral mammary gland and the ipsilateral internal mammary lymph nodes. The medial supraclavicular and axillary lymph nodes were not included in the field. The difference between the density values before and after treatment of the center of the irradiated field was calculated, and compared with the planned three-dimensional dose distribution. Dose response function between CT value of zero and the lung dose was calculated.

Results: In the entire study, five patients (5/456, 1.1%) developed symptomatic radiation pneumonitis. Adjuvant tamoxifen was given to all five patients (5/63，7.9%). Mean irradiated volumes more than 5, 10, 20, 30, and 40Gy was 180, 130, 80, 60, 20ml. And those of five radiation pneumonitis patients were 270, 200, 130, 100, and 40ml. Mean maximum Dose in the lung was 43Gy. The maximum doses of the lung of five radiation pneumonitis patients were from 50 to 45Gy. Mean cumulative ipsilateral lung DVHS of Tc-1 showed larger volume of a lower dose (less than 20 Gy) region. That of Tc-3 showed larger volume of a middle dose (between 20 and 30 Gy). Tc-2 seemed the best radiotherapy among the three. The density value of the lung before treatment was less than -700. All patients showed lung density changes. From dose response function between CT value over zero and the lung dose, the frequency of the density of zero increased rapidly over the dose of 20Gy.

Conclusions: Lung density changes with CT were verified in all patients. Local lung fibrosis seemed to be the essential late toxicity after local breast irradiation. But there were very few patients who developed symptomatic radiation pneumonitis after local breast irradiation.

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REPRODUCIBILITY IN BREAST CANCER CONSERVATIVE TREATMENT: PERSPECTIVE STUDY

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Purpose/Objectif: The set-up of the patient is a common problem during the radiation therapy and it's essential for the efficacy of the treatment and for the reduction of the toxicity. It's necessary, therefore, a Quality Assurance Program to ensure.

This study wants to analyse interfraction reproducibility of breast cancer treatment with tangential fields and total dose of 50,4 Gy with standard fractions, to define our range of tolerance in this treatment and to identify the better frequency of the Electronic Portal Imaging (EPI) controls in Quality Assurance Program.

Materials/Methods: Thirty patients with breast cancer, after conservative surgery, were enrolled in this study and analysed using VARIS/VISION SYSTEM with blend function.

Three groups of ten patients each one were differentiated on the basis of the frequency of Electronic Portal Imaging (EPI) controls: five consecutive EPI after radiotherapy start and two times weekly (GROUP A); three consecutive EPI and one weekly in the rest period (GROUP B); two consecutive EPI and one every ten fractions (GROUP C). In every EPI the outline of the breast and the internal margin of the thoracic wall (match structures) were contoured. In VARIS/VISION SYSTEM there is the function of blend that was used to estimate correspondence between match structures contoured on Digitally Reconstructed Radiographs (DRR) and EPI. Errors < 7 mm were considered acceptable on the basis of the literature data.

The correspondence of DRR/EPI was estimate: - at the level of cranial breast outline (the distance between the superior border of the field and the chest wall profile was used for errors of patients' rotation); -

on the axis Z (the central distance between the internal field margin - lung direction - and the chest wall profile was used for this axis);
- on the axis Y: (the distance from the inferior border of the breast to the caudal border of the field for this axis).

Results: 470/480 EPI were performed with a compliance of 97,6%. Ten EPI were not performed because of damages of VARIS VISION SYSTEM. The global differences related to three parameters and in the tollerance limits (+ 7 mm) were of 76,2% (group A), 78,8% (group B) and 78,4% (group C); about the patients' rotation the differences were of 60,8% (group A), 64,4% (group B) and 66,3% (group C); about the central lung distance they were of 85,5% (group A), 91,9% (group B) and 73,8% (group C) and about the distance from the inferior border of the breast to the caudal border of the field the differences were 82,4% (group A), 80,0% (group B) and 95,0% (group C).

Conclusions: The better sequence of EPI seems the sequence of the group B because the frequency doesn't overload the work and produces results near to the results of the group A, where the EPI were performed with major frequency. This outcome will have to be confirmed by statistical analyses. The patients' rotation is the main parameter that influences the reproducibility of this treatment.

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SUBJECTIVE ACUTE AND LATE TOXICITY AND THE SATISFACTION LEVELS IN PATIENTS WITH BREAST CANCER IRRADIATED WITH SHORT FRACTIONATION FOR BREAST CONSERVATION THERAPY -COMPARISON WITH CONVENTIONAL FRACTIONATION -----

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Purpose/Objectif: The aim of this study is to compare the frequency of "subjective" complications and their severity between conventional fractionation and short fractionation, and to clarify the relationships between the sequelae and the satisfaction ratings.

Materials/Methods: From 1992 to 2005, 370 patients with stage I and stage II breast cancer who received breast conservation therapy (BCT) were enrolled in this study. One hundred and ninety-six patients received 50 Gy/25 fractions/35 days, and 54 of the 196 patients also received boost irradiation with 10 Gy/5 fractions/7 days (group C). One hundred and seventy-eight patients received 44 Gy/16 fractions/22 days, and 122 of the 153 patients also received boost irradiation with 9 Gy/3 fractions/3 days (group S). Early sequelae were evaluated by doctor's questions at the end of radiation therapy (point A) and 7-10 days after the treatment (point B). Late sequelae were assessed by conducting a survey int he form of a questionnaire at least 6 months after the end of radiation therapy (point C). The median follow-up period was 5.17 years and 5.98 years in groups C and S, respectively.

Results: The most commonly observed toxicity at point A was erythema 153 (78.1%)/135 (75.8%) [group C/group S], followed by heat sensation 74 (37.8%)/77 (43.3%), sense of discomfort 77 (39.3%)/73 (41%), and pain 72 (36.7%)54 (30.3%). There were no significant differences in these symptoms between the two groups. The frequency of erythema, sense of discomfort, pain and dryness was hardly changed between points A and B. The boost irradiation also did not influence the frequency of erythema, sense of discomfort, pain, dryness, or edema at point A or point B. A sense of hardness more frequently appeared in group S 58 (32.6%)] than in group C [43 (21.9%)] with a significant difference between the values (p=0.021). There was no significant correlation between the satisfaction ratings and sense of hardness in either group C (p=0.24) or group S (p=0.36). Similarly, sense of hardness and breast deformity had no significant correlations in either group C (p=0.26) or group S (p=0.49). Other commonly noted symptoms were pigmentation (27.6%/30.3% [group C / group S]) and intermittent pain(29.6%/27.0%), with no significant different between the two groups.

Conclusions: Small fractionation results in acceptable patient "subjective" sequelae comparable to the sequelae experienced following the conventional fractionation.

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SURIVAL AND LOCAL CONTROL IN BREAST CANCER AFTER CONSERVATIVE TREATMENT IN YOUNG PATIENTS

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Purpose/Objectif: Breast cancer in young patients is often associated with a poorer prognosis, We analiyse mortality rates and local control of early stage breast cancer in young patients after conserving surgery followed by radiation therapy.

Materials/Methods: From July 1986 to July 2005, 540 patients under 50 years (mean 43,3) were treated. The majority of cases carried a infiltrating ductal carcinoma (90%). Staging comprised 63% stage I and 37 % stage II. All received breast conserving therapy - lumpectomy (90%) or quadrantectomy (10%)-. Axillary lymph node dissection or sentinel lymph node biopsy was performed in all cases. Median tumour size was 16,8 mm. and histological grade was 24.5 % grade I, 45.3 % grade II and 28.4% grade III. Intraductal carcinoma was present in 48,2 % of cases. Margin status was: positive in 3.6 %, close (under 3 mm) in 12.6 % and negative in 83.8 % of cases. Hormonal receptors were known in 72 % of cases, and 60 % of them were positive. In 67 % of patients adjuvant chemotherapy was administered. Breast conserving surgery was followed by whole breast irradiation. The radiation dose to the whole breast was 47 Gy (22-55) at standart fractionation and with boost doses of 8-25 Gy administered to the tumor bed in 89 % of cases. Median follow-up for all patients was 4 years (mean: 5 years).

Results: Local relapse (ipsilateral breast tumor recurrence), and distant metastasis occurred in 29 (5.5%), and 62 patients (11.6 %), respectively. Deaths were observed in 37 cases, of which 92% were due to breast cancer. The 5-year overall survival, local-relapse-free survival, distant-metastasis-free survival and disease-free survival rates were 93 % (CI 90-96%), 93.4 % (CI 91.4-96.6%), 87.7 % (CI 84-91.4%) and 84 % (CI 80-88%) respectively. From analysed prognostic factors (age, histological grade, margin status, nodal involvement, intraductal carcinoma presence or hormonal receptors) only histological grade (p= 0.0402) and nodal involvement (p=0.033) showed impact in overall survival. In very young patients (under 40 years) a trend to higher local recurrence was present (p=0.0586) while other prognostic factors didn't show any impact in local control.

Conclusions: In this series young patients reached marked survival rates with high local control. Nevertheless histological grade and nodal involvement show to have impact in overall survival, while very young patients seem to have a higher local failure.

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TARGETED INTRA-OPERATIVE RADIATION THERAPY (TARGIT) USING PRS400 PHOTON RADIOSURGERY SYSTEM (INTRABEAM) AS A TUMOR BED BOOST IN BREAST CONSERVING TREATMENT.

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Purpose/Objectif: The aim of this study was to assess the tolerance and effectiveness of intraoperative radiotherapy (IORT) using as a boost in breast conserving treatment.

Materials/Methods: 95 patients with early breast cancer were treated by TARGIT during breast concerving surgery, followed by conventional postoperative external beam radiotherapy (EBRT). A boost dose of 5 Gy was prescribed to 0.5 cm from the applicator surface. All patients received EBRT to the whole breast to total dose of 50 Gy in 25 fractions. The acute and late effects were assessed using RTOG/EORT score.

Results: The median follow-up was 18 months (range, 5-35 months). Acute skin toxicity after EBRT was modest, limited mainly to grade 1-2 reactions (68%). Slight, moderate and severe fibrosis of subcutaneous tissue were observed in 52%, 8% and 1% of patients, respectively. Of all patients, 56% and 9% had late skin reaction of grade 1 and 2, respectively. One patient (1%) had radionecrosis of skin close to the neck of applicator. No patients developed local recurrence. Two patients (2%) had distant metastases.

Conclusions: Intraoperative radiotherapy using Intrabeam was well tolerated. Side effects were mild to moderate and were mainly asymptomatic. Local control was encouraging. Further investigations of TARGIT using Intrabeam are warranted.

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THE FEASIBILITY AND TOXICITY OF ACCELERATED PARTIAL BREAST IRRADIATION USING HDR BRACHYTHERAPY WITH SIMULTANEOUS INSTALLATION TECHNIQUE

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Purpose/Objectif: Accelerated partial breast irradiation using HDR brachytherapy was delivered for the selected patients with early breast carcinoma. We used lesser number of catheters and planes than in other countries. The aims of this study were to evaluate the feasibility and toxicity of HDR brachytherapy using one or two treatment planes.

Materials/Methods: Between Jun 2002 and Dec 2003, 37 patients with clinical stage I and II breast cancers were enrolled in HDR brachytherapy protocol after lumpectomy. We installed the afterloader catheters simultaneously with lumpectomy. Under the direct view of surgical clips, we inserted 3 to 5 catheters on the surgical bed with 1 to 1.5cm intervals depending on the treatment volume. The treatment planning was done with orthogonal planning films and using Nucletron Plato Brachytherapy v14.2.3.

Results: The median follow-up is 33 months (5-47 months). Twelve patients had undergone HDR brachytherapy alone (brachytherapy group) and 25 patients brachytherapy as a boost treatment (combined group). The total dose of brachytherapy group was 30 Gy/10 fractions/5 days and combined group 8 to 18 Gy. The reasons for adding the external beam radiotherapy of whole breast were pathologic (12 patients), high skin dose more than 50% of the prescribed dose (8 patients), insufficient treatment margins (3 patients), and refusal of treatment (2 patients). Even though we used one or two treatment planes, the skin doses were 12 to 99.7%(median 42.6%) of the prescribed dose. The median distances from surgical clips to 100% isodose line were 7.8, 17.3, 16.2, 7.1, 12, and 8mm respectively (table 1). There has been no evidence of disease at last follow-up in brachytherapy group. In combined group, two patients had local failure at 21 months and 36 months and were salvaged with modified radical mastectomy. The treatment was well tolerated without any acute side effects such as pain or bleeding during brachytherapy treatment. For late side effects, asymptomatic fat necrosis was founded in 13 patients and postoperative seroma in 7 patients. In two patients increased hot uptakes in underlying rib were developed. The cosmetic results were excellent in all brachytherapy group. In combined group, the cosmetic results were good in 3 patients, fair in 1 patient, and excellent in the rest of the group.

Distance from clips to 100% isodose line (mm)	All cases (median)	brachytherapy group (median)	Combined group (median)
Superior margin	1.3-17(7.8)	6.3-17(7.2)	1.3-15.2(9.1)
Medial margin	9.9-31.1(17.3)	12.5-29.9(17.2)	9.9-31.2(17.6)
Lateral margin	5-28(16.2)	14.1-28(15.9)	5-24.5(16.8)
Inferior margin	0-20(7.1)	3-14.1(8.3)	0-20(6.8)
Superficial margin	3.5-23.7(12)	3.5-16.2(11.1)	7-18.8(12.7)
Deep margin	0-13(8)	2.1-13(10)	0-11.3(7.9)

Conclusions: This simple and noninvasive treatment is well tolerated. These preliminary results with using limited numbers and planes of catheters show the possibility of delivering brachytherapy on relatively small breast size with excellent cosmesis and local control rates.

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THE RELATIONSHIP OF V20 AND CENTRAL LUNG DISTANCE IN BREAST RADIOTHERAPY PLANNING

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Purpose/Objectif: The central lung distance (CLD) is used to estimate the volume of lung treated in breast radiotherapy. A central lung distance of less than 3cm is generally accepted as safe standard for an acceptable risk of pneumonitis. It is unclear if CLD corresponds well with V20 (volume of lung receiving >=20Gy), which has been correlated with a risk of pneumonitis in conformal radiotherapy planning.

The objective of this study was to evaluate the relationship between CLD and V20 for four-field breast radiotherapy.

Materials/Methods: Thirty-three patients with breast cancer treated with a standard 4-field technique, between September and November 2005 were identified. The CLD was measured on the central tangent slice and defined as a line perpendicular to the midpoint of the posterior tangent field and the edge of the chest wall. Both lungs were contoured; V20 for the ipsilateral and contra lateral lungs and mean lung dose were calculated. The central lung distance and dose volume histogram parameters were analyzed and their relationship was evaluated. Patient charts were reviewed for clinical status and presence of pneumonitis.

Results: The 4-field radiotherapy technique utilized a photon tangent pair to deliver 40-42.5 Gy/16 to the chest wall +/- IMC (internal mammary chain) and a direct anterior and posterior patch field to deliver 37.5 -40 Gy/16 to the axillary midplane. The mean central lung distance was 2.3 cm (range 1.5-3.5cm). The mean V20 for both lungs was 13.8% (range 8.4-23%). The mean V20 for the ipsilateral lung was 25.8% (range 13.1-41.03%). V20 and CLD were directly correlated. A formula relating CLD and apical lung treated reproducibly predicted V20. With an average of 6 months of follow-up, no patients in this study population have developed clinical evidence of pneumonitis.

Conclusions: The relationship between V20 and CLD confirms our clinical impression that pneumonitis is rare during four field radiotherapy. The V20 of the ipsilateral lung was within tolerance if the CLD was < 3.0 cm. For patients where target coverage requires a CLD of more than 3.0 cm, the V20 would be a useful tool to estimate the risk of pneumonitis. Alternatively, our formula utilizing CLD and apical lung treated may provide a useful estimate of the risk of pneumonitis.

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THE SEQUENCING OF CHEMOTHERAPY AND RADIOTHERAPY IN BREAST CANCER PATIENTS AFTER MASTECTOMY

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Purpose/Objectif: The purpose of this study is to retrospectively evaluate the outcomes according to the sequencing of radiation therapy (RT) and chemotherapy (CT) after mastectomy in high risk patients with breast cancer.

Materials/Methods: From January 1986 through September 2000, 275 women with stage I-IIIB breast cancer were treated with chemotherapy and radiation therapy after mastectomy. In Seoul National University Hospital . Indications of postoperative radiotherapy were as follows: [3] 5 cm of tumor size; close (< 2mm) or positive resection margins; T4 primary; 4 or more positive axillary LNs. A median of 50.4 Gy (49.5-60.4 Gy) in 28 fractions over a period of 5 1/2 weeks, was administered to chest wall, axillary, supraclavicular, and internal mammary LN area. The patients were divided into four groups. Chemotherapy was given first in 116 patients (CTRT), concurrent chemoradiotherapy in 77 (CCRT), sandwich therapy in 65 (SAND), and radiation therapy first in 17 (RTCT). Prognostic factors such as age, primary tumor size, and nodal status were not statistically different among the four groups. There were a higher proportion of patients with close or positive margins in CCRT and RTCT groups than CTRT and SAND (22/77, 5/17 vs. 3/116, 2/65).

Results: Median follow-up was 145 months (10 - 210). The 5-year OS and DFS were 69.4 % and 56.1 % as a whole. OS and DFS were not statistically different among the four groups (5 yr OS/DFS 68.0%/63.0%, 71.3%/60.8%, 65.0%/48.1%, 81.9%/58.8%, in CTRT, CCRT, SAND, and RTCT, respectively). The incidences of locoregional recurrence (LRR) were not different between early RT group (CCRT/RTCT, 11%/12%) and delayed RT group (CTRT/SAND, 7%/8%).

Conclusions: This study suggests that in these high risk breast cancer patients after mastectomy, delay in the start of radiotherapy does not increase LRR and the final treatment outcomes are not affected by the sequencing of CT and RT.

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VOLUNTARY MODERATELY DEEP INSPIRATORY BREATH HOLD (VMDIBH) REDUCES HEART DOSE WHILE MAINTAINING ADEQUATE COVERAGE OF THE CTV COMPARED TO TANGENTIAL BEAM IRRADIATION WITH/WITHOUT A HEART BLOCK IN LEFT SIDED BREAST IRRADIATION.

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Purpose/Objectif: Irradiation of left-sided breast cancer bears a risk of cardiotoxicity. The aim of this study was to evaluate the feasibility of vmDIBH in irradiation of the left breast and to compare this vmDIBH method with free breathing with or without a heart block.

Materials/Methods: Patients < 70 years, with T1-T2N0-1M0 left-sided breast cancer, referred for tangential breast irradiation were eligible for this study. First, standard CT simulation was performed (CT1). A maximal heart distance (MHD) of >1 cm prompted a CT in breath hold at maximal inspiratory volume to evaluate the heart's movement. If the MHD decreased to <1 cm, patients were coached for vmDIBH: maximally attainable inspiratory volume for 30 seconds. After training a new CT-simulation (CT2) was made in vmDIBH in 9 patients. For all patients, heart, lungs and CTV (breast) were delineated on both CTs, and 3 treatment plans were designed: 2 plans with CT1 (2 wedged tangential fields in free breathing with/without heart block) and one plan with CT2 (2 wedged tangential fields in vmDIBH). The V95, V107, Dmax (CTV), V20, MLD (lungs), V30 and MHD (heart) were evaluated for alle 3 plans, and the best plan was executed.

To minimise variation in inspiratory volume, inspiratory displacement of the midline epigastric skin was measured using a specifically designed instrument: a metrically marked vertical bar placed over the epigastrium. During irradiation patients were asked to inhale until their skin touched the tip of the bar, ensuring reproducible positioning. In addition, EPID in video-mode was used for continuous visualisation of the field. Finally, in-house designed metric gold-markers (visible on EPID) were placed on the field edges on the skin to quantitatively evaluate breathing motion. Displacement of >5 mm meant treatment interruption.

Results: For all 9 patients the vmDIBH plan was judged to be the best plan. Consequently, all 9 patients were treated using this technique. Compliance and tolerance were excellent. No treatment interruptions were required.

Conclusions: vmDIBH in tangential left breast irradiation permits a significant decrease in the volume of irradiated heart while maintaining similar/ superior coverage of the CTV when compared to standard fields in free breathing without/with a heart block. A slightly less homogenous dose distribution in the vmDIBH-plans is noted; probably due to stretching breast tissue across the chest-wall, creating areas of higher dose-deposition in thinner areas. In our experience, the technique is well tolerated, reproducible and patients can be treated in a regular time-slot.

Mean Results:	Free breathing	vmDIBH	p-value	Heart Block	vmDIBH	p-value
V95 (%)	93	92	0.83	89	92	**0.02**
V107 cc	0.8	2.6	0.1	1.6	2.6	0.54
Dmax (%)	108	109	0.22	108	109	0.34
V30 (%)	5.7	0.6	**0.002**	2.1	0.6	0.19
MHD (cm)	1.9	0.6	**0.00003**	0.9	0.6	0.4
MLD (Gy)	4.1	4.4	0.71	3.6	4.4	0.27

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ANALYSE OF SITE OF RECURRENCE IN 44 PATIENTS WITH PRIMARY LYMPHOMA OF THE BRAIN.

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Purpose/Objectif: The main objective was to determine the site of recurrence in patients with primary intracranial lymphoma (PICL) treated by chemotherapy and whole brain RT with boost(s)on initial localization(s).

Materials/Methods: Forty-four patients with PICL were treated in Centre Leon Bérard between 08/1992 and 01/2002. The treatment protocol included chemotherapy with high dose of Metotrexate followed by radiotherapy. Radiation therapy delivered 20 Gy to the whole brain followed by a "boost" of 30 Gy delivered at the initial site of disease.

Results: After a median follow up of 50 months, 15 patients relapsed. Intracranial relapses occurred on 11/44 patients. One patient presented a pelvic recurrence. Two patients presented a medullar

recurrence. One patient presented an occular recurrence. Intracranial relapse occurred in five patients at initial site. Two recurrences were in the field of the boost. The recurrence were marginal in three patients. Five patients recurred in the brain but not at the initial site. Two patients died because of leucoencephalopathy. In univariate analysis the response to the chemotherapy is border line significant prognostic factor 0.06.

Conclusions: Five among 11 intracranial recurrences occurred at or near the initial site of lymphoma. Radiation protocol including whole brain irradiation followed by a boost seems to be efficient, but optimal doses and fractionnation for whole brain irradiation has to be established.

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CEREBRAL METASTASES IN PATIENTS WITH BREAST CANCER: PROGNOSTIC FACTORS DERIVED FROM THE BLACK FOREST BRAIN TUMOR REGISTRY

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Purpose/Objectif: To identify prognostic factors with regard to survival for patients with brain metastases from breast cancer.

Materials/Methods: Data of 1174 patients with brain metastases, treated with whole brain radiation therapy (WBRT) between January 1985 and December 2003 at the Department of Radiation Oncology, University Hospital Freiburg, were analyzed retrospectively.

Results: 269 patients (23%) presented with a primary tumor of the breast. For these patients median age at diagnosis of brain metastases was 54.8 years. The median interval between diagnosis of the primary and diagnosis of brain metastases was 31.9 months. Forty-eight patients had a solitary brain metastasis, 221 patients presented with multiple brain metastases. Surgical resection was performed in 43 patients. WBRT was applied with daily fractions of 2 Gray (Gy), planned total dose 50 Gy (n = 169 patients), or 3 Gy, planned total dose 30 Gy (n = 100 patients), respectively. According to the recursive partitioning analysis (RPA) classes of the Radiation Therapy Oncology Group for patients with brain metastases 12 patients met the criteria for class I, 162 for class II, and 95 for class III.

Median overall survival (OS) was 4.4 months (Kaplan-Meier method) for the whole group and 10.4, 6.8, and 1.8 months for RPA classes I, II, and III, respectively ($p = < 0.0001$). The following parameters were analyzed with regard to their prognostic impact: Karnofsky performance status (KPS, ≥70 vs. <70), age (≥ vs. < 54.8 years), number of brain metastases (solitary vs. multiple), status of primary tumor (controlled vs. uncontrolled), extracerebral metastases (present vs. absent), and interval between diagnosis of the primary and brain metastases (≥ vs. < 31.9 months). At univariate analysis, a good KPS, a long interval between diagnosis of the primary and diagnosis of brain metastases, and the presence of only one brain metastasis was associated with a significantly longer survival. At multivariate analysis (proportional hazards model), these parameters turned out to be independent predictors of a better outcome (KPS ≥70 vs <70, RR = 0.33, 95% CI 0.25-0.4, $p < 0.0001$, interval ≥ vs. < 31.9 months, RR = 0.7, CI 0.51-0.91, $p = 0.007$, solitary vs. multiple brain metastases, RR = 0.56, CI 0.39-0.77, $p = 0.0004$).

Survival in patients with brain metastases from breast cancer was significantly longer compared to patients with brain metastases from other primaries (4.4 months vs. 3.2 months, $p = 0.02$).

Conclusions: The analysis of this large cohort of breast cancer patients with brain metastases confirmed known prognostic parameters. Survival was poor, however, the outcome was slightly more favourable than in patients with brain metastases from other primaries.

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CONCURRENT HYPOFRACTIONATED INTENSITY-MODULATED RADIATION THERAPY WITH SIMULTANEOUS INTEGRATED BOOST TECHNIQUE AND TEMOZOLOMIDE FOR GLIOBLASTOMA

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Purpose/Objectif: Glioblastoma was an aggressive tumor, and main pattern of failure was local recurrence. There was a new treatment scheme for glioblastoma, hypofractionated radiation therapy or temozolomide. The rationale of hypofractionated radiation therapy was based on biological benefit and shortening of treatment time. This pilot study was designed to analyze the efficacy of combined hypofractionated intensity-modulated radiation therapy (IMRT) with temozolomide, and the difference in treatment outcome by recursive partitioning analysis (RPA) score.

Materials/Method: Twenty-two patients histologically proven primary glioblastoma were accrued between August 2004 and February 2006. All patients were treated with IMRT with simultaneous integrated boost (SIB) technique, and a dose of 50 Gy was prescribed in 5 Gy per fraction to gross tumor or surgical bed (GTV), 30 Gy in 3 Gy per fraction to 2 cm margin from GTV during 2 weeks. Patients were educated that temozolomide was to be taken 1 hour before radiation therapy everyday. Patterns of failure were classified as in-field, marginal, and out-of-field after radiation therapy using magnetic resonance imaging.

Results: Eighteen patients were analyzed, and fifteen patients received concurrent temozolomide with IMRT. Tumor progression was shown in eight patients (44.4%), and median time to progression was 9.1 months from treatment start. Four patients had in-field recurrence, one in marginal, one out-of-field, and the other two had in-field with out-of-field recurrence. Median time to progression by RPA score were 10.2 months for 3 score, 9.1 for 4, and 6.3 for 5 ($p=0.05$). Mean survival time was 14.3 months form treatment start. RPA score affected on overall survival ($p=0.02$), and surgery type (total or subtotal resection over biopsy alone, $p<0.01$) and number of primary tumor (single versus multiple, $p=0.04$) also affected on survival outcome. Median duration of IMRT with temozolomide was 12 days. No patients experienced grade 3 or 4 acute toxicity, and only one patient who has been surviving for 16.8 months showed a suspicious radiation-necrosis lesion.

Conclusions: Hypofractionated IMRT with concurrent temozolomide regimen in this study could slightly improve survival outcome compared with historical reports using conventional radiation therapy and it could shorten duration of radiation therapy from 6 weeks to 2 weeks without increasing treatment-related toxicities. It might be confirmed that RPA score was related with survival outcome.

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CYBERKNIFE FRACTIONATED STEREOTACTIC RADIOTHERAPY (FSRT): A FEASIBLE TREATMENT OPTION IN RECURRENT/PROGRESSIVE MALIGNANT GLIOMA

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Purpose/Objectif: Fractionated sterotactic radiotherapy is one of the salvage options in previous irradiated patient with recurrent/

progressive malignant glioma. We reported the results and prognostic factors of cyberknife fractionated stereotactic radiotherapy (FRST) in recurrent/progressive malignant glioma in a single institution.

Materials/Methods: From March 2002 to November 2005, 10 patients with recurrent malignant glioma (7 glioblastoma, 3 anaplastic oligodendroglioma) received Cyberknife fractionated stereotactic radiotherapy (FRST) as salvage treatment for recurrent/progressive malignant glioma. The mean age was 54.1 years old (range 32-74). Seven patients received gross total removal of brain tumor and 7 patients had Karnofsky performance score above 70. Post-operative adjuvant external beam radiotherapy 1.8-2.0Gy per fraction, 5 fractions per week with mean dose 59.92Gy (range 50-68.4) was delivered, and four of them received concurrent chemotherapy with Temozolamide 75mg/m^2.

All patients received regular clinical follow-up at interval of 1-3 months and MRI images was arranged every 3-4 months. The median time to local relapse is 13.4 months (range 4.2-36.6). Cyberknife FSRT (Accuray Co. U.S.A.) was applied for health insurance payment and approved when lesions increased size on T1W contrasted MRI images during follow-up. Target volume was delineated to T1W+C enhanced lesion with 2-5mm safety margin. The median tumor volume was 17cc (range 9.6-108.5cc). The mean dose prescribed to the gross recurrent tumor volume was 23.7 Gy (range 16-35) with mean prescription isodose curve 84.5% (range 74-90%) and the median fractions was 4 (range 1-10). The mean BED of tumor (α/β=10) was 40.05 Gy10 (range 22.4-60). Seven patients received 3-22 cycles of Temozolamide 200mg/m^2 systemically after disease recurrence or progression. Other chemotherapeutic agents included oncovin and ACNU.

The median follow-up was 32.4 months (range 10.7-41.8). Overall survival and post-FSRT survival were calculated from the time of initial surgery and the date of FSRT to death or last follow-up. Survival was analyzed using the Kaplan-Meier method. Prognostic factors were compared by log-rank test.

Results: All patients tolerated Cyberknife FSRT well. No severe acute reaction was noted. The median time for post-FRST survival was 18.4 months (range 4.3-28.2) and the median overall survival was 32.4 months (range 10.7-41.8). The only significant prognostic factor for the duration from initial surgery to FRST was pre-EBRT Karnofsky score >70 (p= 0.001) and a trend of using concurrent chemoradiation with Temozolamide (p =0.087). Other factors were insignificant, including age (¡ø50 vs. > 50), RPA class (I-IV vs. V-VI), tumor grade (III vs. IV), operation method (gross total vs. subtotal), EBRT dose (¡ø60 vs. > 60 Gy).At 6, 12, 18 months after FSRT, survival rates were 77%, 61%, 44%, respectively. The prognostic factor for post-FSRT survival was systemic Temozolamide use (p=0.005), while other univariate analysis of age (¡ø50 vs. > 50), RPA class (I-IV vs . V-VI), tumor grade (III vs. IV), previous CCRT, previous EBRT dose (¡ø60 vs. > 60 Gy), FSRT tumor volume (¡ø17 vs. >17cc), FSRT BED dose (¡ø40 vs. > 40Gy) were all insignificant. The overall survival rate at 1 year was 88%, and was 58% and 13% at 2 and 3 years. The only significant prognostic factor for better overall survival was pre-EBRT KPS score >70 (p=0.04), and borderline significance of CCRT with Temozolamide (p=0.066) and age <50 years (p=0.085). Tumor grade, RPA class, EBRT dose, FSRT BED dose, FSRT tumor volume, systemic Temozolamide treatment had no significance.

Conclusions: Pre-treatment performance statuses, age, CCRT with Temozolamide are important prognosic factors for malignant glioma. Cyberknife fractionated stereotactic radiotherapy is an option for local salvage treatment when malignant glioma recurrence or progression. Aggressive treatments including fractionated stereotactic radiotherapy and systemic use of Temozolamide may result in substantial improved duration of survival.

719 poster

DOSE-INTENSIFICATION WITH CONFORMAL CONCOMITANT STEREOTACTIC BOOST IN HIGH GRADE GLIOMAS

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Background: High grade gliomas are usually refractory to standard multimodal therapies, with a high rate of recurrence and death. Although, dose-levels highest then 60 Gy, increased, as reported in many reports acute and late neurological toxicity.

Aim: our study evaluates response, acute neurological toxicity, OS and DSF of patients with III-IV grade WHO gliomas treated by 3D-EBRT with concomitant stereotactic conformal boost and concomitant Temozolomide, followed from a sequential stereotactic conformal boost.

Materials/Methods: Between December 2003 and April 2006, 23 patients with new diagnosed histological confirmed high grade gliomas (20 GBM, 3 AA), with bed tumour ≤ 6 cm in diameter, after surgery were alternatively assigned to receive a schedule of 3D-EBRT to a dose of 5040 or 5400 cGy at standard fractionation, plus conformal stereotactic concomitant boost of 900 cGy (90 cGy/day 3 times a week from 3rd week) or 630 cGy (90 cGy/day 2 times a week from 3rd week), followed from sequential stereotactic boost of 1000 cGy (250 cGy/day), to a total dose of 6940 or 7030 cGy. All patients was received oral chemotherapy with Temozolomide 75 mg per square meter BSA/day. Adjuvant chemotherapy with Temozolomide (150-200 mg per square meter BSA/day) was administered from 2 weeks after the end of radiotherapy. A MRI-scan was performed about 45 days from the end of the treatment to evaluate response. Acute neurology toxicity was evaluated by RTOG scale.

Results: All patients completed the treatment. Median FUP was 17.3 months. G3 acute neurological toxicity according to RTOG score was observed only in 2/23 pts (8.7%), while no patients presented late neurological toxicity. There were no significant differences between the 2 groups of patients.

Conclusions: Ongoing analysis of local control and survival, with the demonstrated acceptable toxicity will define the future of this study.

720 poster

EARLY MRI CHANGES FOR MONITORING THERAPEUTIC RESPONSE DURING CHEMOTHERAPY AND RADIOTHERAPY FOR GLIOBLASTOMA MULTIFORME

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Purpose/Objectif: The diagnosis of Glioblastoma Multiforme invariably leads to rapid local recurrence and fatal progression despite best standard of care with radiation therapy (RT) and concurrent temozolomide (TMZ) chemotherapy. Early measures of response may permit both an individualized adaptation of radiation delivery through a course of radiotherapy, and also serve as predictive factors of treatment outcome.

The overall goal of this study is to evaluate the spatial-temporal pat-

terns of local failure defined by tumor volume changes on standard and investigational MR sequences in patients with GBM receiving adjuvant chemoirradiation. Specifically in this analysis, the aim was to evaluate the changes demonstrated on T1 post-contrast MRI scans through a course of RT and early follow-up.

Materials/Methods: 10 patients with GBM receiving 3D-Conformal RT (60Gy in 30 fractions over 6 weeks) with concurrent TMZ (75mg/m^2) then adjuvant TMZ (150-200mg/m^2) were evaluated. Each patient underwent a series of study MRIs distinct from RT treatment planning: baseline prior to RT, week six RT, 1 month post-RT (PRT), then two monthly intervals PRT, or until radiologic evidence of progressive disease (PD). At each time point, the MRI protocol included: T2-weighted FLAIR, 3D MRSI, post-Gd-DTPA T1-weighted, diffusion weighted imaging, and dynamic contrast enhanced MRI. Regions of interest were manually contoured for T1-weighted contrast enhancement (T1) using Pinnacle v.7.6 RT treatment planning system, serially co-registered using an automated normalized mutual information algorithm, and then compared volumetrically with baseline images.

Results: All 10 patients (8 males, 2 females; 41-63 years; median 56.5 years) underwent week 6 scans, 8 at 1 month PRT (1 patient died, 1 withdrew), 6 at 3 months PRT, and 1 at 5 months PRT. 4 patients developed PD at a median of 3.4 months PRT. Relative to baseline, volume of T1-weighted contrast enhancement (T1) abnormality at week 6 RT reduced in 8 of 10 patients (range 1.6%-57.8%), and increased in 2 patients (by 38.8% and 8.7% respectively). At 1 month PRT, volumes reduced in 5 of 8 patients (range 23.9%-79.1%), and increased in 3 patients (by 4.5%, 37.0%, 60.6%). Compared to baseline, two patients have demonstrated volumetric increases at both week 6 RT and 1 month PRT - despite disease control at 1.7 and 6.6 months respectively. Moreover in one patient, T1-weighted abnormality consistently increased from baseline to: 38.8% (week 6 RT), 60.6% (1 month PRT) and 64.0% (3 months PRT), with a subsequent volumetric decrease at 5 months PRT (20.3%).

Conclusions: Preliminary results demonstrate that volume of contrast-enhanced T1-weighted abnormality reduces during RT in the majority of patients. Although volumetric increases are documented during RT in 20% of patients, this early change does not seem predictive of poor outcome. Ongoing follow-up and analyses of all MRI sequences will enable more detailed spatial and temporal mapping of tumor and treatment related effects, and identification of potential early predictors of local progression.

721 poster

FRACTIONATED CONFORMAL RADIOTHERAPY IN VESTIBULAR SCHWANNOMA; LONGTERM OUTCOME WITH RATE OF HEARING PRESERVATION AND CRANIAL NERVE FUNCTION.

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Purpose/Objectif: To assess the local control and longterm cranial nerve toxicity in vestibular schwannoma patients treated with fractionated conformal radiotherapy delivered using a linear accelerator.

Materials/Methods: 95 patients were referred to Oncology in Addenbrookes Hospital from 1996-2006. 21 opted for surveillance, 12 had surgery, 52 were offered Radiotherapy, and 10 of these were referred elsewhere for single fraction radiosurgery. The 42 cases who received fractionated conformal radiotherapy are the subject of this analysis. All patients had progressive tumours and/or symptoms. Average tumour size was 21.5mm on magnetic resonance (MRI) scan. Radiotherapy was prescribed at 50Gy in 30 Fractions over 6 weeks. patients were immobilised with either a beam direction shell in edentate patients or a relocatable stereotactic frame in dentate patients.

Results: The median age was 59 years (range 28-81) with 57% male. In the pre treatment setting, 18 cases (43%) had tinnitus with 15 (36%) mild, 3 (7%) moderate and no severe cases on subjective scoring.Rhombergs test proved positive in 9 (21%) patients.Prior to treatment 22 (52%) patients were deemed to have useful hearing in the affected side. Treatment was delivered using fractionated conformal radiotherapy and 23 (55%) cases were immobilised with a Gill Thomas Cosman relocatable stereotactic head frame. The remainder of patients were immobilised using a beam direction shell.

The mean follow-up was 2 years (range 0.6-6.8yrs) and the actuarial local control rate at 36 months is 97% (only 1 patient demonstrated radiological progression following treatment). The actuarial rate of freedom from trigeminal neuralgia was 97% at 36 months. The actuarial rate of hearing preservation was 90% in previously hearing patients. No patient who had normal facial nerve function pre radiotherapy developed toxicity post radiotherapy. There were 3 Neurofibromatosis type 2 patients treated, and 2 of these 2 had useful hearing pre radiotherapy which has not yet been affected by radiotherapy.

Conclusions: In this single institution series, fractionated linear accelerator radiotherapy gives excellent local control in vestibular schwannoma. Although follow-up is relatively short, the rate of hearing preservation and excellent post radiotherapy cranial nerve function is promising.

722 poster

FRACTIONATED STEREOTACTIC RADIOTHERAPY (FSRT) FOR TREATMENT OF ACOUSTIC NEUROMAS. THE BARCELONA EXPERIENCE.

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Purpose/Objectif: This is a retrospective analysis to evaluate the results of FSRT in patients with acoustic neuromas, treated in two institutions, in terms of local control and toxicity.

Materials/Methods: Between 1997 and 2005, FSRT has been performed in 57 patients with acoustic neuroma. Thirty seven patients with a minimum follow-up of 1 year are the aim of analysis. Median age was 62 years (r 28-83). Seven patients had neurofibromatosis type 2 (NF2) (18.9%) and 6 patients had undergone resection before FSRT (16.2%). Eleven patients (29.7%) had serviceable hearing before treatment and facial nerve was preserved in 81% of them. Median PTV was 5.8 cc (r 0.5-47.3 cc). During this treatment period we have used 2 different fractionation schemes: total dose of 50Gy, 2 Gy/fraction in 17 patients, and total dose of 30 Gy, 2.5 /fraction in 20 patients, mainly in either old, medical deteriorated or deaf patients.

Results: After a median follow up of 29.4 months (r13.8-78.4 months), 14 patients demonstrated partial tumour remission, 20 had tumours that remained stable and 2 demonstrated tumour enlargement. One patient died due to the tumour progression and other one died due to an intercurrent disease. Tumour control rates were 91.8%. Useful hearing was preserved in 8/11 patients. The rate of radiation induced toxicity to the Vth and VIIth cranial nerves was 15.3% and 10% respectively.Tinnitus improved in 4/14 patients and trigeminal symptoms in 2/8 patients.

Conclusions: FSRT achieves high rates of tumour control for the treatment of acoustic neuromas, preserving useful audition in a large proportion of patients. FSRT causes low rates of damage of the fifth or the seventh cranial nerves.

723 poster

GLIOBLASTOMAS TREATED BY RADIOTHERAPY WITH CONCOMITANT AND ADJUVANT TEMOZOLOMIDE

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Purpose/Objectif: Glioblastoma represents the most malignant brain tumour in adults. We tried to improve the survival and the time to progression of our patients with high grade gliomas by the inclusion of an alkylating drug Temozolomide in the therapeutic approach of this malignancy .

Materials/Methods: From October 1999 to January 2006 we treated with a radical intent 68 patients (46 males , 22 females), age range 7-69 years (median 52 years) with a diagnosis of glioblastoma. All patients received a radiotherapy of a total dose 43,2-64,8 Gy (median 61 Gy) /1,8-2 Gy/ fraction/ day with the concomitant Temozolomide (TMZ) 75 mg/m^2 qd and then they continued by 6 cycles (12 cycles in 1999-2000) of the adjuvant TMZ 150 - 200 mg/m^2 qd x 5 day repeated every 28 days or till the progression. Before our treatment 44 patients underwent or a macroscopic radical or subtotal resection, 21 patients a partial resection and in 3 cases a biopsy was made. Their performance status (PS) was 0 in 29%, 1 in 66% and 2 in 5%.

Results: 28 of 64 patients (44 %) finished the planned treatment , 1 patient refused to continue after 3 cycles of the adjuvant TMZ, 4 patients are still under the treatment, 31 (48%) patients progressed 1-6 months after the initial chemoradiotherapy (15 till one month), 3 patients did not continue and 1 died of a chemotherapy related hematotoxicity. We follow patients for 2-55 months (m), median follow up is 13 m. Median overall survival (OS) is 18 months, 65% patients survived 1 year, 37 % patients 2 years and 23 % patients are alive more then 36 m. Median progression free survival (PFS) is 11 months, PFS 12 m. - 40%, PFS 24 m.- 20%. We analysed impact of sex, performance status, surgical radicality and histology (primary vs secondary GBL) on OS and PFS. None statistically significant factor except for PS has been found . 29 patients with a progression underwent a salvage treatment - 6x resection alone, 7x resection + chemotherapy (4 patients were operated two times), 15x chemotherapy (CCNU, BCNU, TMZ, PCV), 1x reirradiation, 1x radiosurgery. 26 patients can be evaluated: 4 patients are alive 3,4,12,30 m after a local recurrence was diagnosed, 21 pts died 2-24 m after the progression. We observed a severe myelosuppression (thrombocytopenia grade 3-4 + leucopenia grade 3-4) in 3 cases (4,4 %) during the concomitant chemoradiotherapy (1 patient died) and only one time during the adjuvant treatment. A nonhematogical toxicity (nausea and vomiting) was irrelevant , well controlled by standard antiemetics.

Conclusions: The radiotherapy with the concomitant and adjuvant Temozolomide has shown a good efficacy and tolerance with a low toxicity. Our results confirm conclusions of the phase III trial of the EORTC Brain and RT group and NCIC Clinical Trials group presented at ASCO congress 2004 by Dr.Stupp.

724 poster

HIGH GRADE GLIOMA: IMAGING APPEARANCES SHOULD BE COMBINED WITH PATHOLOGICAL GRADE FOR PREDICTING PROGNOSIS

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Purpose/Objectif: There is ambiguity in the pathological grading of high grade gliomas, especially those with oligodendroglial differentiation which are classified as grade III in the WHO classification of 2000, even if cardinal pathological features of glioblastoma (GBM) are present. Radiological appearances may contribute to the final clinical classification.

Materials/Methods: All high grade gliomas presenting between 1996 and 2005 and treated radically were assessed. Cases in which pathology defined the tumour as grade III but radiology suggested GBM were classified as grade III/IV; pathology from these cases was reviewed. All patients were treated with debulking surgery where possible, followed by radiotherapy. Patients had a WHO performance status of 0 or 1. Grade III patients received 54Gy, grade III/IV and GBM patients 60Gy, in 30 fractions.

Results: There were 245 patients (52 grade III, 18 grade III/IV, 175 GBM). Of these, 35 grade III, 14 grade III/IV and 152 GBM patients are dead. Data were analysed using a Cox Proportional Hazards ratio model.

Of the 18 grade III/IV cases, the pathologist indicated suspicion of GBM in 8. Oligodendroglial components were present in 10; 6 exhibited both necrosis and vascular endothelial proliferation; in only 1 was suspicion of GBM raised. MIB1 counts were available in 10 cases, mean 27%, all greater than 15%.

The median survivals were: grade III 34 months, grade III/IV 10 months, and GBM 10 months. Survival was not significantly different between grade III/IV and GBM. Patients with grade III/IV tumours had significantly worse outcome than grade III, with an instantaneous hazard of death 3.7 times higher ($p = 0.0001$). In this model, the increase in hazard from Grade III to GBM is approximately equivalent to aging 40 years in the model.

Conclusions: The results highlight the current inconsistency in pathological grading of high grade tumours, especially those with oligodendroglial elements. The study suggests that patients with histological grade III tumours but radiological appearances suggestive of GBM have an outcome equivalent to those with GBM, and should be managed as glioblastoma.

725 poster

NEUROLOGICAL TOXICITY FROM STEREOTACTIC RADIOSURGERY IN PATIENTS TREATED FOR BRAIN METASTASIS LOCATED IN FUNCTIONAL AREAS

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Purpose/Objectif: Even if the efficacy and safety of stereotactic radiosurgery (SRS) are well established, its toxicity for specific target locations has not been well defined. In this study we evaluated the neurological toxicity following SRS for brain metastasis located in functional areas.

Materials/Methods: We retrospectively reviewed all patients treated with SRS between January 2001 and December 2005 in our center. We identified 39 patients with 42 brain metastasis located in eloquent cortex. Functional areas included the hand, the leg, Broca and Wernicke areas, and the inferior parietal lobule in the dominant hemisphere. They were anatomically defined using CT imaging or MRI.

Results: Median follow-up was 6 months. Ninety two percent were previously treated with whole brain radiotherapy. Seventy one percent have a pulmonary primary. Median dose was 18 Gy prescribed at a median isodose of 90%. Data were available for thirty-five lesions for neurological function evaluation. Twenty-six (74.3%) metastasis in 24 patients showed improvement or stability in neurological function following SRS, and 9 (25.7%) showed deterioration. Six metastasis from these last 9 progressed radiologically, which means only 3 metastasis without radiological progression were associated with a neurological deterioration. One of them had confirmed radiation necrosis.

Conclusions: SRS for brain metastasis located in eloquent cortex appears to be safe and could be proposed as an alternative to surgery.

726 poster

RADIOSURGERY IN PATIENTS WITH SKULL BASE MENINGIOMAS: THE FREIBURG EXPERIENCE

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Purpose/Objectif: To evaluate survival, local control and permanent morbidity in patients undergoing radiosurgery for skull base meningiomas.

Materials/Methods: Between May 1994 and October 2003 108 consecutive patients with 111 skull base meningiomas <3 cm were treated at the Department of Radiation Oncology, University Hospital Freiburg. On the day of radiosurgery, a stereotactic head frame was applied under local anesthesia. This technique of immobilization allows a spatial positioning with an accuracy of 1mm. Contrast-enhanced computed tomography (CT) scans were obtained with axial slices every 3mm. 41 patients had magnetic resonance images, however, digital image fusion was not routinely available at that time. The target volume was defined as the area of contrast enhancement without safety margin. Dose calculation was performed using special treatment planning programs (Stryker-Leibinger Freiburg). The target volume was encompassed by the 80% isodose line. Radiosurgery was performed with 6-MV photons of a linear accelerator (Elekta SL20) using a six non-coplanar arc technique with circular-shaped collimators. Statistical methods: Kaplan-Meier method, log-rank test.

Results: Median age of the patients war 56 years, 78% were female. 66% of the meningiomas were located in the cavernous sinus. 51% of the patients had previous resections. Median interval between resection and radiosurgery was 2.5 years. Median radiosurgery dose at the tumor margin was 13 Gy. Multiple isocenters were used 60% of the meningiomas. Median follow-up was 4.6 years (range 2.8-10.0 years). 2 patients were lost to follow-up. 5-year overall survival was 92%. Treatment-associated mortality was 0% and none of the patients died due to tumor progression. 5-year local tumor control based on CT imaging was 88%. Uni- and multivariate analysis revealed that 5-year local control was significantly higher in patients with a Karnofsky performance status (KPS) of 90-100 than in patients with a KPS of 70-80 (91% vs. 58%, RR = 0.43, p = 0.02). Higher local control was also found in patients who never had a tumor outside the brain compared to patients with a history of benign or malignant extracerebral tumors (94% vs. 58%, RR = 0.4, $p < 0.001$). Recurrences were diagnosed in 9 patients. In 12 patients with locally controlled tumors new neurological symptoms occurred, mostly affecting cranial nerves II, V, and VII. One patient developed unilateral blindness 28 months after radiosurgery. Permanent morbidity at 5 years was 11%. No prognostic variables influencing permanent morbidity could be identified by univariate analysis.

Conclusions: LINAC-based radiosurgery of skull base meningiomas is both safe and highly effective. The negative prognostic impact of extracerebral tumors on local control is a new finding that needs to be studied further.

727 poster

RADIOTHERAPY WITH CONCOMITANT AND ADJUVANT TEMOZOLOMIDE IN GLIOBLASTOMA MULTIFORME PATIENTS: COMPLIANCE ANALYSIS.

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Purpose/Objectif: Our intent is to evaluate the compliance of the patients (pts) cohort affected by glioblastoma multiforme (GMB) , treated with radiation (RT) and Temozolomide (TMZ).

Materials/Methods: Through May 2000 and December 2005 we selected (from 104 malignant brain tumours) 43 pts. (14 females and 29 males), affected by GBM, treated with RT (conventional fractionation, total dose 60 Gy) , combined with TMZ . Following the RT-CT combined regimen, 6 cycles of 5 consecutive days of temozolomide are scheduled (the same schedule of the EORTC protocol).

The pts age ranged between 37 and 77 years, with a median age of 62; the median Karnofsky Performance Status was 70 (range 50-90). 15 pts (35%) underwent a total resection, 17 (40%) a partial resection with a macroscopic tumor residual and 11 (25%) had only diagnostic biopsy.

Results: All pts but six well tolerated the combined regimen ; 1 death not drug related , 3 did not completed the concomitant therapy because rapid progression disease ;1 pt did not receive the scheduled CT because neurological deterioration before starting the treatment and 1 because refused to continue the RT . 9 (21%) pts did not received adjuvant TMZ : 2 because thrombocytopenia grade III/IV after RT; 7 (16%) for disease progression .In 11 (25.5%) pts the adjuvant TMZ (six cycles) was not completed for progressive disease (usually ≥ 3). 16 (37%) pts completed the schedule.

During the combined treatment no pts presented nausea or vomiting higher than grade I (the nausea, present in few patients, was easily managed with non 5-HT3 antagonist antiemetics). So no antiemetic prophilaxis with ondansetron or granisetron was used. . In a negligible number of pts, at the end of the combined RT and CT, a transient elevated hepatic enzymes have been observed. 3 pts presented trombocytopenia grade III-IV, 6 pts grade II. 1 pt died for mielo-suppressive adverse event which occurred at 40 Gy and 2,4 gr.TMZ, total dose, despite the intensive therapy in the hematologic unit and without a clear and understood explanation. No deterioration of the neurological status was observed too. 1 pt died one week after the end of treatment for unrelated cause (cardiovascular disease)

Conclusions: From our series the association of RT and temozolamide during the combined regimen is tolerable and feasible, without increased haematological or gastroenteric toxicities. The pts who completed the scheduled cycles after the RT, also, mostly, did not presented relevant toxicity. . Probably the very low incidence of nausea and vomiting was dependent on the corticosteroid therapy . The expired patient, because toxicity, represents a unique and not understood event. Trombocytopenia usually associated with leukocytopenia.

Usually the transient transaminase elevation decreased lowering the corticosteroid doses ; no allergy was observed.

728 poster

RADIOTHERAPY IN A MULTIMODAL TREATMENT APPROACH IN PRIMARY CENTRAL NERVOUS SYSTEM LYMPHOMA (PCNSL): A LONG TERM EVALUATION

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Purpose/Objectif: Prognosis of PCNSL is very unfavorable. Chemotherapy or radiotherapy alone offer poor results. This retrospective study investigated the role of external beam radiotherapy (EBRT) on

response rate and overall survival in patients treated with a multimodal therapy.

Materials/Methods: Thirty-two consecutive patients (15 male, 17 female) with a pathological diagnosis of PCSNL (9 single, 23 multiple) were observed between March 1995 and October 2003. Median age was 56 years (range 38-63 years). IELSG score was prevalently 2-3 (68%). All patients were treated with EBRT after chemotherapy with high dose methotrexate (MTX) with or without cytarabine (ARA-C). EBRT (whole brain) was administered to a median dose of 39.6 Gy (9-54 Gy) plus a boost (22/32 pts) with a median dose of 19.8 Gy (range 8-30 Gy) to a total median dose of 59.4 Gy. The median follow-up time was 57 months (range 2-108).

Results: Twelve patients (37.6 %) achieved a complete response (CR), seven patients (21.8%) a partial response (PR) or stable desease (SD), six patients (18.8 %) a progression desease (PD). Five-years overall survival (OS) was 40% (95 % C.I.: 21-58 %). Variables such as age , number of lesions or CR before radiotherapy were not found to influence survival. CR after radiotherapy was found to influence survival: 5-years SVV 65 % (95 % C.I.: 35-85 %) vs 34 % (95 % C.I.: 6-62%) in patients with non CR, (p= 0.005). Also IELSG score significantly influenced survival (score 0-1 vs 2-3 vs 4-5 , p=0.0008).

Conclusions: External beam radiotherapy seems to be effective in increasing response rate and overall survival in this combined therapy approach . Treatment timing, chemotherapy schedule and radiation dose reduction need to be furthermore investigated in perspective trials.

729 poster

RADIOTHERAPY PLUS CONCOMITANT AND ADJUVANT TEMOZOLOMIDE FOR UNRESECTABLE GLIOBLASTOMA: A RETROSPECTIVE ANALYSIS OF OUR EXPERIENCE.

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Purpose/Objectif: The treatment of patients with unresectable or partially resectable primary biopsy proven glioblastoma is questionable. The data of literature shows a median survival time of three months with best supportive care and seven months with radiotherapy alone.

Materials/Methods: Through May 2000 to December 2005 in our department 104 malignant brain tumors patients have been treated. We analysed retrospectively 24 consecutive patients (17 men and 7 women) who underwent biopsy or partial gross resection and were treated with radiotherapy combined with temozolomide (similar to EORTC protocol). The intent of the treatment was to avoid tumor progression.

We considered as major violation a number of TMZ cycles ≤ 3.

The median age of these patients was 61 years (32-74) at the time of diagnosis; the median Karnofsky Performance Status was 70 (50-90). Because of the deep localization of the tumor, 8 pts (33%) were only biopsied and 16 pts (67%) underwent a partial resection valuated by postoperative MRI .

A standard dose of 60 Gy in 30 fractions was delivered in 21 patients (87,5%); only three patients (12,5%) received 45 Gy in 15 fractions for poor KPS. All patients but one received TMZ 75 mg/mq concomitantly.

We observed major violation in six patients in adjuvant setting.

The statistical analysis of survival data was conducted with Kaplan Meyer method. We considered only patients with minimal follow up of 3 months at the end of radiation therapy; the mean follow up was 14 months (3-27).

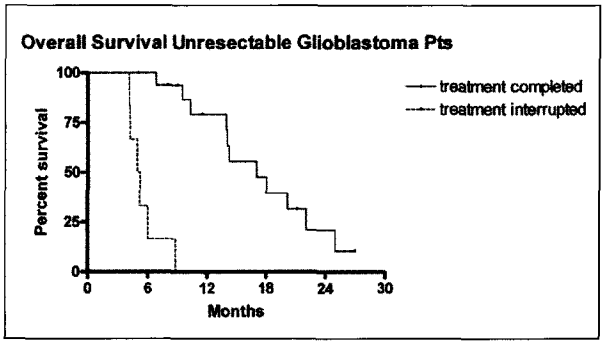
Results: Concomitant and adjuvant TMZ was generally well tolerated. Eighteen patients (75%) received the intended treatment; 4 (17%) patients interrupted the schedule at the third cycle for progression disease, 1 pt (4%) at the the first cycle for toxicity and 1 pt (4%) died by cardiovascular disease (not related to the TMZ).

The salvage chemotherapy consisted in combination of procarbazine, CCNU and vincristine (PCV) in 12 patients, administered with surgery in 3 patients and with radiosurgery in one.

The analysis with intention to treat method was showed with a median survival of 14 months and 2 yrs overall survival of 12,5% from diagnosis.

Between patients who completed the protocol we observed a median survival of 17,4 months and 2 yrs overall survival of 16,7%.

Conclusions: Our analysis was focused on true end point as median and overall survival because of the poor prognosis of these patients. The median survival and overall survival is better than literature data related to treatment with best supportive care and radiotherapy alone. Surprisingly the median survival is comparable with data related to EORTC study where patients had a more favourable prognostic features.Therefore we support the combination of Radiotherapy and TMZ as the standard of treatment for this group of patients. Anyway, a specific trial is needed to verify and better quantify the observed benefit.



730 poster

RECENT ADVANCES IN STEREOTACTIC FRACTIONATED RADIOTHERAPIE OF GLOMUS JUGULARE TUMORS.

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Purpose/Objectif: Microsurgical excision is the treatment of choice for patients suffering from a glomus jugulare tumor. For minimizing postoperative lower cranial nerve palsies stereotactic radiosurgery (SRS) was performed as an alternative to excision. Stereotactic fractionated radiotherapy (SRT) could be a further alternative treatment modality. This study aims to local control, radiological regression, toxicity, symptomatology and the assessment of quality of life (QoL).

Materials/Methods: Between 1999-2005, 17 patients were treated with SRT. 11/17 patients underwent previous operations, another 5/17 previous endovascular embolizations, 6/17 patients were treated with SRT alone. Treatment was delivered by a linear accelerator with 6 MV photons. Median cumulative dose was 57.0 Gy. Local control, radiological regression, toxicity and symptomatology were evaluated half-yearly by clinical examination and MRI scans. TV shrinkage was evaluated quantitatively by the planning system. QoL was assessed by Short Form 36 (SF36).

Results: Median follow-up was 34 months (range, 6-76 months). Follow-up data were available from 16 patients. Actuarial progression-

free survival and the overall survival for 3 and 5 years were 100% and 93.8%, respectively. Median TV was 7.42 ml. Radiological regression was seen in 5/16 cases, 11/16 patients were stable. Median TV shrinkage was 17.9% (p=0.14). Clinically significant severe acute toxicity (III-IV°) was never seen. Late toxicity did not occur in any case. 9/16 patients improved their main symptoms, 7/16 were stable. QoL was not affected by SRT.

Conclusions: The SRT offers an additional treatment option of high efficacy with less side effects for patients suffering from a glomus tumor especially in the case of recurrences or larger TVs. The QoL will be granted.

731 poster

REGRESSION PATTERN OF INTRACRANIAL MENINGIOMAS TO PRIMARY DEFINITIVE RADIOTHERAPY BY VOLUMETRIC RESPONSE ANALYSIS

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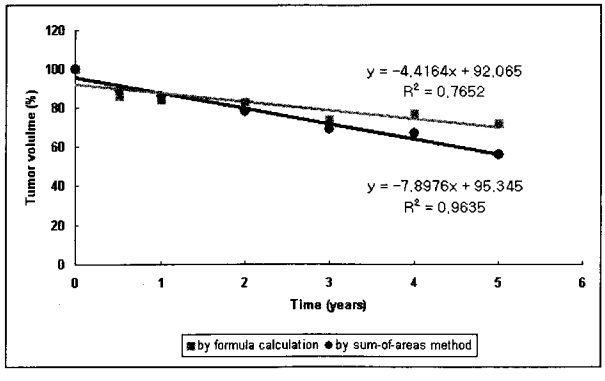
Purpose/Objectif: To evaluate the effectiveness of definitive radiotherapy for primary intracranial meningiomas and its volume regression pattern.

Materials/Methods: The records of 28 patients with intracranial meningiomas who underwent definitive radiotherapy between 1994 and 2003 were analyzed. Median follow-up duration was 39 months. Three patients had pathologically confirmed benign meningiomas and others were clinically diagnosed. The dose ranged 48.6 to 61.2 Gy (median 54) over 3-7 weeks. We measured the tumor volume using either the formula calculation, $\pi/6*X*Y*Z$ or a software (Osiris, the University Hospital of Geneva) based on sum-of-areas method.

Results: The tumor volume by formula calculation ranged from 12 to 123 % of the initial volume at 1 year, from 12 to 92 % at 3 years after radiotherapy and did from 11 to 126 % at 1 year, from 10 to 93 % at 3 year by sum-of-areas method. There were 2 cases of excellent response, which showed more than 65% decrease in tumor volume. Even though we excluded 2 cases, the mean tumor volume at 1, 3, and 5 years after radiotherapy were 84, 74, and 72% by formula calculation and were 86, 69, and 56% by sum-of-areas method, respectively. There were 3 cases of progression. The 5-year overall and progression-free survival rates were 69 and 87%, respectively. Except two grade 3 middle ear effusions, there was no documented severe toxicity.

Conclusions: Intracranial meningioma showed slow but continuous regression without severe toxicity after definitive radiotherapy. External beam radiotherapy is a well-tolerated and effective treatment for inoperable intracranial meningioma with various reasons, and its efficacy can be further improved with high precision techniques.



732 poster

RETROSPECTIVE EVALUATION OF NEWLY DIAGNOSED HIGH GRADE GLIOMA PATIENTS TREATED BY RADIOTHERAPY, CONCOMITANT AND/OR ADJUVANT TEMOZOLOMIDE: A SINGLE CENTER STUDY.

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Purpose/Objectif: Standard treatment in high grade glial tumor is surgery followed by radiotherapy. The place of chemotherapy is still controversial. Temozolamide (TMZ) is an alkillating agent which is used in the treatment of anaplastic astrocytoma (AA) and Glioblastoma Multiforme (GM) patients. We evaluated the tolerance and effectiveness of TMZ concomitantly and/or adjuvant treatment with radiotherapy.

Materials/Methods: Fifty patients who were diagnosed histologically as AA and GM were treated between January 2004 - February 2006. 41 (82%) of these patients were GM and 9 (18%) were AA. Their median age was 47 years (range: 25-27). All patients were treated surgically. The type of surgery was partial resection in 17 (34%) and total resection in 33 (66%) patients. TMZ was used concomitantly with radiotherapy at a dose of 75mg/m^2/day for approximately 6 weeks. The total dose of radiotherapy was planned as 50-66 Gy (median 60 Gy) with 2 Gy per fraction. Four weeks after the radiotherapy, patients were treated adjuvant TMZ every 28 days for 5 days at a dose of 200 mg/m^2/day. Primary endpoint was accepted as tolerability and overall survival (OS).

Results: Median OS was 17 months (95%CI10-24). One year OS was 85% in GM and 100% in AA. In Univariate analysis (Kaplan-Meier method) the type of the surgical operation (p>0.05) and total radiotherapy dose (p>0.05) had no statistically significant effect on survival. On the contrary the performance status (PS) (ECOG, > or ≤1, p> 0,05), number of adjuvant TMZ courses (>or≤3, p>0,05) and age (≥or<50 years) had statistically a significant effect on survival. The most common non-hematologic adverse effect was fatigue and this was at a grade I-II level and it was seen in 58 % and 74% of patients during the course of radiotherapy and adjuvant TMZ consequitively. During concomitant temozolomide treatment one patient (2%) experienced grade III or IV neutropenia and one patient (2%) had grade III or IV thrombocytopenia. Grade III or IV thrombocytopenia was seen in 2 patient (6,5%), during adjuvant TMZ treatment

Conclusions: The type of surgery and total radiotherapy dose had no statistically significant effect on survival. The performance status of ECOG I and above and age 50 and below are significant prognostic factors. We found that starting adjuvant TMZ, keeping adjuvant TMZ at a number of 4 courses and above had a statistically significant effect on survival. Treatment enconpanssing concomittant plus adjuvant chemotherapy was well tolerated. Subjective toxicity and neutropenia and thrombocytopenia associated with myelosuppression was rerely seen. However this data must be confirmed randomised studies.

733 poster

STEREOTACTIC RADIOSURGERY FOR PATIENT WITH CEREBRAL METASTATIC TUMOURS.

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Purpose/Objectif: The aim of our poster is to evaluate the efficacy of stereotactic radiosurgery (SRS) using LINAC equipment for the treatment of patients with brain metastases.

Materials/Methods: 85 patients with brain metastasis underwent stereotactic radiosurgery in the years 2004-2006. Among them there were 53 men and 32 women. The median CTV (clinical target volume) was 6.78 cm^3 (range 32,67 to 0,32 cm^3).The dose of radiation ranged from 24 to 10 Gy with average 16 Gy. Most of the metastatic tumours originated from lung cancer (58,8%), melanoma malignum (14,1%), kidney (9,4%), mammary gland (4,7%), alimentary canal (4,7%) and from other locations (8,2%). We are analysing: status of systemic disease, intracranial tumour volume, number of lesions, tumour location, Karnofsky scale, age, gender and histological diagnosis.
Results: The median overall survival time was 13 months after SRS. 15 % of patients had the neurological progression after a 3 months control, 30% of patients after a 6 months control. Additional treatment was provided for 8 patients. Better survival time was noted in patients with intracranial tumour volume less than 3 cm^3 and inactive systemic disease.
Conclusions: Radiosurgery is an effective treatment for patients with intracranial metastatic tumours with high rate of local tumour growth control. SRS is efficiant in management of brain matastasis, especially for radioresistant tumours (melanoma malignum and renal cell carcinoma).

734 poster

STEREOTACTIC RADIOSURGERY LINAC-BASED FOR BRAIN METASTASES: RETROSPECTIVE ANALYSIS OF A SINGLE ROMANIAN CENTER EXPERIENCE

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Purpose/Objectif: The spread of systemic cancer to the brain is a common complication for cancer patients. Conventional radiotherapy offers modest palliation, and surgery is helpful only for patients with single metastasis in accessible location. Stereotactic radiosurgery, a technique that permits the precise delivery of a high dose of radiation to a small intracranial targetwhile sparing the surrounding normal brain, is used as an alternative treatment for brain metastasis (BM).
Materials/Methods: Between January 2004 and February 2006, 20 patients, 12 males, 8 females with a total of 40 lesions underwent linac based stereotactic radiosurgery (LB-SRS) for BM in our centre. Our system consists of circular cones ranging from 4 mm to 35 mm, carbon head ring, target localizer, planning system BrainScan 5.3.1. (BrainLab, Heimstetten, Germany), and dual photon energy linear accelerator Clinac 2300 C/D (Varian, Palo Alto, Ca, USA). The characteristics of these patients are: age range 34-72 years, Karnofsky Performance Status of 70 or higher, three of fewer BM, the median tumor volume of 10,56 cmc (range 0.11-29.02 cmc). Most of the patients had either lung (60%) or breast (30%) cancer. The treatment was delivered using multiple noncoplanar 6 MV photon arctherapy, cones of 7.5-35 mm, the mean prescription dose was 19 Gy (range 14-22 Gy) at 100% with 80% isodose encompassing the tumor periphery. All patients had follow-up imaging with computed tomography (70%) or magnetic resonance (30%). Local control (LC) was defined as the absence of enlargement of the BM on follow-up scans. Factor s analysed includeed histology, volume, prescription dose, target volume ratio.
Results: Median survival from radiosurgery was 6.4 months with 2 failures. The most significant factors correlated with LC were prescription doses and tumor volume. The absence of active systemic disease, age < 50 years, two or fewer lesions were significantly associated with increased survival.
Conclusions: Our results confirm that LB-SRS is associated with excellent LC rates in the majority of patients treated. Results of this study also confirms that radiosurgery not only provides LC rates equivalent to ythose from surgical series but is also effecticve in treating patients with inaccessible lesions, multiple lesions, and tumor types that resistant to conventional treatment.

735 poster

STEREOTACTIC RADIOTHERAPY FOR INTRACRANIAL MENINGIOMAS: ROLE OF INTRA-OBSERVER AND INTER-OBSERVER VARIABILITY IN CHOICE OF MARGINS

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Purpose/Objectif: To date, sparse data exists on the safety margins we should include for benign meningiomas treated with fractionated stereotactic radiotherapy (FSRT). The purpose of this study was to investigate intra-observer and inter-observer variability in contouring benign meningiomas in order to select an appropriate margin.
Materials/Methods: Twelve consecutive patients who had undergone FSRT for benign intracranial meningiomas were studied. Two radiation oncologists and one neuroradiologist independently contoured the target volume on two occasions, separated by at least a one week interval, on merged MRI and CT-scan. The stereotactic planning system used was Brainscan, version 5.31, BrainLAB AG. Absolute and relative variability in intra-observer volume measurements were calculated. Concerning inter-observer variability, we analyzed the mean absolute difference between volumes as well as the absolute positional shift in three dimensions.
Results: The mean intra-observer variability was 5.2% (0.56cc) with a maximum of 12.97% (0.59cc). For inter-observer measurements, the mean maximal difference was 2.13cc with a maximum of 7.14cc. The average standard deviation for all volumes was ±0.84cc. The mean absolute positional shift was 1.03mm ± 0.44mm with a maximum of 2.79mm.
Conclusions: Optimal radiotherapy planning relies on accurate delimitation of tumor volumes in order to spare critical structures and normal tissue. These results demonstrate that intra-observer variability does not seem to be significant. Inter-observer volume determination is more variable. However, the absolute positional shift is of small magnitude. We conclude that the application of a 2mm margin on the target volume seems safe in order to cover 95% of the inter-observer variability.

736 poster

TEMOZOLOMIDE AND RADIOTHERAPY IN GLIOBLASTOMA MULTIFORME' PATIENTS. RESULTS OF TWO MONOINSTITUTIONAL FASE II PROSPECTIVE TRIALS.

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Purpose/Objectif: Surgery, adjuvant radiotherapy (RT) and Temozolomide (TMZ) represent the standard treatment for glioblastoma multiforme' patients (pts). The aim of this analysis was to compare two different regimens of TMZ with standard RT in terms of feasibility, toxicity and effectiveness.
Materials/Methods: From March 2000 to May 2003 36 pts (group 1) were treated with concomitant TMZ (75 mg/m^2/d x 7d/wk for 6 wk)

plus "partial brain" RT (total dose 60 Gy, 2 Gy daily for 5 days/week for 6 weeks) followed by adjuvant TMZ (200 mg/m^2/d for 5 days every 28 days for 6 cicles). From April 2003 to April 2006 31 pts (group 2) were treated with neo-adjuvant TMZ (200 mg/m^2/d x 5d after surgery) followed by the same schedule of concomitant TMZ-RT but followed by 12 cycles of adjuvant TMZ. Each patient underwent weekly clinical evaluation and laboratory exams. Toxicity was assessed by the RTOG/EORTC scale.

Results: In the group 1: all pts were evaluable; median age was 60 years (range 33-76), 26 (74 %) pts were male and 26 (74%) had a KPS >80%. All but one patient underwent surgery and gross tumour resection (G.T.R.) was performed in 23 (66%) pts. According to the RPA by Curran, 11% belonged to class III, 54% to class IV, and 35% to class V. Adjuvant TMZ was administered in 23 (66%) pts. Globally, 15 (43%) pts completed concomitant RT plus TMZ followed by adjuvant treatment as planned in the protocol. In the group 2: 27/31 pts were evaluable; median age was 59 years (range 36-76), 17 (63%) pts were male, 21 (78%) underwent G.T.R. while 6 (22%) pts received sub-total resection (S.T.R.). According to Curran, 56% pts belonged to class IV, 41% to class V and 3% to class VI. Seven pts did not receive adjuvant TMZ and 14 (51,8%) did not complete this phase. Myelosuppression was the dose-limiting toxicity of this combined treatment, even if it was low in both trials. Grade III-IV non-haematological and haematological toxicities were rare. The statistical analysis showed the was not differences between the two regimens in terms of OS, DFS, median survival (18 vs 19 ms), and time to progression (11 vs 8 ms).

Conclusions: Both schedules of treatment are feasible and well tolerated, but no differences on OS and DFS were shown. Our aim is to evaluate the impact of treatment in the group 2, in terms of survival after a longer follow-up. Based on these results, a cost-benefit analysis between the two TMZ schedules is advisable.

737 poster

THIRTY-THREE YEARS OF FOLLOW-UP OF POST-OPERATIVE IRRADIATION FOR LOW GRADE GLIOMAS

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Purpose/Objectif: Post-operative policy for Low Grade Gliomas (LGG) is still controversial.

In 1986 a randomised trial was initiated by the EORTC (22845) comparing immediate post-operative irradiation for LGG to delayed radiotherapy at progression. Long-term results of this trial were published in 2005 after a median follow-up of 7.7 years and showed no difference in overall survival but a longer progression-free survival period in the immediate irradiated group. We present the results after long-term follow up with a maximum of 33 years in a series of 204 patients irradiated immediately after surgery.

Materials/Methods: We retrospectively analysed 204 patients with histologically proven LGG.

All patients in the analysis were consecutively included and were random unselected patients from daily practise, irradiated between 1964 and 1985 with mega-voltage (range 40-66G) equipment.

The overall survival curves were calculated for more than three decades of follow-up and the prognostic factors that influence the outcome were identified.

Results: The overall survival curve shows a median follow-up of maximum 33 years, with a median survival of 5 years. This survival curve decreases further exponentially, with a 28% survival at 10 years, 14% survival at 20 years, then followed by a stabilisation of the survival curve at 12% without further decrease up to 33y.

There is however a large significant advantage in survival for patients with an irradiated volume of maximum 500 cc brain tissue compared to those with larger irradiated volumes. The 5-year survival is respectively 86,4 and 45.3 % (log rank p= 0.019) and the 20-year survival is 32.3 and 15.4% while the median survival is 147m. and 50 m. respectively.

Patients <35 years old show a significantly better survival than patients between 35-45y and >45y with a 5 y survival of respectively 64.4, 53.5 and 29% while the 20y survival is respectively 23.7, 7.7 and 3.9% (log-rank p < 0,0001).

There is no difference in 5 year survival according to the extent of resection. However patients with total resection do show a significantly better survival after 10 and 20 y compared to those only biopsied or partially resected. The 10 year survival is respectively 40.7% and 27%, while the 20 year survival is respectively 30% and 10% (log-rank p 0.056).

Conclusions: This is the first analysis of a large series of megavoltage irradiated low grade gliomas with a follow up of more than 3 decades.For the first time is shown that an irradiated volume of brain tissue of maximum 500cc is the most important prognostic factor with a median survival of 147months, compared to only 50months for the larger irradiated volumes, and still a 20 year survival of more than 30%. For the first time is shown that LGG can be a curable disease if surgery and irradiation is not delayed at the time of early diagnosis. This should encourage the clinician not to postpone treatment in these LGG patients.

738 poster

THREE INSTEAD OF SIX WEEKS TREATMENT SCHEDULE FOR GBM PATIENTS.

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Purpose/Objectif: To determine an apropriate treatment schedule for patients with glioblastoma multiformae.

Materials/Methods: 232 patients with histologically proven glioblastoma multiformae were treated in the Radiotherapy Division of the Centre of Oncology - Maria SkÂ³odowska-Curie Memorial Institute in Warsaw, between 1998-2002. During dose years the standard dose for majority of GBM patient was 42 Gy in 15 fractions.Patients were retrospectively assignet to prognostic groups previously indentified by Curran et al. in the RTOG partitioning analysis.

Results: In the multivariate analysis the most important prognostic factors were RTOG prognostic group, performance status and extent of surgery. The median survival for all patients were 12,8 months and the median time to disease progression were 2,5 months. The median survival for each prognostic groups were similar to the results achieved by Curran et al. with more aggressive treatment schedule.

Conclusions: The short radiotherapy regimen in an apropriate option for majority of GBM patients.

739 poster

TREATMENT OF RECURRENT GLIOBLASTOMA MULTIFORME WITH FOTEMUSTINE AND BRACHYTHERAPY

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3 - Neurosurgery, Neurosurgery, Pisa, Italia

Purpose/Objectif: The gold standard treatment of recurrent glioblastoma multiforme (GBM) is surgery. Unfortunately after this treatment the prognosis is poor. The aim of this work was to assess the efficacy and toxicity of fotemustine and interstitial brachitherapy (HDR) in patients with recurrent GBM.

Materials/Methods: Patients with recurrent GBM, previously treated with external radiotherapy and temozolomide, able to chemother-

apy and with KPS ≥ 70 were value for surgery. Patients operable ab initio were treated with surgery + intraoperative HDR brachytherapy (a single fraction of 18 Gy performed by means of a ballon device) and then chemotherapy with fotemustine (100 mg/m^2 as induction chemotherapy administered weekly for 3 weeks and then, after 4-5 weeks, with the same drug and the same dose as maintenance treatment every 3 weeks until disease progression, unacceptable toxicity or patient refusal). Patients unable to operation were treated with fotemustine with the same schedule. After induction treatment patients were value by RMN or TAC. The patients became able to surgery were also treated with surgery and brachytherapy.

Results: 15 were enrolled between 2005 and 2006. 8 patients were not operable ab initio, 2 of these became able to surgery after induction chemotherapy.

After induction chemiotherapy 13 (87%) obtained a stable disease and 2 (13%) partial response. The median survival from the first surgery were 17,8 months (range 6-46 months). The died patients were 5 (median survival time from diagnosis of relapse were 5 months), 4 of these were treated with surgery and HDR brachytherapy. A total of 48 cycles of fotemustine were administered, Major toxicity was myelosuppression resulting in 1 thrombocytopenia G4 and 4 leukopenia G1-2. No other toxicity occurred.

Conclusions: Although our experience is at the beginning and the follow-up is less than 12 months, treatments are well- tolerated with acceptable toxicity and less recurring hospitalization.

740 poster

TWO HYPOFRACTIONATED RADIOTHERAPY (RT) SCHEDULES (8 GY X 2 VS. 8 GY) IN METASTATIC SPINAL CORD COMPRESSION (MSCC). UPDATING OF AN ONGOING PHASE III RANDOMIZED MULTICENTRE TRIAL.

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4 - Radiation Oncology Centre, *Taormina, Italy*

5 - Radiation Oncology Centre, *Lucca, Italy*

6 - Radiation Oncology Centre, *S.Giovanni Rotondo, Italy, 7*

- Radiation Oncology Centre, *Rionero in Vultrure, Italy*

Purpose/Objectif: This randomized trial was planned to determine whether a single dose (8 Gy) is as effective as a short-course (8 Gy x 2) RT schedule in MSCC patients (pts) with regard to symptom control, duration of response and toxicity. This is the updating of an ongoing trial.

Materials/Methods: From November 2002 to April 2006, 265 MSCC pts with a short life expectancy (£ 6 months) because of (a) the presence of unfavourable histologies (i.e., lung, kidney, gastrointestinal and head and neck carcinoma, melanoma, sarcoma), or (b) favourable ones (i.e., lymphoma, seminoma, myeloma, and breast or prostate carcinoma) provided that motor/sphincter dysfunction and/or low performance status were also manifest, underwent short-course or single dose RT without surgery. Parenteral dexamethasone (8 mg bid) was given in all cases. Antiemetic therapy was prescribed in pts treated with fields covering the upper abdomen. Median follow-up was 3 months (range, 1-38).

Results: 219 pts, with updated data are evaluable for response and toxicity, 104 were randomized to receive a short-course and 115 a single dose RT schedule. Male/female ratio was 142/77, median age 67 years (range, 33-88), and median Karnofsky PS 60% (range, 20-100%). Considering back pain relief and ability to walk maintenance, a significant difference was observed in favour of the short-course with respect to the single dose RT (78% vs. 60% and 76% vs. 57%, respectively; $p < 0.01$ and $p < 0.01$). No difference was found in ability to walk recovery between two RT schedules (overall response, 7%). Median duration of response was 4 months for both groups. The incidence of acute toxicity was low in both regimens: WHO grade 2 and 3 stomatitis/esophagitis was registered in 5% of and 1% of pts, respectively; 9% of pts suffered from nausea that interfered with normal daily life; 2% and 1% of pts referred > 2 and ≤ 10 and > 10 episodes of vomiting/d, respectively. No late toxicity was registered in pts with at least 12 months of follow-up (i.e., 22% of cases).

Conclusions: The short-course RT schedule seems to give better response rates than single fraction RT in back pain control and in ability to walk maintenance. The accrual will continue until the established simple size of 300 pts will be reached.

Posters Combined Chemo-Radiotherapy

741 poster

COMBINED RADIOTHERAPY - CHEMOTHERAPY WITH VINORELBINE IN LOCALLY ADVANCED, INOPERABLE NON SMALL CELL LUNG CANCER (NSCLC) STAGE IIIB

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Purpose/Objectif: Vinorelbine, a potent inhibitor of microtubule polymerization causing accumulation of cells in the G2/M phase of the cell cycle, has been used successfully with radiotherapy acting as a radiosensitizer. Based on these data, we conducted a pilot study to evaluate the activity and safety of combined radiotherapy-oral vinorelbine, in patients with locally advanced, inoperable NSCLC stage IIIB.

Materials/Methods: Thirteen patients with locally advanced non-operable NSCLC were included in the study. The primary site and the mediastinum were irradiated with 18 MV photons to a tumour dose of 60 - 65 Gy in 30 - 33 fractions. Ten patients received chemotherapy: 90 mg vinorelbine per os weekly - 30mg every other day in 5 days- and three patients received 100 mg vinorelbine per os weekly - 20mg every treatment day. The median age was 68,77 years (40-84) and the median Karnofsky score >70. Nine of the patients were over 65 years old [median age 74,33 years, range 65-84]. Physical examination and full blood count were performed every week. In total, we administrated 231 doses of vinorelbine (141 of 30 mg, 90 of 20mg).

Results: From the patients studied so far, nine completed their combined therapy. None of them showed complete response. One patient died from cardiovascular disease before the first evaluation. Five patients had a partial response, one stable disease and two progressive disease. One patient developed anaemia (grade I), seven patients esophagitis grade I and one patient grade II. This results are consistent with previous studies using intravenous vinorelbine. Four patients didn't complete the combined treatment schedule, one because of PD, one because of TBC infection, one because of esofhagitis grade II and one because of abdominal pain during chemotherapy. All patients completed the planned radiotherapy treatment.

Conclusions: From this pilot study we conclude that thoracic radiotherapy with concomitant chemotherapy with oral vinorelbine is efficacious with manageable toxicity. Further studies are needed to identify subgroups of patients and the appropriate vinorelbine schedule in order to improve efficacy.

742 poster

CONCOMITANT RADIOCHEMOTHERAPY IN HIGH GRADE GLIOMAS WITH TEMOZOLOMIDE GIVEN IN THE FIRST AND LAST WEEK OF TREATMENT: FINAL REPORT

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Purpose/Objectif: The standard of care for newly diagnosed glioblastoma is surgical resection to the extent feasible, followed by adjuvant radiotherapy. Nevertheless, the prognosis for patients is poor, with a median overall survival of only 9-12 months.In this study we evaluated the efficacy of a not-conventional schedule of concomitant radiochemotherapy with temozolomide on the survival.
Materials/Methods: A fractionated focal irradiation in daily fractions of 1.8 Gy given 5 days per week was administered for 6 weeks, for a total of 59.4 Gy.Concomitant temozolomide was given 75 mg/m^2 per os during the first and the last week of radiation treatment, followed by six cycles of adjuvant temozolomide, 150-200 mg/m^2 per os for 5 days during each 28-days cycle. Survival was estimated using Kaplan-Meier statistical method from time of diagnosis. Survival related to surgery, RPA score and adjuvant chemotherapy was calculated by log-rank test.
Results: From January 2000 until November 2003, a total of 28 patients (3 anaplastic astrocytoma) was observed. The median age was 62 years (range, 28-74); 14 patients (50%) were female, 14 male. Only 25% (7 patients) had R0 surgery. Compliance to concomitant treatment was 96.4%; one patient interrupted treatment for worsening of general status, due to progression of disease.Median follow-up was 26,5 months (range, 19,1-56,5).Median progression-free survival was 6,7 months. 1 and 2-year actuarial local control was respectively 40% and 14%.Median survival was 16 months. 1 and 2-year actuarial survival was respectively 60% and 27%.Haematological toxicity (23,8%), graded according to RTOG score, was only observed during adjuvant temozolomide therapy: 3 patients presented Grade 1-2 and 3 patients Grade 3-4 toxicity. No patient died for toxicity. In univariate analysis, adjuvant chemotherapy (YES vs NOT, $p<0.01$), RTOG-RPA class (≤ 3 vs ≥ 4, $p=0.015$) and surgical residual (YES vs NOT, $p=0.03$) had a statistically significative role.
Conclusions: Our not-conventional schedule of concomitant radiochemotherapy confirms the role of temozolomide. Adjuvant chemotherapy seems to promise favourable outcomes.

743 poster

EFFICACY AND TOXICITY IN POSTOPERATIVE CONCOMITANT TREATMENT WITH RADIOTHERAPY AND DACARBAZINE -FOTEMUSTINE IN NEWLY DIAGNOSED GLIOBLASTOMA MULTIFORME.

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Purpose/Objectif: Efficacy and toxicity of chemoradiotherapy (CRT) with dacarbazine and fotemustine as treatment for glioblastoma (GBM) was assessed as alternative in case temozolomide was not available or not reimbursed. This rationale is based on a previous phase II trial (Fazeny et al., 2003) that showed a comparable outcome to the current standard treatment with temozolomide (Stupp et al., 2005).
Materials/Methods: A total of 11 patients with newly diagnosed glioblastoma multiforme (GBM) were treated with a combination of dacarbazine and fotemustine, concurrent with radiotherapy. The median age was 63 year (range 30 - 70 year). Karnofsky performance status was 60% or higher. After surgical tumour reduction each patient received radiotherapy up to a total dose of 60 Gy (2 Gy/day, 5 days/ week using 3 limited fields with 18 MV photons after 3-dimentional planning). Chemotherapy consisted of three cycles of dacarbazine (200 mg/m^2) and fotemustine (100 mg/m^2) and was administered at day 1, day 22 and day 43 of the radiotherapy treatment. Time to progression (TTP) and 6 month progression free survival (PFS-6) as well as toxicity according to the NCIC-CTC version 3 were analysed.
Results: The levels of extent of surgery are: macroscopic total resection (n = 3), partial resection (n = 4), stereotactic biopsy (n = 3), radiological diagnosis without histology (n = 1). Median TTP from start of therapy was 23,6 weeks (range 6,7 - 43,1). One patient (with macroscopic total resection) remains free of progression with a follow up of 38 weeks. PFS-6 is 40 %. Median overall survival has not been reached, with a median follow up of 11 months. The main toxicity was thrombocytopenia. Two patients were excluded for further concomitant chemotherapy (after the first and second cycle respectively) because of prolonged thrombocytopenia NCIC-CTC grade 3 of whom one patient received chemotherapy for breast cancer in the past. No significant pulmonary toxicity was observed.
Conclusions: Our PFS-6 and TTP results are worse than those achieved in the earlier phase II trial and in the EORTC 26981 trial (2005). It might be speculated whether an older median age of our patients (63 y vs 44 y) and a low percentage of macroscopic total resection (only 27 %) might have contributed to these less favourable results. In conclusion, CRT with dacarbazine and fotemustine for GBM is feasible but more toxic than CRT with temozolomide. However, if temozolomide is not available, this regimen may serve as a possible alternative.

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INDUCTION IRINOTECAN/GEMCITABINE FOLLOWED BY TWICE-WEEKLY GEMCITABINE AND RADIATION IN LOCALLY ADVANCED PANCREATIC CANCER

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Purpose/Objectif: Early clinical studies combining Irinotecan (CPT11) and Gemcitabine (GEM) have yielded encouraging results. GEM administered via a twice-weekly schedule results in an enhanced radiation-sensitizing effect. In an attempt to improve systemic control of disease and to impact on overall survival, investigators at several Centers are currently testing neoadjuvant chemotherapy strategies. This is a phase II study of induction CPT11 and GEM followed by twice-weekly GEM and radiotherapy (RT).
Materials/Methods: 23 patients (pts) with cytological and/or histological evidence of unresectable pancreatic adenocarcinoma, entered the study. Median age was 58 years (39-69) and median Karnofsky score 90 (80-100). All patients received two cycles of induction CPT11(100 mg/sm) and GEM (1000 mg/sm) on days 1 and 8 of each 3-week cycle. Three weeks later patients underwent RT at daily doses of 180 cGy, to a total dose of 54 Gy combined with bi-weekly GEM on Tuesday and Friday at a daily dose of 40 mg/sm. Dose reduction or delay was required with toxicity of grade II.
Results: All patients completed the neoadjuvant chemotherapy (CT) - RT treatment as scheduled whereas the scheduled concurrent RT-GEM treatment was completed by 2 pts only; the median number of GEM cycles was 8 (3-12). Median follow-up time was 8 months and median survival time 14 months. Radiological confirmed response was: PR in 10 pts and NC in 10, 3 pts had progression of disease during treatment. 16 pts had a subjective PR. Haematological toxicity of grade III was observed in 1 pt and grade II in11 pts. Gastrointestinal toxicity was grade III in 1 pt and grade II in5 pts.
Conclusions: Induction CPT11/Gem followed by twice weekly Gem and RT is feasible in pts with locally advanced pancreatic cancer, but with modest activity on local control and overall survival. Based on this experience, we would recommend to further explore induction CT by using other treatment schemes including novel agents.

745 poster

PHASE I STUDY OF WEEKLY TOPOTECAN IN COMBINATION WITH CONCOMITANT EXTERNAL CRANIAL RADIOTHERAPY FOR PATIENTS WITH GLIOBLASTOMA MULTIFORME OF THE BRAIN

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Purpose/Objectif: A phase I study was performed to evaluate the dose limiting toxicity (DLT) and the maximum tolerated dose (MTD) of Topotecan (Hycamptin; GlaxoSmithkline) that could be safery administered concurrently with conventional external cranial irradiation for patients with Glioblastoma Multiforme (GM). A secondary objective was to determine the acute and delayed toxicities of the concurrent chemotheradiation (CCRT) treatment.

Materials/Methods: 36 patients with histological confirmed and previously untreated GM of the brain were enrolled. After surgery or stereotactic biopsy, patients received conventional external cranial RT (59.4 Gy/ 33 Fractions in 6.6 weeks). Two cycles of Topotecan (T) were administered at days 1 and 4 of each week. Each cycles consisted of 30 minute i.v. infusion before RT. The (T) dose was escalated in 3-dose increments from 2.0 to 2.5 and 3.0 mg/m^2 divided in a twice a week schedule, in different patient groups. All the patients were evaluated, of whom 25 (70 %) were ≥ 50 years, 24 (67 %) were men, and 28 (78 %) had an ECOG PS of 0-2. Nine (25 %) had undergone biopsies, 18 (50 %) partial resections, and 9 (25 %) gross total resections.

Results: Three dose levels of (T) were tested. 10 patients accrued to level 1 (T-dose: 2 mg/m^2, divided in 2 days per week). No grade 4 toxicities were seen. Grade 2/3 hematologic toxicity was observed in 4 patients. From 11 patients included at level 2 (T-dose: 2.5 mg/m^2), 3 presented with grade 3 neutropenia and 2 with grade 3 thrombocytopenia; One patient experienced an episode of severe (grade 3) asthenia and another one presented with pulmonary thromboembolism respectively. From 15 patients accrued to level 3 (T-dose 3 mg/m^2), 6 had episodes of grade 4 neutropenia (2/6 febrile neutropenia) and 2 patients developed grade 3/4 thrombocytopenia. Chemotherapy was interrupted in one while two patients were transferred onto the level 1 and 2 of (T), respectively No other serious early non-hematologic or late toxicities were seen in 21 months median follow up time. All the patients had post radiation adjuvant chemotherapy with the PCV regimen until deterioration and then continued to Temozolomide as second - line treatment.

Conclusions: The MTD of (T) given concurrently to RT was determined at the 2.5 mg/m^2/week dose level. The above CCRT schema is a well-tolerated regimen, easy to administer in ambulatory patients and with acceptable early and late toxicities. A phase II trial is ongoing, to find the response rates, the local failures and the median survival of the above patients.

746 poster

RADIOCHEMOTHERAPY FOR STAGE III PANCREATIC CANCER

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Purpose/Objectif: To investigate the survival improvement in locally/regionally advanced, unresectable pancreatic cancer, time to progression (TTP), overall survival (OS) and adverse events (AEs) in stage III, unresectable pancreatic cancer were evaluated using initial chemotherapy (CT), concurrent radiochemotherapy (RCT) and then subsequent CT.

Materials/Methods: Nineteen consecutive pts (9 males) with a median age of 65 ys (range: 42-79) were treated for T4 N0-1 M0 pancreatic adenocc between July 2003 and March 2006. The median initial CA 19-9 level was 407 U/ml (range: 4-8854). The treatment consisted of 13 cycles of gemcitabine (1000 mg/m^2/week), 5-fluorouracil (5-FU, 500 mg/m^2/week) and folinic acid (FA, 30 mg/m^2/week) therapy, with a 2-week intermission after the 7th week. Following the completion of the initial CT, concurrent RCT was performed with a 4-week intermission applying 500 mg/m^2 5-FU continuous infusion and 30 mg/m^2 FA bolus on days 1-5 of weeks 1 and 5 of radiotherapy. The planning target volume (PTV) encompassed the macroscopic tumor with a 15 mm safety zone. The plans of 18 MV energy were carried out with a 1.8 Gy daily dose using a linear accelerator (Precise Treatment Machine, Elekta, Crawley, UK). The mean 745 cm^3 (range: 390-926) PTV was irradiated with a mean total dose of 43.7 Gy (range: 37.8-46.8). With a 4-week intermission following RCT, pts received a subsequent, 6-week long CT with the same agents and dose as initially. AEs were recorded using the CTCAE v3.0, and TTP and OS were calculated by the Kaplan-Meier method.

Results: 19 pts received initial CT with a median 13 (range: 2-19) cycles, 4 of them with gemcitabine-only due to the cardiac contraindication of 5-FU. Thirteen pts received RCT with a median 2 cycles (range 1-2) of 5-FU, and 8 pts had subsequent CT with a median 6 (range: 2-9) cycles. The cause of the cessation of therapy was disease progression (12 pts) or grade 3 toxicity (1 pt for thrombocytopenia and another for diarrhoea). Five pts completed the whole, 34-week long therapy, 2 of them are currently survivors. The median TTP was 6.5 months (95% confidence interval [CI]= 5.2, 12.1), the median OS 10.4 months (95% CI = 7.3, 13.2), and the 1-year TTP was 31% and the OS 41%. No grade 4 acute AEs developed, but grade 3 were observed (3 neutropenia, 1 thrombocytopenia, 1 diarrhoea, 4 vomitus).

Conclusions: sequential gemcitabine-based CT and 5-FU-based concurrent RCT in stage III, unresectable pancreatic cancer is an efficient treatment with acceptable toxicity. It seems that responding pts has to retain on CT till progression or serious AEs to ensure survival prolongation. Our median OS rate is close to that (12.8 months, 95% CI=8.2, 18.9) of Schneider et al. with comparable treatment method (Int J Radiat Oncol Biol Phys, 2005;63:1325-1330)

747 poster

RADIOTHERAPY WITH CONCOMITANT WEEKLY GEMCITABINE FOR UNRESECTABLE PANCREATIC CANCER

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Purpose/Objectif: To evaluate the feasibility and efficacy of radiotherapy concomitant with weekly Gemcitabine for unresectable pancreatic cancer.

Materials/Methods: We reviewed 23 patients (male 10, female 13, ages 45 to 77, median 66 years-old) with pancreatic cancer who received chemoradiotherapy from April 2001 to November 2005. Most of patients were unsuitable for surgery because of recurrences, metastases to liver or lung, and peritoneal disseminations. One patient of stage ‡UA was unsuitable for surgery because of cardiac failure. Their clinical stages according to UICC TNM classification (6th Ed.) were Stage ‡UA: 1, ‡V: 8, ‡W: 11, and local recurrence after surgical resection: 3.

Patients received radiotherapy (median total dose 50.0 Gy in 25 fractions) from a linear accelerator by four portal or rotation method. GTV was defined to cover the primary tumor and regional involved lymph nodes, and mean radiation field was 56 cm^2. Weekly intrave-

nous administration of Gemcitabine was carried out during the irradiation period (200mg/ body each week, mean total dose 400 mg/ body). Five patients received selective arterial infusion chemotherapy of Gemcitabine through arterial port implanted transcutaneously (mean total dose 800 mg/body, 4 times). If patients condition was permitted, adjuvant chemotherapies consisted of Gemcitabine or platinum agent were also done. CTCAE ver.3.0 and RTOG / EORTC criteria were used to evaluate toxicity. Initial local response was evaluated by tumor size reduction on CT images according to RECIST. Kaplan-Meier analysis was used to calculate cumulative local control (LC) and overall survival (OS).
Results: Median follow-up time was 8 months (2 - 24 months). The local tumor response was PR: 4 (17%), SD: 18 (83%), PD: 0, except for one patient who did not undergo the follow up CT examination. Grade 3 early adverse effects were noted as follows; white blood cell in 10 (42%) and platelet in 2 (8%). Three patients had break longer than 8 days during radiation treatment course because of acute adverse effect. There was no termination of radiation treatment course. Grade 3 late gastrointestinal tract toxicity (small bowel obstruction) was noted in only one case (4%). No other severe late adverse effect was noted, and no treatment-related death was occurred. The median local control and overall survival time was 7 months and 8.6 months, respectively.
Conclusions: Radiotherapy with concomitant weekly Gemcitabine seems to be feasible and effective treatment for patients with advanced pancreatic cancer. Additional clinical studies are required to confirm the therapeutic efficacy.

748 poster

REGULATION OF RADIATION INDUCED COX-2 EXPRESSION IN HUMAN PROSTATE CARCINOMA CELLS IN VITRO

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Purpose/Objectif: In earlier investigations celecoxib treatment led to a significant growth inhibition as well as reduction of radiation induced prostaglandin E^2 production in human prostate carcinoma cell lines. However, no radiosensitizing effects could be observed in response to celecoxib treatment. We investigated potentially involved signal transduction pathways in the regulation of COX-2 expression with and without exposure to ionizing radiation.
Materials/Methods: Radiosensitivity and PGE_2 production was investigated in human prostate carcinoma cell line PC-3 with and without celecoxib pre-treatment, using colony forming assays and PGE_2 ELISA. Expression of COX-2 protein as well as proteins involved in the PI3 kinase pathway were analysed by Western Immunoblotting using selective inhibitors (LY 294002; celecoxib).
Results: Increased COX-2 protein expression could be observed following ionizing radiation with 2 to 15 Gy as well as after celecoxib treatment. Concerning the functional aspect of radiation induced COX-2 expression, a celecoxib dependent decrease of PGE_2 production following radiation with doses of at least 4 Gy was apparent. Radiation induced COX-2 expression in prostate carcinoma cells PC-3 seems to be regulated via an EGFR mediated PI3K signal cascade since treatment with EGF alone also induced COX-2 expression, and moreover, selective inhibition of PI3K completely abolished IR induced COX-2 expression.
Conclusions: IR induced increase of COX-2 protein expression and activity in prostate carcinoma cells seems to be regulated by the PI3K pathway, probably mediated by EGFR. However, the cell lines investigated did not show radiosensitization after inhibition of COX-2 activity and suppression of PGE_2 production by celecoxib treatment.

749 poster

THE EFFICACY OF CONCURRENT RADIOCHEMOTHERAPY IN WOMEN WITH ADVANCED CERVICAL CANCER

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Purpose/Objectif: Meta-analysis of 19 randomized controlled trials of chemoradiation for cervical cancer show that concurrent treatment improves treatment results. Concomitant modality is beneficial in Ib with poor prognostic factors and IIB cervical cancer group, the improvement in women with advanced cervical cancer is less significant. There were differences among analyzed clinical trials: several type of systemic therapy, brachytherapy methods and radiotherapy doses and fractionation were used. The number of women with advanced cervical cancer was not high.
The aim of this study is evaluation of efficacy of treatment of women with advanced squamous cell cervical cancer treated equal concomitant radiochemotherapy.
Materials/Methods: 130 women with IIIB FIGO stage, treated with radiochemotherapy in our Centre between 1999-2002, were analyzed. The minimal follow up was 48 months. Cisplatin 40 mg/m^2 (mean 5,3±1,1 courses) was given weekly. All patients received teletherapy (9 or 15 MV), delivered with 4 fields, 2 Gy per fraction and LDR brachytherapy in 2 applications. The radiotherapy median doses were as follows: 80,7 (±0,8)Gy to the point A, 62,6 (±0,6) Gy to the point B and the median treatment time was 53,7 days.
Results: Seventy (53,8%) of treated women remained alive: 57 (43,8%) was disease free survival, 13 (10%) patients live with disease. Because of cancer died 46 (35,4%) persons, of other reasons 4 (3,1%). 10 patients were lost to follow up, however the latest controls have not shown active cancer processing. The overall survival was presented on the Kaplan Meier survival curve.
Conclusions: Concomitant radiochemotherapy is an effective treatment modality in women with IIIB FIGO stage cervical cancer. Additional chemotherapy concurrent to radiotherapy did not modify radiotherapy doses and treatment time.

Posters DNA Repair

750 poster

A COMPARISON OF GENOTOXICITY OF THE LOW DOSES VS. STANDARD DOSE OF RADIOTHERAPY WITH OR WITHOUT CIS-DIAMMIN EDICHLOROPLATINUM(II) (CIS-DDP) IN HUMAN LYMPHOCYTES

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Purpose/Objectif: The aim of the study was to estimate the genotoxicity and repair efficiency of low doses (LD) vs. standard dose irradiation (SD) with or without cis-Diamminedichloroplatinum(II) (cis-DDP) in human peripherial blood lymphocytes.
Materials/Methods: Human peripheral blood lymphocytes (PBL) were obtained from 19 healthy, range from 25 to 40 years, nonsmoking volunteers. The cells were separated by the standard method (centrifugation over Gradisol L at 1200 rpm for 15 min) and were suspended in the RPMI 1640 medium without L-glutamine. Analysed cells were exposed to LD of radiation alone as a single agent (0 Gy as negative control and 0.1 Gy, 0.25 Gy, 0.5 Gy, and SD of 2 Gy which was used as a positive control) or combined in the same fashion with cis-DDP in concentration of 30 mM which was applied 60 minutes before irradiation. Single-cell gel electrophoresis assay (comet assay) was applied to estimate DNA degradation from lymphocyte for analysed probes.
Strand breaks were measured as total comet length (increase in DNA

migration). Median values were calculated for 100 comets per slide. An influence of DNA repair at 37°C was analysed within the range of 5 -180 minutes. The data were collected and than analysed with the ANOVA test (-Kramer Multiple Comparison Test) and unpaired t test. Results were considered significant when reached $p<0.05$.

Results: The results of the study demonstrated linear relationship between DNA cell damage and irradiation dose both in irradiation alone and irradiation combined with cis-DDP. The exposed cells were capable to perform repair single and double DNA breaks after 5, 30, 90, and 180 minutes of incubation. However, only after 180 minutes in the LD level arm and in the standard arm the effective repair was observed for all probes. Although even after that the repair level in the range of low doses were lower than for the standard dose irradiation alone. The similar results were obtained for probes which were irradiated concurrently with cis-DDP.

Conclusions: Our study indicated a relatively higher level of genotoxicity due to lower level of repair for low dose range irradiation both for irradiation alone and irradiation combined with cis-DDP.

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CORRELATION BETWEEN TUMOUR CELL RADIOSENSITIVITY ASSESSED BY COMET ASSAY AND RADIOTHERAPY OUTCOME IN CERVICAL CANCER PATIENTS

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Purpose/Objectif: The aim of this study was to assess tumour radiosensitivity in squamous cell carcinoma (SCC) of the cervix by alkaline comet assay. The extent of endogenous (without irradiation), initial (measured immediately after irradiation) and residual (assessed after radiation dose of 2 Gy and 60 minutes of repair) DNA damage was studied. Correlations between the values of endogenous, initial and residual DNA damage and in vivo tumour response were investigated. Also overall patients` survival and grade of normal tissue reaction in cervical cancer patients after radiotherapy (RT) were studied.

Materials/Methods: Tumour biopsy was obtained from 42 patients with SCC of the cervix . Four patients had FIGO stage IB, 10 IIA, 15 IIB and 13 stage IIIB. Median patients` age was 56 years (ranged from 34 to 78).

Results: Individual differences between tumours in the value of endogenous, initial and residual DNA damage were found. Linear relationship between the initial DNA damage and radiation doses was observed. Therefore, we decided to use coefficient "a" (the slope of dose-response curve) as a parameter of tumour cell radiosensitivity. The percentage of residual DNA damage was used as a second radiosensitivity parameter. In younger patients subgroup (<= 50 years) patients having steeper dose response curves (coefficient a > 13.5) had tendency to survive longer ($p = 0.084$).

None of radiosensitivity parameters correlated with tumour response after RT. Also there was no relationship between radiosensitivity parameters and grade of acute normal tissue reaction. However, higher percentage of residual DNA damage was observed for patients with late tissue reaction (>G0) then for those not heaving late effects (G0) ($p = 0.017$).

Conclusions: These preliminary results suggest that alkaline version of comet assay might be useful to assess tumour radiosensitivity in clinical practise, although larger studies are needed to show predictive significance of this test.

Posters Electronic Portal Imaging & Dosimetry

752 poster

DAILY 'IN-VIVO' VERIFICATION OF DYNAMICALLY DELIVERED IMRT FLUENCE PROFILES

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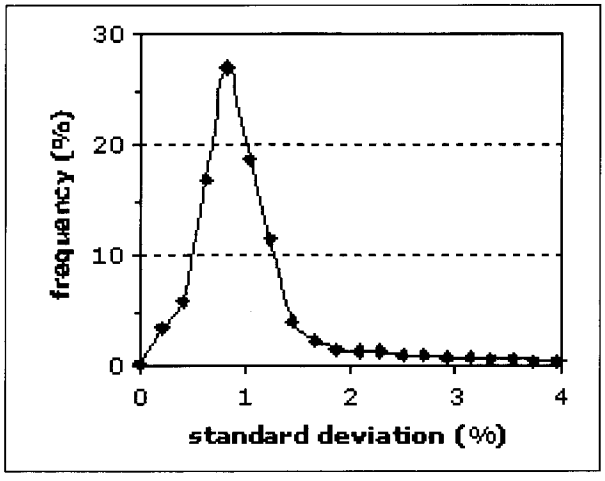
Purpose/Objectif: As part of a comprehensive system for individualised dosimetric quality control and quality improvement in IMRT, portal dose images (PDIs) are routinely acquired in our clinic during patient treatment to verify the accuracy of delivered fluence profiles. For this purpose the Split IMRT Field Technique (SIFT) is used (IJROBP 60: 981-993). Each IMRT beam is split into a 6 MU static field and a residual modulated field delivered with dynamic multileaf collimation. The PDI ratio image for the beam is then calculated by dividing the PDI for the modulated field by the PDI of the static field. Deviations in portal dose ratios are proportional to deviations in the delivered fluence profile, and can be used for verification within a 1% accuracy, even if large changes in patient geometry with respect to the planning CT exist. In this study, the SIFT technique is used to investigate day-to-day variations in the delivery of IMRT profiles. Methods to automatically detect significant deviations in fluence delivery are developed and tested.

Materials/Methods: PDI ratio images, acquired on a daily basis for each beam direction, are analysed for a group of 50 head and neck cancer patients. In total nearly 5000 images are evaluated. For each pixel of a 2-dimensional IMRT profile, the standard deviation describing the day-to-day variation in the measured portal dose ratio over all treatment fractions is calculated. Distributions of standard deviations are analysed as a function of the dose level and the dose gradient in the pixels. In addition, for each treatment field, the mean reproducibility of the delivered fluence profile is derived. Day-to-day variations in portal dose ratios are also quantified by comparison with the PDI ratio reference image.

Results: The mean reproducibility of the delivered IMRT profiles ranges from 0.7 up to 1.8%. Below the frequency distribution of observed standard deviations for all pixels is shown. On average the variation in fluence delivery is 1.2%, while for 92% of the pixels the reproducibility is within 2%. Subanalysis to show the impact of the dose level and the dose gradient will be presented. On a few days, deviations in the measured PDI ratio up to 10% were observed, which were related to malfunctioning of one of the leaves. Due to our daily analyses, these errors could be detected and solved before delivering the subsequent treatment fractions. For automatic analysis of day-to-day variations in delivered IMRT profiles, quantification of the magnitude and spatial extent of observed dose differences per individual leaf pair turned out to be a sensible choice.



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EVALUATION OF RADIOTHERAPY QUALITY – ANALYSIS OF SET UP ERRORS

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Purpose/Objectif: An evaluation of the impact of CTV location, immobilization area, field parameters and in vivo dosimetry for geometric set up errors using Portal Vision Images.

Materials/Methods: Geometric set up errors for 2703 fields of 1062 patiens were analyzed. The mesurements of transversal (X) and longitudinal (Y) axis shifts on portal verifications images were performed. All cases were divided into 8 groups according to locations of CTV and into 6 groups according to type of thermoplastic cast immobilization. Due to statistical analysis all measurements were separated into three classes according to the values of the shift (accepatable, requiring observation and unacceptable). Additionally head and neck cancer patients were divided into two subgroups: one group had izocentric point above the angle of mandible and the second one below it. Pelvic cancer patients were also divided into two subgroups; in one group patients were treated in supine and in second in prone position. From all thoracic cases a tangential fields used for breast cancer treatment (without termoplastic mask immobilization) were separated. 2133 in vivo measurements of entrance doses using semiconductor detectors were performed. Comparisons were done using non-parametric tests. Correlation and dependences between the parameters was performed using Spearman analysis and linear or logistic regression.

Results: The mean X shift for all locations was 1,66 mm (SD ±2,73), the mean Y shift was 3,17 mm (SD ±4,78). The smallest X and Y shifts were obserwed in brain and head and neck regions (0,86, 1,28 mm in X and 0,99 and 1,61 mm in Y axis respectively). The largest shifts were observed in abdomen and pelvic regions (2,07, 2,08 mm in X and 4,09 and 5,85 mm in Y axis respectively). Also the percentage of unacceptable errors was higher for abdomen and pelvis than in brain and head and neck irradiation regions. Kruskal-Wallis tests revealed significant difference between mean X and Y shift according to CTV location and an immobilization area. There were no differences between two subgroups of head and neck cancer patients and thoracic cases. A Mann-Withney test showed that X and Y shifts of pelvic cancer patients treated in a prone position are larger than in a supine one (p=0,008 i p=0,01). The Spearman test and regression analysis showed statistically significant correlation (p=0,00, R=0,39; β=0,26, p=0,00), between X and Y shift. The field size also correlated positivelly with X and Y shifts. There were no correlations between X and Y shifts and DIV results.

Conclusions: The obtained results allow to form conclusion that Portal Vision Image system is very useful and important method of geographic errors assesment during irradiation. Immobilization of thorax, abdomen and pelvic cancer patients is insufficient and requires frequent checks or changing set up system. Due to lack of correletion between dosimetric and geometric uncertainties, it is impossible to predict one according to second and both of them should be systematically and independently measured.

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EVALUATION OF SET-UP ERRORS USING ELECTRONIC PORTAL IMAGING IN HEAD AND NECK CARCINOMA

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Purpose/Objectif: To evaluate the set-up errors using Electronic Portal Imaging Device (EPID) to form a basis for the 3DCRT (Three dimensional conformal radiotherapy) protocol of the head and neck carcinoma to be used in Dokuz Eylül University School of Medicine Radiation Oncology Department.

Materials/Methods: Ten consecutive head and neck cancer patients to be treated using 3DCRT with orthogonal fields between July 2004-September 2005 were included in this study. For each patient a total of 7 EPID in 5 weeks were planned to be evaluated by two independent observers. Reference Digitally Reconstructed Radiography (DRR) images were compared and the differences between the EPID and the DRR using bony landmarks were measured in cranio-caudal (CC), anterior-posterior (AP) and medio-lateral (ML) directions. The random (Σ) and the systematic (∑) components of the errors were calculated using margin formula ($2.5 \times \Sigma + 0.7 \times \Sigma$) proposed by Van Herk to find out the planning target volume (PTV) margin.

Results: A total of 93 EPID with 186 measurements were evaluated. Out of total 186 measurements 93 (50%) was CC, 78 (42%) was AP and 15 (8%) was ML measurements. In 28 (15%) measurements the difference between the two observers was more than 3 mm. Random errors (Σ) were AP: 2,6 mm, CC: 2,9 mm, ML: 1 mm. Systematic errors (∑) were AP: 3,9 mm, CC: 1,8 mm, and ML: 1,9 mm. The PTV margins calculated were AP: 11,7 mm, CC: 6,6 mm and ML: 5,8 mm.

Conclusions: The 3DCRT protocol for head and neck cancer was amended using these PTV margins accordingly.

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EXAMINATION OF THE THREE SET-UP VERIFICATION METHODS USING DISCRIMINATION ANALYSIS FOR OBSERVER DEPENDENT EVALUATION PROCESS IN THE PROSTATE CANCER

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Purpose/Objectif: Set-up verification is one of the most important parts of quality assurance performed during radiotherapy process. Many studies have shown that obtained disagreements could be caused by systematic and random errors. If there is a possibility of using several verification methods it has to be chosen that one which decreasing the errors caused by an observer. The purpose of this study was to evaluate three verification methods and their random and systematic errors.

Materials/Methods: Ten patients with prostate cancer were chosen for the analysis. The evaluation of disagreement was made using three methods: 1/ line based - manual - in which the lines corresponding to bone structures are marked on the EPID and DRR pictures, then the pictures are manually fixed, 2/ points based - two semi-automatic methods - in which the corresponding points are marked on the pictures (10 for second and 6 points for third method) and then the pictures are automatic fused by computer.

Seven observers evaluated images displacement. Displacements in the sagittal and frontal planes (deviations in direction of L-R, C-C, A-P and rotation) were assessed. Each patient was evaluated by using all three verification method. The evaluation was repeated after one week. The results for each observer were analyzed by calculating means of deviations and their systematic and random errors depended on each of the method. This parameters allowed to compare this three methods using the discrimination analysis.

Results: For random errors, no significant differences between their means calculated for all three verification methods were observed (p>0.05). The analysis revealed significant differences between the variance of the calculated means for each verification methods (p<0.001). The highest variance was obtained for the 6 points based, the lowest - for the line based method. For example, in the frontal plane, in direction of L-R, the random error was 1/ Line-based 0.12+0.04 [cm], 2/ 10 points-based 0.11+0.08 [cm], 3/ 6 points-based

0.20+0.14. 0.12 [cm], respectively. For systematic errors, significant differences between their means calculated for all three verification methods were observed ($p<0.001$). The highest systematic error was obtained with 6 point based, the lowest - with line based method. The results indicated significant difference between the variance calculated for the line based and 10 points based versus 6 points based methods ($p<0.001$). For example, in the frontal plane, in direction of L-R, the systematic error was: 1/ Line-based 0.12+0.03 [cm], 2/ 10 points-based 0.19+0.04 [cm], 3/ 6 points-based 0.23+0.08 [cm], respectively.

Conclusions: The line-based method produced the lowest systematic and random errors, and therefore lead to highest accuracy.

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FIDUCIAL MARKERS FOR HEAD-AND-NECK RADIOTHERAPY

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Purpose/Objectif: The purpose of this work is to investigate whether fiducial gold markers implanted under local anaesthesia in the pharyngeal wall can be used for daily position verification using EPID images of the small IMRT treatment fields.

Materials/Methods: For 8 patients, two fiducial markers were placed before treatment in the pharyngeal wall at positions representative for the tumour position (not in tumour). For some patients additional markers were placed in the lower neck. CT scans were made before treatment, and in the third and sixth week of treatment to investigate marker migration. EPID images using large orthogonal verification fields were acquired during treatment according to our position verification protocol as well as EPID images of the much smaller non-orthogonal IMRT treatment fields. Matching of the EPID images to the reference DRR was performed for both the verification fields and for all treatment fields. This was done using the marker positions as well as using the bony structures with the marker information removed from the DRR. Markers were manually matched using our marker position verification software. Five observers performed both bone structure matching and marker matching for one fraction of each patient. The standard deviation of the resulting displacements was defined as the interobserver variation.

Results: The interobserver variation over all patients and directions for marker matching amounted to 0.3 (SD 0.3) mm in the verification fields and 0.4 (SD 0.4) mm in the IMRT fields. The interobserver variation for matching bony structures was 0.7 (SD 0.4) mm in the verification fields and 1.2 (SD 0.9) mm for the IMRT fields. These results indicate that especially for the IMRT treatment fields, the marker matching is more reproducible than matching bony structures because in the small IMRT treatment fields not enough bony structures are visible for reliable matching. The average time for the matching was 3 min for the markers and 9 min for the bony structures.For three patients, the average set up errors determined using bony structures deviated more than 3 mm from that determined using markers. This was clearly due to marker migration.

Conclusions: The use of fiducial markers in the head-and-neck region allows for fast and daily position verification using IMRT treatment fields. Incorrect placement of the markers with associated marker migration can, however, occur leading to systematic incorrect patient positioning.

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PRE-TREATMENT AND IN VIVO EPID DOSIMETRY FOR HEAD AND NECK CANCER

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Purpose/Objectif: For head and neck IMRT treatments, we currently perform dose verification with an a-Si EPID both prior to and during actual patient treatment. The purpose of this study was to compare pre-treatment and in vivo verification methods, both before and after modification of a parameter in our treatment planning system (TPS).

Materials/Methods: Three IMRT head and neck plans were optimised with our TPS, Pinnacle v7.4f. Each plan consisted of 6 fields, with 5-12 segments per field, using 6 MV photon beams. Plans were calculated with the original beam-fit (a), and then re-calculated following modification of parameters modeling the off-set of multi-leaf collimator (MLC) leaves, producing beam-fit (b). EPID images (Elekta iView GT) were acquired for each segment for fields delivered to a homogeneous slab phantom (pre-treatment) and for 3 treatment fractions (*in vivo*). Segment images were converted to dose distributions, reconstructed at a plane intersecting the isocentre, perpendicular to the beam axis, using EPID dosimetry software developed in-house. The dose image for each field was the sum of the corresponding segment dose distributions. No corrections were made for inhomogeneities within the patient. The γ evaluation method was used to compare EPID and planned 2D dose images within the phantom and *in vivo*. γ criteria were 3% maximum dose difference and 3 mm distance to agreement. The average γ (γ_{avg}), maximum γ (γ_{max}) and percentage of points with $\gamma<1$ ($P_{\gamma<1}$) were used to compare results. Cone beam CT (CBCT) scans, acquired prior to treatment, were used to assess errors induced by changing anatomy

Results: For all 18 fields calculated with beam-fit (a), $\langle\gamma_{avg}\rangle^a = 0.47$, $\langle\gamma_{max}\rangle^a = 2.09$ and $P_{\gamma<1}{}^a = 93\%$. Small regions of discrepancies (up to 13%) were detected at abutting segments in 11/18 pre-treatment fields. All errors were also located in *in vivo* measurements. Following modification of the MLC off-set table for beam-fit (b), all discrepancies were reduced, $\langle\gamma_{avg}\rangle^b = 0.30$, $\langle\gamma_{max}\rangle^b = 1.40$ and $P_{\gamma<1}{}^b = 99\%$. Other discrepancies found with *in vivo* dosimetry could be attributed to inhomogenieties and patient anatomy changes, as determined from CBCT scans. These included opening of air cavities (i.e. re-positioning of the epiglotis), neck positioning and change in tumour and/or neck swelling.

Conclusions: Modification of the MLC off-set was shown to improve the dose calculation of all fields measured. In highly modulated fields delivered to inhomogeneous treatment sites and changing anatomy, the combination of pre-treatment and *in vivo* EPID dosimetry is able to detect and reduce clinical meaningful deviations.

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PRETREATMENT DOSIMETRIC VERIFICATION OF IMRT PLANS WITH A BEAM IMAGING SYSTEM

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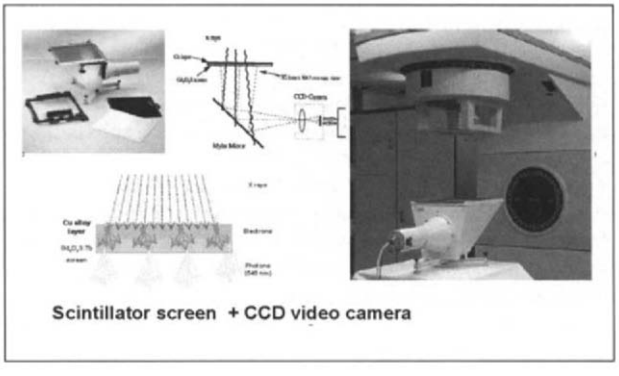
Purpose/Objectif: Existing methods for IMRT treatment verification are highly labor intensive. The potential exists with some new and suitable electronic portal imaging devices (EPID) to reduce the measures efforts making two-dimension images of the radiation fields. The aim of this study is to test the feasibility of using a beam imaging system to obtain, from the images, all the positions of leaves of the multileaf collimator (MLC) and to measure dose distributions of IMRT step-and-shoot treatments.

Materials/Methods: Our instrument is a beam imaging system (BIS) of Scanditronix-Wellhöfer, independent from the accelerator, made up of a terbium-dopped gadolinium oxysulphide scintillator optically coupled with a CCD digital camera: the spatial resolution is 0.366 mm and the area of detection is 30x30 cm^2. The grey level intensities of the image may be carefuly converted in relative dose values. The dosimetric characteristics of the imaging device were studied

for photon beams with energies of 6 and 15 MV from a Simens Linac (dose and dose rate linearity, Output Factors...). Square field profiles at water-equivalent buildup depths, extracted from BIS maps, have been compared with the corresponding scans performed with a diode detector in water. Disagreement is always shown in the regions outside the field penumbra (tails) and also near the field edges, but only for field sizes >15x15 cm^2, due to the metal/phosphor screen higher sensitivity to low energy scattering x-rays. A straightforward correction method for the "tails effect" was developed for square fields and then generalized to MLC-shaped fields. The verification procedure followed the next steps: first, we planned with the inverse planning module of the Plato Sunrise v.2.0 system (TPS) an IMRT treatment of a patient; then, the fields and the segments were transposed on a cubic water phantom; the recalculated dose distribution on an axial plane was compared to the dose distribution resulting from imaging with BIS.

Results: Comparison was realized calculating pixel-by-pixel percentual dose differences and using the "gamma index" method. Moreover, a software routine was written to automatically extract positions of the collimator leaves from the images, thus directly testing both the MLC positioning and the treatment parameters transfer from TPS to the linac. Other homemade software tools were written to perform all the elaboration of data and images.

Conclusions: It is our opinion that IMRT clinical implementation needs methods to measure two-dimensional dose distributions with high spatial resolution and to compare them with the distributions calculated from TPS using both geometric and dosimetric criteria. We think that the technique we described in this work provides a better time-saving mean to verify geometric and dosimetric accuracy of treatment delivered in IMRT with the use of a high resolution beam imaging system.



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ROUTINE IN VIVO DOSIMETRY USING ELECTRONIC PORTAL IMAGING DEVICES

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Purpose/Objectif: To analyze the results of routine EPID measurements for pre-treatment verification and in vivo dosimetry.

Materials/Methods: Calibrated camera-based EPIDs were used to measure the central field dose, which was compared with a dose prediction at the EPID level. For in vivo dosimetry, transit dose data were calculated using patient transmission and scatter, and compared with measured values. Furthermore, measured transit dose data were back-projected to a dose value at 5 cm depth in water (D_s) and directly compared with D_s from the treatment planning system. Dose differences per treatment session were calculated by weighting dose values with the number of monitor units per beam. Reported errors were categorized and analyzed for approximately 37500 images from 2511 patients during a period of 24 months.

Results: Pre-treatment measurements showed a mean weighted dose difference of 0.0±1.7%. Transfer errors were detected and corrected prior to the first treatment session. A machine output variation of about 4% was found between two weekly QC measurements. In vivo dosimetry showed mean weighted transit and D_s dose differences of -0.7±5.2% and -0.3±5.6%, respectively. Dose differences were related to set-up errors, organ motion, erroneous density corrections and changes in patient anatomy.

Conclusions: EPIDs can be used routinely to accurately verify treatment parameter transfer and machine output. By applying in vivo dosimetry, more insight can be obtained with respect to the different error sources influencing dose delivery to a patient.

760 poster

SIZE REDUCTION OF THE PROSTATE DURING EXTERNAL BEAM RADIOTHERAPY DETECTED WITH RADIOGRAPHIC MARKERS AND THE EFFECT ON POSITIONING ACCURACY

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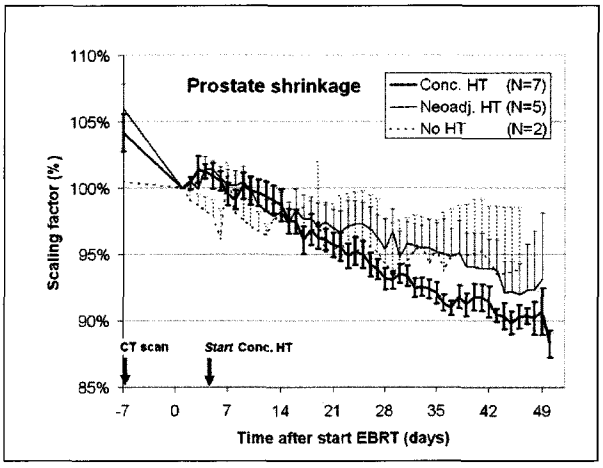
Purpose/Objectif: To improve the accuracy of the dose delivery to the prostate in external beam radiotherapy treatment (EBRT).

Materials/Methods: For 14 patients 4 radio-opaque gold markers were implanted in the prostate. Seven patients received hormonal therapy (HT) starting in the first week of the EBRT ("Concurrent HT" patient group), 5 started the HT at least one month before the EBRT ("Neoadjuvant HT") and 2 patients did not receive HT ("No HT"). The EBRT was a four-field box technique (35 x 2.0 Gy). The prostate markers were imaged daily with an EPID during the AP and left-lateral therapeutic fields. The reconstructed 3-D marker positions from the EPID images were matched off-line with the 3-D positions obtained from the planning CT, allowing translations, rotations, and a single scaling factor. Trends were monitored by comparing the average marker positions in weeks 1 and 7. All indicated confidence levels/error bars are ±1 standard error of the mean.

Results: The scaling factor reduced during the 7-week EBRT for all patient groups (see figure) indicating volume shrinking. The largest reduction of 10.1 ± 1.2% was observed for the "Conc. HT" patient group. This value was comparable with a reduction of the prostate diameter of 12.1% ± 4.1% observed in another group of patients in a period before and 3 months after HT (N=28 patients; volumes determined with TRUS prior to treatment with seed implants; data not shown). Hence the 10%-reduction can partly be ascribed to the concurrent HT. For a typical prostate diameter of 40-50 mm, the shrinkage means a displacement of 2-3 mm of the prostate surface. In the entire population a statistically significant trend ($p<0.05$) was observed in the SI direction, which was a translation of -2.5 ± 0.9 mm (shift toward the apex). For the separate groups the values were -4.2 ± 0.8 mm ("Conc. HT"), -1.4 ± 2.0 mm ("Adjuv. HT") and -0.8 ± 0.1 mm ("No HT"). The largest trend was seen for the "Conc. HT" group, which could be an indication that the shift is related to prostate shrinkage. For all patients combined, the systematic (Σ) and random (σ) translation errors in the 3 principal directions (LR, AP, SI) were Σ = 2.5, 3.9, 3.0 mm, and Σ=1.7, 3.0, 2.6 mm. The rotations were Σ = 5.3°, 3.3°, 3.4°, and σ = 3.6°, 0.9°, 1.2°. The use of off-line and on-line correction strategies is discussed.

Conclusions: The volume change and the trend in the prostate position plead for daily position verification and correction.



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USE OF SKIN MARKERS AND ELECTRONIC PORTAL IMAGING TO IMPROVE VERIFICATION OF TANGENTIAL BREAST IRRADIATION.

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Purpose/Objectif: Verification of breast irradiation is one of the most challenging problems in radiotherapy due to the differences between motion of breast (target volume) and bony tissue. Therefore, the aim of this study was to investigate the additional value of the use of skin markers in electronic portal imaging (EPI) in breast cancer patients treated with tangential fields.

Materials/Methods: For 45 patients, copper skin markers were placed at the cranial, caudal, medial, and lateral border of the palpable breast tissue (CTV) prior to the plannings CT-scan. These locations were marked with ink as a short line, to allow placing gold markers with the same geometry as the copper markers, at identical places at the linear accelerator for EPI. The copper markers were delineated at the CT-scan and visualized on digitally reconstructed radiographs (DRR, reference image for EPI). EPIs with the gold markers were performed in on average 5.6 fractions, resulting in a total number of 504 EPIs. First, the EPIs were analyzed qualitatively, to check whether the skin markers (=CTV) were located within the radiation portal. Second, the displacement of the EPI with respect to the DRR was quantified by matching the EPI to the DRR manually 1) by observer 1, only using anatomical landmarks such as lung and breast contour ("anatomy match") and 2) by observer 2, using the anatomical landmarks with additional help of the skin markers ("clinical match"). Displacements were recorded in horizontal and cranio-caudal direction, and the difference between the anatomy match and clinical match was calculated for each EPI.

Results: In all EPIs, the skin markers were located within the radiation field, indicating that large set-up errors did not occur. The quantitative analysis showed that for both the anatomy match and the clinical match, the average value of the displacement on the EPI compared with the DRR (m) was < 1.5 mm in horizontal and cranio-caudal direction, both for the medio-lateral beams and the latero-medial beams, with a systematic error S < 3.5 mm, and a random error s < 3.2 mm. In 15 out of the 45 patients, a > 5 mm difference was seen in the cranio-caudal direction between the two matches, in 30% of the measurements. This difference was explained by the lack of specificity of the anatomical landmarks to correctly define the cranio-caudal position, suggesting that the skin markers improve the match especially in cranio -caudal direction.

Conclusions: The use of skin markers allows quick detection of large set-up errors. Furthermore, the additional use of skin markers next to anatomical landmarks improved the match of the EPI to the DRR in a substantial number of patients, especially in cranio-caudal direction. The measured systematic and especially random errors are smaller than perhaps expected, and comparable to literature data for e.g. prostate, allowing a future implementation of an off-line set-up correction protocol.

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VALIDATION OF A NEW FORMALISM FOR IN VIVO DOSIMETRY USING TRANSIT DOSE MEASURED WITH EPID

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Purpose/Objectif: The aim of this work was to assess the use of an amorphous silicon electronic portal imaging device (EPID) for in vivo dosimetry. A new formalism is proposed to determine the dose delivered to the patient during treatment. The dose in the patient on the central axis of the beam can be estimated from transit dose measured on the EPID. This formalism has been tested on a water equivalent phantom for different high-energy photon beams configurations. Preliminary results on patients treated for prostate cancer will be presented.

Materials/Methods: The formalism will be first described. It has then been tested by transit doses measurements using an ionization chamber. Subsequently, this detector was replaced by an aSi portal imager (aS500, Varian Medical Systems) which is more suitable to measure dose during treatment. Integrated dose images were acquired with a special mode after a preliminary calibration of the detector was done.Measurements in a water equivalent phantom of varying thicknesses were performed on different beams with different energies (4, 6, 10 and 20MV). Different configurations of square and asymmetric fields have been tested. Complementary measurements were then performed to check the validity of the method for conformal fields. Central axis doses estimated by this formalism were compared with dose measured with an ionization chamber. To evaluate the feasibility of the method and its applicability in clinical use, the formalism has been evaluated with patients treated for prostate cancer with conformal therapy.

Results: The results showed that differences between measured and estimated doses were within 2% for square fields and less than 3% for asymmetric fields. For conformal beams, the measurements are under way and the results will be presented.

Conclusions: These preliminary results are encouraging and demonstrate that the proposed formalism using transit dose measured on EPID is suitable for in vivo dosimetry. This method would provide a very quick and simple way of dose verification usable in clinics.

Posters Experimental Animal Models

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ANTI-INFLAMMATORY EFFECTS OF LOW-DOSE RADIOTHERAPY IN EXPERIMENTAL MODEL OF SYSTEMIC INFLAMMATION IN MICE

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Purpose/Objectif: To determine the effects of low-dose radiotherapy (LD-RT) on the inflammatory response and to characterize the potential mechanisms underlying these effects.

Materials/Methods: Mice were irradiated with 0.1, 0.3, 0.6 Gy, or

sham radiation prior to lipopolysaccharide (LPS) challenge. Leukocyte-endothelial cell interactions in intestinal venules were assessed using intravital microscopy. ICAM-1 expression was determined using radiolabeled antibodies 5 hours after irradiation. Production of transforming growth factor (TGF)-β_1 was measured by ELISA and its *in vivo* functional relevance by immunoneutralization.
Results: Compared with vehicle treated animals, LPS induced a marked increase in leukocyte adhesion (0.13±0.59 vs 5.89±1.03, $p<0.0001$) in intestinal venules. The number of adherent leukocytes was significantly reduced by the 3 doses of LD-RT tested; the highest inhibition was observed with 0.3 Gy (0.66±1.96, $p<0.0001$). LPS-induced ICAM-1 upregulation was not modified by LD-RT. Circulating levels of TGF-β_1 were significantly increased in response to LD-RT in controls and LPS challenged animals. Neutralization of TGF-β_1 partially restored LPS-induced adhesion (4.83±1.41, $p<0.05$).
Conclusions: LD-RT has a significant anti-inflammatory effect, inhibiting leukocyte recruitment, which is maximum at 0.3 Gy. This effect results in part from increased TGF-β_1 production and is not related to modulation of ICAM-1 expression

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COMBINED EFFECT OF LOVASTATIN AND X-IRRADIATION ON U87 HUMAN MALIGNANT GLIOMA CELLS IN VITRO AND IN VIVO

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Purpose/Objectif: Statins were shown to have the ability to induce growth arrest, apoptosis, and decrease clonogenicity in several tumour-derived cell lines. Till now, little is known about its combination with irradiation. Therefore, the aim of this project was to investigate the effects of lovastatin and lovastatin combined with X-radiation on the cell cycle distribution, apoptosis, and growth of U87 cells *in vitro* and *in vivo*.
Materials/Methods: U87, a human malignant glioma cell line was used in all experiments. Lovastatin was dissolved in ethanol. Proliferation was determined by cell counts and cell cycle distribution by flow cytometry. To measure reproductive cell death colony formation and dilution assays were performed. Western blotting was performed to detect the expression of $p21^{WAF1/Cip1}$ protein. One day after transplantation of U87 to the right leg of nude mice, 50 mg/kg/day of lovastatin or carrier (divided in 3 injections per day, 7 x weeks, over whole experiment) were applied i.p. Tumours were irradiated with single dose 20 Gy. Experimental endpoint was tumour growth delay.
Results: Lovastatin in unirradiated U87 cells leads to an increased proportion of cells in the G_0/G_1 phase, and decreased in S-phase and increased apoptotic cell number. The G2 block induced by irradiation was modified and abrogated by the addition of lovastatin. These changes were accompanied by a reduction of cell proliferation and number after treatment with lovastatin alone and in combination with 4 Gy. Western blotting analysis showed an increase of the p21 protein level in lovastatin treated cells and after combination of lovastatin and irradiation. CFE was slightly lower after combined treatment than after IR alone, however this was not significant. *In vivo* lovastatin had a marginal effect on growth of U87 in NMRI nu/nu mice. Combination of single dose with lovastatin did not prolong tumour growth delay.
Conclusions:
Lovastatin given alone has antiproliferative (G0/G1) and cytotoxic (apoptosis, CFE) effects on U87 cells in vitro. Both effects are dose dependent. When combined with 4 Gy IR, neither apoptosis nor CFE were significantly changed. *In vivo* lovastatin alone or in combination with single dose did not change tumour growth delay in U87 tumours. Lovastatin was tolerable when given over one month, longer application leads to the death of animals.

765 poster

INHIBITORY EFFECT OF TRANILAST ON RADIATION-INDUCED CARDIAC INJURY IN C57BL/6 MOUSE

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Purpose/Objectif: Tranilast is an anti-allergic drug clinically used because it inhibits the release of chemical mediators from mast cells and of cytokines from macrophages. Tranilast is also shown to cure or prevent keloids and hypertrophic scars by inhibiting collagen synthesis. Thus, to observe whether tranilast can prevent radiation-induced cardiac injury and fibrosis that are caused by radiation-induced cytokines, we examined the effect of tranilast on the release of transforming growth factor-beta1(TGF-beta1), collagen I and III that are induced by ionizing radiation (RT) in C57BL/6 mouse.
Materials/Methods: The thoraces of C57BL/6 mice were irradiated with 20 Gy (dose rate 200 cGy/min). Mice were injected with tranilast (100mg/kg) or vehicle intra-peritoneally, once a day, six days a week for 18 weeks from 3 days before thoracic irradiation. The cardiac tissues from the different groups were analyzed by immunohistochemical stain, Masson's trichrome stain and hematoxylin-eosin (H-E) stain. The protein levels of TGF-beta1, collagen I and III were correlated with the histopathological alterations.
Results: In cardiac tissue of irradiated mice, active inflammation, collagen deposition and septal thickness were shown. Protein level of TGF-beta1 and collagen I and III were increased. On the contrary, in mice treated with tranilast after cardiac irradiation, there was no inflammatory reaction, collagen deposition or septal thickness. In immunohistochemical stain, the level of proteins in mice treated with tranilast and radiation was much more reduced than that of irradiated mice. Among control, vehicle injected and tranilast injected groups, there was no difference of protein levels of TGF-beta1, collagen I and III. In histopathologic finding, the extent of inflammation, collagen deposition and septal thickness were almost same in these groups.
Conclusions: These results suggest that tranilast can prevent the radiation-induced cardiac injury and fibrosis by suppressing the release of TGF-beta1, collagen I and III that are induced by ionizing radiation in the cardiac tissue.

766 poster

LIVER REPOPULATION BY TRANSPLANTATION OF DONOR HEPATOCYTES AFTER EXTERNAL BEAM RADIOTHERAPY AS PREPARATIVE REGIMEN FOLLOWED BY PARTIAL HEPATECTOMY

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2 - University Hospital Göttingen, *General Surgery, Göttingen, Germany*
3 - University Hospital Göttingen, *Radiology, Göttingen, Germany*
4 - University Hospital Göttingen, *Laboratory Animal Science, Göttingen, Germany*

Purpose/Objectif: The transplantation of donor hepatocytes is considered a promising option to correct chronic liver failure through repopulation of the diseased organ. We established a novel selective external beam irradiation technique as a preparative regimen for hepatocyte transplantation.
Materials/Methods: Livers of DPPIV (CD26) -deficient rats were pre-conditioned with external beam single dose irradiation (25 Gy) delivered to 2/3 of the liver. Four days later, a 1/3 partial hepatec-

tomy (PH) was performed to resect the untreated liver section and 15 million wild-type (DPPIV+) hepatocytes were transplanted via the spleen into the recipient livers. Radiation effects were determined by TUNEL- and f×H2AX-staining for apoptosis and DNA-DSB, respectively. Donor cell integration and growth was proven over a period of 9 month either by immunocytochemistry (CK18, Cx32, CYP40) on frozen liver sections or in vivo by detecting Cy5.5 marked CD26-antibodies using the eXplore Optix System by GE.
Results: Transplanted hepatocytes integrated rapidly into the irradiated liver and proliferated as clusters, finally repopulating the host liver to approximately >20% hepatocyte mass thereby expressing functional markers to the same extent as host hepatocytes. By in vivo imaging, repopulation was also demonstrated as strong signals specific for Cy5.5 in the liver region of the transplanted animals could be detected. In contrast, in non-transplantated control animals only weak signalling could be measured. Animals showed no acute or chronic toxic effects, and induced apoptosis was not detected in the irradiated liver. DNA-DSBs, as visualized by g-H2AX-foci, were repaired within 24 hours.
Conclusions: External beam liver irradiation is sufficient to achieve partial repopulation of the host liver following hepatocyte transplantation, under the additional stimulus of 1/3 PH. The method described has potentially good prospects for its application in a clinically viable form of treatment, although the exact mechanism of radiation action remains to be determined.

767 poster

MELATONIN AMELIORATES HEPATIC TOXICITY IN IRRADIATED RAT LIVER

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Purpose/Objectif: Radiation therapy is a common and important tool for cancer treatment but the radiosensitivity of normal tissues adjacent to the tumor limits therapeutic gain. Over the years, a number of compounds have been tested for their radioprotective efficacy. Melatonin(N-acetyl-5-methoxytryptamine), the chief secretory product of the pineal gland in the brain, has been documented as a direct free radical scavenger and an indirect antioxidant. Several clinical reports indicate that melatonin administration, either alone or in combination with traditional radiotherapy, results in a favorable efficacy/toxicity ratio during the treatment of human cancers. The aim of this study was to investigate the antioxidant role of melatonin against oxidative damage caused by gamma irradiation in liver tissue after total body irradiation (TBI).
Materials/Methods: After performing required dose response experiments, thirty two adult male rats were equally divided into 4 groups; group I was injected with (30mg/kg, ip) melatonin, while group II received isotonic NaCl solution. Groups I and II were exposed to 10 Gy whole body ionizing radiation in a single fraction sixty minutes later. Group III was injected with (30mg/kg, ip) melatonin but was not irradiated, the final group was reserved as sham treated. Animals were followed for 72-h after irradiation, while melatonin (30mg/kg, ip) injections were repeated once daily.
Results: Tissue levels of malondialdehyde (MDA) and glutathione (GSH) activity were estimated in live. The results demonstrated that Hepatic MDA levels in irradiated rats that were pretreated with melatonin (30mg/kg) were significantly decreased, while GSH activity was significantly increased.
Conclusions: The results suggest that administration of melatonin before and after irradiation may prevent liver damage caused by gamma irradiation.

Posters Functional Imaging

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18-FDG-PET AS A PREDICTOR OF THERAPY RESPONSE TO SINGLE DOSE IRRADIATION OF HUMAN SQUAMOUS CELL CARCINOMA (HSCC) FADU IN NUDE MICE?

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Purpose/Objectif: To investigate whether FDG uptake at early time points may predict outcome of irradiation in hSCC FaDu.
Materials/Methods: The hSCC cell line FaDu was transplanted subcutaneously into the hind leg of NMRI nude mice. Animals entered the study at a tumour diameter of 7mm. PET scanning was performed on a dedicated animal PET scanner (MicroPET® P4, CTI Molecular Imaging, measured attenuation correction, 8 MBq ^{18}FDG i.v., list mode acquisition for 60 min, evaluation of acquisition from 30-60 min p.i.). After an initial FDG-PET (day 0) the tumours were stratified according to the median FDG uptake for irradiation with either 25 Gy (TCD20) or 35 Gy (TCD80) single dose. The follow up FDG-PET were performed at day 1, 4 and 7 after irradiation. The Standard Uptake Value (SUV) and the FDG accumulating volume of the tumours was calculated for each PET measurement. Mice were observed for 120 days, experimental endpoints were growth delay and local control.
Results: To date 35 of the 80 animals planned for this study are included. After irradiation with 25 or 35 Gy, the FDG accumulating tumour volume determined on day 0 has decreased at day 7 by 47%. Although within the group of tumours heterogeneous SUVmax values are found, for the individual tumour as well as between the two dose groups up to now no significant difference between day 0 and the follow up scans is observed. The average time to recurrence was 41 days after 25 Gy and 45 days after 35 Gy. The impact of FDG uptake before and after irradiation on time to recurrence will be evaluated after recruitment of all animals.
Conclusions: PET offers the possibility of longitudinal evaluation of possible predictive factors before, during and after radiation. The present study on FDG shows intertumoral heterogeneity of SUVmax values but little changes of the values early after irradiation. Data correlating SUV with the outcome of irradiation will be presented.
This work was performed within the 6th framework EU-project BioCare, proposal# 505785.

769 poster

3D-SEGMENTATION OF [18F]-CHOLINE PET SIGNALS FOR TARGET VOLUME DEFINITION IN RADIATION THERAPY OF THE PROSTATE

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Purpose/Objectif: The volumetric assessment of PET signals becomes increasingly relevant as PET imaging is increasingly demonstrated to offer improvements in radiotherapy (RT) treatment planning. One of the major advantages of using PET signals in RT treatment planning is that they offer the possibility, because they are amenable to automated segmentation routines, to improve standardization of tumor volume definition. In the present study, we have investigated the use [^{18}F]-choline PET imaging and a novel,

asymmetrical, automated segmentation algorithm for tumor volume delineation in the prostate. We have assessed the anatomical and spatial accuracy of the algorithm in contrast to tumor volumes defined using standard CT imaging data sets.

Materials/Methods: [^{18}F]-choline PET and CT scans of ten patients with prostate cancer were acquired using a combined PET/CT scanner. Target volumes were manually delineated on CT images using standard software tools. Volumes were also obtained from [^{18}F]-choline PET images using an asymmetrical segmentation algorithm which offers the ability to independently vary the signal threshold in lateral, cranial-caudal, and anterior-posterior directions, hence use of the term asymmetrical. Planning target volumes (PTVs) were derived form CT and [^{18}F]-choline PET based volumes using an automated region growing algorithm. Comparative planning was performed with [^{18}F]-choline PET and CT derived PTVs and, as a measure of dose to non-target structures, dose to the rectal wall was assessed.

Results: Target volumes derived from CT and [^{18}F]-choline PET yielded comparable volumes. Optimal matching of CT and [^{18}F]-choline PET derived volumes in the lateral and cranial-caudal directions was obtained using a background subtracted signal threshold of 23 +/- 2.6%. In the anterior-posterior direction, where signal adaptation requires compensation for rectal signal overflow, optimal matching was achieved using a threshold of 49.5 +/- 4.6%. 3D-conformal treatment planning with CT and [^{18}F]-choline PET resulted in comparable dose to the rectal wall.

Conclusions: PET-defined target volumes are potentially useful for generating standardized PTVs. Volumes derived automatically from [^{18}F]-choline PET signals require the use of asymmetrical segmentation, optimized background subtracted signal thresholds, and adequate expansion to qualify as suitable PTVs for radiotherapy.

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A METHOD FOR AUTOMATIC SEGMENTATION OF 18F PET SIGNALS FOR TARGET VOLUME DELINEATION

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Purpose/Objectif: Positron Emission Tomography (PET) alone or in combination with Computer Tomography (PET/CT) is increasingly used not only for staging but additionally for target volume assessment. The visual impression of PET images is dependent on window and level settings. Thus a standardized way of converting PET signals into volumes is essential. An automated, observer independent software solution is presented.

Materials/Methods: A model-based method was developed to determine a relative threshold level (Threl) from the background subtracted image for volume delineation. Measurements were made using cylinders (diameter 4.5mm to 45mm) filled with ^{18}F activities ranging from 0.001MBq/ml to 0.15MBq/ml. These were placed in a tank filled with ^{18}F water of different activities. From these measurements Threl was derived. Software (SW) was generated to automatically delineate PET activity volumes based on this threshold. The SW was validated in vitro and *in vivo*. *In vitro* validation was done with spherical sources (diameter 16mm to 36mm). *In vivo* validation of the SW was done using patient data. Tumour volumes derived with the automatic SW were compared with CT based clinician derived volumes.

Results: The Th_{rel} best representing the source diameter was 41 2.5% of the background-subtracted signal. The Th_{rel} was constant for diameters ^{3} 12.5mm. In an in vitro set-up the SW was capable of segmenting solitary PET volumes to within 1.4mm (1SD). For non-homogeneous signals in a clinical set-up minimal manual intervention is presently required to separate target from non-target signals. Examples of automatically generated clinical target volume will be presented. The volume can be manually adapted to give the ultimate target volume.

Conclusions: SW-based automatic delineation of the volume of ^{18}F activity is feasible and highly reproducible. Volumes can be subsequently modified by the clinician if deemed necessary to produce the ultimate target volume. This approach will increase the efficiency and reproducibility of the planning process.

771 poster

A NOVEL METHOD OF PERFUSION MRI ANALYSIS USING DYNAMIC CT SCANNING IN PATIENTS WITH CERVIX CARCINOMA

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Purpose/Objectif: Dynamic contrast enhanced MRI (DCE-MRI) and CT (DCE-CT) may have prognostic value in radiation therapy. Kinetic analysis typically requires an arterial input function (AIF) but determination of the AIF in DCE-MRI is challenging as the T1-weighted signal saturates with high contrast concentration in arteries. A novel method of generating the MRI-AIF from the DCE-CT data set is proposed for the analysis of DCE-MRI when both of these studies are done on the same patient.

Materials/Methods: Thirteen patients with cervix carcinoma took part in an REB approved study in which they received a DCE-MRI scan followed by a DCE-CT scan at the time of staging. DCE-MRI was acquired (3D SPGR) on a 1.5T GE MRI system at 8 second temporal resolution for 400 s, 10 mm thickness slices and 6 slice locations; 0.1 mmol/kg body weight of gadodiamide was injected at a rate of 2 ml/s. DCE-CT was performed on a GE Lightspeed XQ/i scanner at 120 kVp, 60 mA, 2 slices of 10 mm each, and 1s per scan for 120 s followed by 8 scans for another 120 s. The CT scanning was synchronized with injection of 1.5 ml of Omnipaque 300 per body weight at a rate of 4 ml/s. A corresponding slice was identified in CT and MRI; an external iliac artery was contoured on the CT slice only (as CT-AIF) while the tumor was contoured on both CT and MRI slices.

With the CT-AIF, the patient characteristic function (PF) describing the delay and dispersion of injected bolus to the external iliac arteries was calculated. An AIF was generated for the amount and injection rate for gadodiamide in the DCE-MRI study using the same PF. The generated MRI-AIF was used for DCE-MRI analysis while the DCE-CT was analyzed with the conventional method. A two-compartment model was used for analysis based on averaged image intensity over regions of tumor, and a voxel based analysis was also investigated on these predetermined regions. The k_{tran} values resulted from DCE-MRI and DCE-CT were recorded and correlation was calculated.

Results: The average k_{tran} values over these patients was found to be 0.42 and 0.40 ml/min/g based on the DCE-MRI and DCE-CT method respectively. The average MRI k_{tran} was 5% higher than that of DCE-CT and they were found to be significantly correlated with $r = 0.80$, $p < 0.001$. Voxel based analysis on 7 patients reviewed a correlation with $r = 0.76$ ($p < 0.001$) in the coefficient of variation for k_{tran} obtained by the two methods over the tumor regions.

Conclusions: The significant correlation for k_{tran} values between DCE-MRI and DCE-CT show the consistency of the two methods when DCE-MRI used the generated MRI-AIF which is believed to have been accurately determined from DCE-CT in these unique sets of data. Investigation of the voxel based analysis is on going. The

results might serve as a benchmark for future investigation of DCE-MRI study design and analysis for cervix carcinoma.

772 poster

COMPARISON OF DIFFERENT SEGMENTATION METHODS OF FDG-PET VOLUME DELINEATION AND EVALUATION OF THE IMPACT ON IMRT TREATMENT PLANNING.

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Purpose/Objectif: To compare the gross tumor volumes (GTVs) of Head an Neck (HN) patients resulting from different segmentation methods of PET volume and to investigate their influence on the radiotherapy treatment planning.

Materials/Methods: Twelve HN patients were scanned and PET images were coregistered with CT scans. Four different methods of segmentation were used. The first defines a GTV by a threshold of 40% of the maximum standardize uptake value (SUV)[GTV_{40}]; the second defines an isocontour of SUV=2.5[$GTV_{2.5}$], the same cut-off value normally used in nuclear medicine to define malignant lesion. Daisne introduced the third method [$GTV_{S/B}$] :a threshold is defined as function of the background signal and in-house phantom measurements were performed to derive this relation. The last method defines a SUV threshold value by the linear relationship SUV_{tsh}=0.307*SUV_{mean}+0.588 [GTV_{NSCLC}]. Such method was actually suggested for lung tumor with volumes sizes and S/B values completely different from HN cases. Quantitative analysis were done by GTVs volume differences and Boolean operators to evaluate the mismatch. The impact of different GTVs on a SIB-IMRT plan were analyzed in term of normal tissue sparing and related potential of dose escalation.

Results: Significant differences were observed between the delineated GTVs. The GTV_{40} appears , on average, bigger then the $GTV_{S/B}$ probably because of the low S/B signal. Differences of the order of 20-30% were evaluated. The GTV_{NSCLC} delineation method appeared not suitable probably because of the small lesion size. Mismatches between different GTVs were observed. An explanation is the limit of the regular geometry of the phantom used to obtain threshold values. Dose distribution analysis on the different IMRT plan doesn't show a significant impact of the $GTV_{S/B}$, GTV_{40}, $GTV_{2.5}$ volume variations. A different result observed for GTV_{NSCLC} in 3 cases is due to the evident mismatch.

Conclusions: The analyzed segmentation methods produce different volumes. In some cases a mismatch is observed between different GTVs. Despite of this volume differences no significant variations were observed in a SIB-IMRT radiotherapy planning. Data indicates that segmentation is an unsolved crucial problem.

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FDG-PET-CT AFTER NEOADJUVANT CHEMORADIATION OF LOCALLY ADVANCED RECTAL CANCER. HOW ACCURATE CAN IT PREDICT TUMOR DOWNSTAGING AND INVASION OF THE MESORECTAL FASCIA ?

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Purpose/Objectif: To assess the accuracy of post chemoradiation FDG-CT-PET for the prediction of tumor downstaging and invasion of the mesorectal fascia (MRF).

Materials/Methods: 23 patients with locally advanced rectal cancer treated with long term chemoradiation were included. An abdominal radiologist and radiotherapist both experienced in CT-PET imaging retrospectively evaluated pre and post CT-PET images for T stage, N stage and tumor invasion of MRF based on visual assessment of Standard Uptake Values (SUV) displayed semi-quantitatively in a colour coded scale fused with the CT images . Residual tumor disease on post chemoradiation CT-PET was defined as an increased level of tracer uptake (SUV) against background activity in the initial tumor area or a positive lymphnode prior to chemoradiation. A confidence level score was used for invasion of the mesorectal fascia. Post CRT CT-PET findings were compared to histology of surgical specimen. Sensitivity, specificity, PPV, NPV and area under the ROC curve were calculated.

Results: Sensitivity/specificity of postCRT CT-PET for pT0, pT1-2, pT3 and pT4 were 50/95%, 56/93%, 70/85%, 100/86% respectively.The area under the ROC curve, sensitivity, specificity, PPV and NPV of postCRT CT-PETfor invasion of the MRF was 0.76 [95%CI:0.55-0.98], 86%, 50%, 43%, and 89% respectively.

Conclusions: CT-PET had a limited accuracy for the prediction of downstaging. PostCRT CT-PET had a better performance for prediction of advanced tumors and tumor invasion of the MRF. The main problem of CT-PET seemed to be overstaging due to chemoradiation induced tissue reaction.

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IMMOBILIZATION DEVICE FOR IN VIVO AND IN VITRO MULTIMODALITY IMAGE REGISTRATION OF RODENT TUMORS

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Purpose/Objectif: With the use of functional imaging for image-guided IMRT, a major issue is to validate that subtle biological changes, both quantitative and spatial, can be visualized in vivo. In that framework, the use of animal model is of growing interest. The aim of this study was to develop a multipurpose immobilization device for in vivo (CT, MRI, PET) and in vitro (autoradiography, immunofluorescence) multimodality images registration of rodent tumors.

Materials/Methods: FSA sarcoma syngeneic to C3H mice was generated in the right leg. When the tumor has reached a diameter of 8-10 mm, the mouse was anesthetized with ketamine-xylazine and positioned in a home made Styrofoam mould with its legs diverging and its tail getting out of the mould. Four Teflon tubes (0.4 mm cross section) were positioned around the mouse to constitute a reference coordinate system. A solution of 90% tepid gelatin and 10% glycerol was poured in the mould, immerging the fiducial markers and the animal from its belt downward, and allowing a normal free breathing. After few minutes at room temperature, the gelatin had solidified. The tubes were filled with a mixture of radioactive tracer, iodinated contrast agent and oil, allowing their visualization in each modality. The mouse was imaged with a CT-scanner (Mx8000 IDT, Philips), and a 4.7 T MRI (Biospec, Brucker) using a T2 sequence. The mouse was then injected with 500 µCi of FDG through the tail vein and a 10 min acquisition was performed with a Mosaic PET (Philips). The mouse was then euthanized with a lethal dose of anesthetic, and the mouse containing mould was frozen at -25°C. After five hours, the block could be sliced (0.8 mm thick slices); the slices were then autoradiographied for 30 min (FLA-5100, Fujifilm). From each slice, 10 µm thick cryostat sections were obtained and processed for further immunofluorescence analysis. The various in vivo and in vitro images were stacked taking into account their thickness and registered using the Teflon tubes as markers. Average distances between the Teflon tubes visualized in two different imaging modalities were calculated to assess the registration accuracy.

Results: The registration accuracy was assessed on 5 mice. Average minimal euclidian distance between two skew lines was 0.23 ± 0.11

mm, 0.28 ± 0.07 mm, and 0.21 ± 0.06 m for PET-CT, PET-MRI, and CT-MRI registration, respectively. Evaluation of the registration accuracy with autoradiography is in progress.
Conclusions: With the use of a specific immobilization device for tumor bearing mouse, the registration accuracy between anatomic and functional images were in the sub-millimetric range, thus allowing proper validation studies of the dynamics of various biological pathways with a micro-PET technology.

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METABOLIC 3D CSI MRS IMAGING OF BRAIN IN RELATION TO IMRT PLANNING FOR BRAIN GLIOMAS

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Purpose/Objectif: To characterize alteration of whole brain metabolism using 3D CSI MRS (Chemical Shift Imaging Magnetic Resonance Spectroscopy) for patients before radical RT for brain gliomas.
Materials/Methods: 30 patients after the surgery because of brain gliomas (WHO grade II-IV tumors) had MRI scans before radiotherapy treatment planning. MR studies consisted of standard imaging, perfusion studies and CSI MRS using Siemens MAGNETOM AVANTO 1.5 T. Volume of brain selected for 3D CSI TE=135 ms MRS was the biggest possible volume, free from non-brain lipids artifacts. Relative intensities of the signals (choline [Cho], creatine [Cr] N-acetyl aspartate [NAA], and lactate) were obtained by automatic numeric integration of fitted signals in 3D array of 1x1x1 cm voxels. Images were fused to treatment CT scans using HELIOS treatment planning system. 19 patients were treated with IMRT, and 11 with 3D conformal techniques (both IMRT and 3D conformal plans were prepared for each patient, and better was selected). PTVs were drawn using T1 MR images with contast enhancement or T2 MR images (for some WHO II tumors). Margins were dependent on tumor grade. Planned doses of 54-60 Gy in 2 Gy/fx were delivered using 6-20 MV photons.
Results: Mean PTV volume was 104 ml SD=80, mean total brain dose 18 Gy SD=9 Gy. In majority of patients (73%) decrease of NAA/Cr and increase of Cho/Cr ratio was registered in PTV, metabolic alterations decreased progressively with the distance from PTV borders. Alterations were registered up to 3-5 cm outside PTV borders. Lactate signals were registered for 43% of patients inside and for 33 % outside PTV up to 4 cm. CSI showed significant variation of metabolite signals inside PTV. Also perfusion studies suggested variation in blood flow inside PTV. Patient will be followed using similar imaging protocol, in order to correlate results of functional imaging with treatment outcome and location of possible recurrent tumor.
Conclusions: Functional imaging suggests great variation of metabolic activity and blood flow inside and outside PTV. Alteration of metabolic ratios are registered several cm outside PTV.

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PET/CT FOR STAGING AND TARGET VOLUME DELINEATION IN PREOPERATIVE 3D-CONFORMAL RADIOTHERAPY OF RECTAL CANCER

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Purpose/Objectif: To investigate the potential advantage of using FDG-PET/CT for delineating GTV and CTV for preoperative 3D-conformal radiotherapy (RT) of rectal cancer.
Materials/Methods: Twenty-one patients, 16 males and 5 females, diagnosed with rectal cancer cT3-4 N0 M0 were enrolled. All patients were candidates for RT or chemo-RT in preoperative setting. RT was planned to a total dose of 45.0-50.4 Gy, 1.8 Gy/fx. FDG-PET study was done by a PET/CT scanner (Biograph, Siemens) with contiguous slices of 5 mm thickness after injection of 5.18 MBq/Kg of FDG. PET/CT fusion images were coregistered by a dedicated software (Syntegra, Philips). The accuracy of image fusion was checked by bony landmarks such as pubic symphisis, acetabula and sacrum. GTV and CTV delineation was firstly performed on CT images (CT-GTV, CT-CTV) and then on PET/CT (PET-GTV, PET-CTV). CTV included GTV and potentially involved lymph nodes (perirectal, presacral, obturator, internal iliac). Then, PET-GTV, PET-CTV were compared to CT-GTV, CT-CTV.
Results: In 6/21 cases (29%) the use of PET/CT affected tumour staging. In 2/21 cases (10%), no FDG uptake was detected in lymph nodes found 1.5 cm in size at CT or MRI. In 3/21 cases (14%) staged N0 at CT or MRI, PET/CT showed FDG uptake. In 1 of the latter 3 cases and in another one, liver metastases were detected by PET/CT changing the stage from M0 to M1. In a case already diagnosed by CT with a potentially resectable liver metastasis, PET/CT showed multiple lesions changing the treatment intent from curative to palliative. In 20/21 cases (95%), PET-GTV was significantly smaller than CT-GTV (p=0.02). PET-CTV and CT-CTV were nearly overlapping in 16/21 cases (76%), while PET/CT implied a CTV variation in size and shape in 5/21 cases (24%). Particularly, PET-CTV was smaller than CT-CTV in 4/5 cases in relation to a smaller GTV identified by PET and larger in 1/5 cases in relation to a PET positive node found outside the CT-CTV.
Conclusion: This study shows that PET/CT for preoperative radiotherapy of rectal cancer can lead to a relevant change in staging and planning. Stage variation was observed in 29% of our cases and change of treatment strategy in 5%. The change of GTV, observed in 95% of cases, could be relevant in case of a radiotherapy boost. The change in size and shape of CTV, observed in 24% of cases, could become of greater interest when using a highly conformal technique such as intensity-modulated radiotherapy.

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QUANTIFICATION OF VASCULAR CHARACTERISTICS IN CERVICAL CANCER DURING RADIOTHERAPY BY DYNAMIC CONTRAST-ENHANCED MR IMAGING.

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Purpose/Objectif: Standard treatment for locally advanced cervical cancer consists of external beam irradiation (EBRT) and brachytherapy. The tumor volume covered by the applicator can be insufficient. For large tumors partial external boosting may resolve part of this problem. Tumor perfusion could be a prognostic factor to predict response during radiotherapy. This helps the choice for an optimal boosting strategy. For this purpose we investigated tumor perfusion using a quantitative analysis of blood flow and other parameters related to the vasculature.
Materials/Methods: In 13 patients with cervical cancer we performed a dynamic contrast-enhanced MRI (DCE-MRI) before radiation treatment and in the first week of treatment. The vascular properties of the tumor were determined by analyzing the DCE-MRI data quantitatively per voxel (sized 0.9x0.9x5-9mm^3), using the tissue homogeneity model, which resulted in 3D parameter maps for blood

flow, mean transit time, extraction efficiency factor, interstitial volume and delay time.Here we determined the correlation between these parameters and measured the changes during radiotherapy.
Results: The mean values of the five parameters were determined before radiotherapy and after 5-7 fractions (see table).

Mean values vascular parameters

	Before radiotherapy	After 5-7 fractions
Parameters	Mean (range)	Mean (range)
Blood flow (F) (ml/min/100g)	25.0 (5.06-39.3)	25.8 (16.6-54.8)
Mean transit time (Tc) (s)	26.1 (14.8-41.1)	28.9 (16.7-56.1)
Extraction efficiency factor (E) (%)	54.0 (37.0-73.0)	55.0 (32.0-79.0)
Interstitial volume (Ve) (ml/100g)	35.0 (16.0-75.0)	32.0 (16.0-49.0)
Delay time (D) (s)	2.14 (0.52-3.06)	2.04 (0.50-3.25)

The blood flow values were distributed over a wide range, with a trend towards an increase of blood flow during radiotherapy. The other parameter values didn't show a significant difference before or after the start of radiotherapy. A significant correlation was found between E and Tc at both time points. We speculate that an increase of the blood fraction leaking into the interstitial space leads to an increase of the time it takes for the blood to travel from the arterial end to the venous end of the capillary bed.
Conclusions: We measured quantitative vascular blood perfusion using DCE-MRI. There is a trend of an increasing blood flow in the tumor during radiotherapy and a correlation between E and Tc. The correlation of these parameters with tumor response is the subject of further study.

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SUBVOLUME BOOSTING OF FDG-POSITIVE TUMOUR AREAS IN PATIENTS WITH NON-SMALL CELL LUNG CANCER (NSCLC): A PLANNING STUDY USING IMRT

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Purpose/Objectif: A high uptake of FDG is associated with a poor prognosis of patients with NSCLC. Our group has previously shown that a high FDG uptake correlates with a higher expression of hypoxia and proliferation-related cellular markers. Delivering higher doses of radiotherapy to areas within the tumour that have high FDG uptake may increase local tumour control. We have shown the areas of high FDG uptake in the tumour remain stable during a course of radiation, allowing for treatment plans with an extra dose on these areas of high uptake. In the present planning study, we evaluated the feasibility of boosting FDG-positive tumour subvolumes, taking into account dose constraints for normal structures.
Materials/Methods: In 9 patients with NSCLC and a tumour diameter of ^{3} 4 cm, referred for radical radiotherapy, IMRT plans using 7 beams (7B) were generated for each patient. The $CTV_{whole\ tumour}$ was defined by the GTV + 0.5 cm and the $PTV_{whole\ tumour}$ was the CTV + 1.0 cm. The $CTV_{subvolume}$ was defined by the 50%SUV or the 70%SUV, as delineated by a validated automatic system (esoft). The $PTV_{subvolume}$ was the $CTV_{subvolume}$ + 1.0 cm. Treatment plans (superposition algorithm) were designed to deliver 57.5 Gy / 38 fractions (1.5 Gy BID) to the $PTV_{whole\ tumour}$ and on top of that to boost the $PTV_{subvolume}$ either by:

1. Increasing the dose per fraction on the $PTV_{subvolume}$, while keeping 38 fractions constant. (Integrated boost)
2. Adding high dose fractions of 20 Gy each only to the $PTV_{subvolume}$, thus adding more fractions. (Hypofractionated boost)

In each method, the dose was escalated until normal tissue constraints were reached, being MLD=16.5 Gy, Dmax oesophagus=80Gy, Dmax spinal cord=55Gy.
Results: In 4/9 patients a considerible dose escalation was possible. By the integrated boost technique: from 57.5Gy (1.5Gy BID) to 100 Gy /38 fractions, 130 Gy/38 fractions, 140 Gy/38 fractions, 145 Gy/38 fractions respectively; by the hypofractioned boost: 3 x 20 Gy, followed by 57.5 Gy (1.5 Gy BID).
Conclusions: Boosting areas of high FDG uptake in the tumour, respecting normal tissue constraints, is feasible for some patients and allows for RT dose escalation, which may result in better prognosis for these patients. More patients are being included in this study and will be presented, together with the effect on Tumour Control Probability.

779 poster

THE EFFECT OF RADIOTHERAPY AND COMBRETASTATIN A-4 PHOSHATE (CA4P) ON PROSTATE GLAND VASCULARITY

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Purpose/Objectif: To document changes in prostate gland vascularity by dynamic MRI following 5 fractions of external beam radiotherapy and a single dose (50mg/m^2) of combretastatin-A4-phosphate (Oxigene Inc., USA) in a Phase Ib study.
Materials/Methods: 8 patients (mean age 68y) undergoing radical radiotherapy following neoadjuvant hormonal therapy for prostate cancer (Gleason >6, PSA >20ng/ml or T3/4), were evaluated by multislice dynamic contrast-enhanced MRI on five occasions (two baseline; following 5 fractions RT; 4h & 72h following CA4P); total 40 scans. Transfer constant (permeability surface-area product K^{trans}) and extracellular leakage space (v_e) were calculated pixel-by-pixel for the whole prostate gland. Changes in median values of parameters were analysed with reference to the statistical measurement error.
Results: Significant group increases in K^{trans} (p=0.004) and v_e (p<0.001) following RT were noted (with 7/8 and 3/8 patients showing individual increases in K^{trans} and v_e respectively). Further significant group increases in K^{trans} were seen at 4h following CA4P (p=0.004) and v_e (p=0.048). 72h after CA4P, K^{trans} decreased significantly (p=0.002) with no change in v_e, which remained higher than at baseline

	pre1	pre2	pre1-pre-2 mean	post RT	post RT%	CA4P 4h	CA4P 4h%	CA4P 72h	CA4P 72h%
K^{trans}	0.439	0.388	0.414	0.977	136.0	1.297	32.8	0.771	-40.6
v_e	0.626	0.607	0.617	0.741	20.1	0.673	-9.1	0.743	10.4

Conclusions: Quantifiable acute changes in the MR vascular kinetic parameters are noted following RT demonstrating an early increase in vascular permeability. The increase in vascular permeability following CA4P is in contrast to the effects seen with CA4P alone without prior radiotherapy. Radiotherapy seems to modulate the expected vascular shutdown. Increases in leakage space may indicate cellular apoptosis. Radiotherapy and CA4P are showing synergism

with a prolonged effect at 72 hours. The combination of radiation with this vascular disrupting agent has demonstrated enhancement of tumour vascular damage compared to CA4P alone and merits further study.

780 poster

TUMOR RESPONSE PREDICTION BY USE OF A COMBINED FDG-PET-CT SIMULATOR BEFORE AND AFTER RADIOCHEMOTHERAPY IN RECTAL CANCER PATIENTS

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Purpose/Objectif: We investigated the potential predictive value of a pre- therapeutic and a post- therapeutic pre-surgical FDG-PET-CT simulation for the histological tumor response in locally advanced rectal cancer patients treated with preoperative radiochemotherapy (RCT).

Materials/Methods: A total of 25 patients with locally advanced rectal cancer, referred for pre-operative radiochemotherapy with curative intent, were studied. All patients underwent a pre-treatment simulation (pre) as well as post-treatment simulation FDG-PET-CT (post) in identical patient position on a combined FDG-PET-CT-simulator before surgery (mean 44 d after RCT). For each patient pre and post visual contouration of the PET - positive tumor area was performed. After RCT, only on the PET-positive areas within the original tumor localization were contoured. For each patient, pre and post qualitative (FDG uptake) and semi- quantitative assessment with standard-uptake values (SUV) of the scans were done. Values of SUV were plotted in volume histograms and the area under curve (AUC) was also calculated. The histological evaluation of the tumor response on surgical specimen was done according to Mandard.

Results: The pre mean SUV_{max} of 14.6 +/- 4.5 SUV contour volume of 83 +/-47cm decreased to a mean SUV_{max} of 3.7 +/- 1.5 with a volume of 25.1 +/- 17.7 cm after RCT. Histological evaluation of all tumor specimen revealed a TRG score distribution of 9.5, 28.5, 43 and 19% for TRG 1 (complete regression), 2, 3 and 4 (no regression), respectively. Comparison of the TRG scores with the SUV parameters showed no difference in the SUV_{max} and the pre and post SUV_{mean} values between the patients with a TRG score of 1 and 2 (1/2 responders) and a TRG score of 3 and 4 (3/4 non -responders). The post SUV_{max} values however were significantly different with 2.8 +/-0.4 for TRG 1/2 and 4.4 +/-0.6 for TRG 3/4, respectively ($p<0.05$). The SUV contour volumes above the cut-off 2 for the post FDG-PET-CTs were also significantly different with 3.7cm +/- 1.3 and 14.2 cm +/- 4.9 for TRG 1/2 and TRG 3/4, respectively ($p<0.05$).

Conclusions: Differences in the FDG-uptake values and the SUV contour volumes between the histological responding and non-responding tumors were only seen in the post FGD-PET-CT scans. The pre FDG-PET-CT had no additional value for the prediction of tumor response.

Posters Genomics and Proteomics

781 poster

RADIATION RESPONSE AND POTENTIAL RADIATION SENSITIVITY GENES IN PRIMARY HUMAN FIBROBLASTS: A WHOLE GENOME MICROARRAY STUDY

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Purpose/Objectif: We were going to identify radiation-induced early transcriptional responses and genes related to individual radiation sensitivity in normal and sensitive human fibroblasts.

Materials/Methods: Skin biopsies were taken and primary fibroblast cultures established from cancer patients undergoing radiation therapy. Radiation sensitivity of the fibroblasts were determined by colony forming assay and correlated to the radiation induced sequelae of the patients. The SF2s ranged between 8-45%, and for the purpose of the present study, fibroblasts were considered normal if their SF2 was >30% and radiation sensitive if it was <15%. Seven normal and three radiation sensitive primary human fibroblast cell lines were chosen for the genome microarray study. The patients from whom the sensitive fibroblast strains were established did not show any signs of inherited genetic diseases, but severe (grade ³3) radiation-induced late sequelae developed after radiotherapy (Ésik et al. Strahlenther Onkol, 179: 690-693, 2003; Póti et al. Int J Radiat Oncol Biol Phys, 58: 1022-1033, 2004). Cells were irradiated with 2 Gy gamma-radiations and RNA was isolated 2 h later. Radiation-induced transcriptional alterations and differences in basal gene expression profiles were investigated using Agilent's Whole Human Genome Oligo Microarrays.

Results: Limited number of genes showed statistically significant radiation-induced responses in normal (109 up-, 114 down-regulated) and sensitive (144 up-, 56 down-regulated) fibroblasts. Only 28 genes were up- and 2 were down-regulated in all cell lines: sixty-six percent of these consensus radiation-response genes were categorized to known gene ontology groups. The majority of the ontology group related genes (60%) belong to the DNA damage response (GADD45A, BTG2, PCNA, IER5), regulation of cell cycle and proliferation (CDKN1A, PPM1D, SERTAD1, PLK2, PLK3, CYR61), and programmed cell death pathways (BBC3, TP53INP1); most of them are regulated by, or regulates p53. When basal gene expression profiles of radiation sensitive strains were compared to normal fibroblasts 60 genes were up- and 150 genes were down-regulated in all sensitive cell lines. Thirty-eight and fifty percent of the up- and down-regulated genes could be annotated to gene ontology groups. The list of potentially important genes includes DDIT4 (DNA damage inducible protein) and TP53I3 (mediates p53 responses), which were expressed at lower level in sensitive fibroblasts.

Conclusions: Genes responding to radiation both in normal and sensitive fibroblasts might have an inevitable function in radiation response. Genes responding to radiation either in normal or sensitive cells, and genes whose basal expression profile was altered in sensitive fibroblasts might contribute to individual radiation sensitivity. These data may contribute to the development of biomarkers to identify radiation susceptible individuals.

Posters Geometric Uncertainties in Radiotherapy

782 poster

A METHOD FOR UTILISING CONE-BEAM CT PROJECTION IMAGES TO DETERMINE INTRA AND INTER FRACTION ORGAN MOTION

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Purpose/Objectif: To determine intra and inter fraction organ motion from the trajectory of seeds or markers on kV cone-beam CT projection images (rotation fluoroscopy) of the patient in the treatment position. Pancreatic data was used as a case study.

Materials/Methods: The position of a seed or edge of stent was determined manually on each projection image giving $P(u_i,v_i)$ where u and v are the imaging panel tangential and axial directions respectively. The resulting u and v curves were then fitted to a function describing the projection of a point, P(x,y,z), into the imaging panel at different gantry angles. The function fitted parameters provide the mean seed position on that fraction with respect to the isocentre. Inter fraction organ motion with respect to the first day was determined from the mean positions while the difference between the mean and actual seed position represent the intra fraction motion. This method was used to determine pancreas motion for 5 pancreatic cancer patients. These patients had either a gold seed marker placed into pancreas at attempted surgery or had stent.
Cone-beam CT scan were taken at the end of treatment using the Elekta Synergy™ (Elekta Systems Crawley,) on a total of 35 fractions.
Results: The seed or stent was not clear in all projection images. Simulation showed that this method is robust with respect to missing data. The pancreas interfraction motion (1 standard deviation) relative to the first fraction was 3.1mm (2.1-5.3) left-right (LR), 2.5mm (1.9-3.7) anterior-posterior (AP) and 5mm (2.7-7.2) superior-inferior (SI). For the intra fraction motion, the range averaged over all patients and all fractions is 3.7±1.2, 5.2±1.0 and 11.3±2.9mm in the LR, AP and SI directions respectively.
Conclusions: Cone-beam CT projection images provide more than a minute of rotational fluoroscopy. These images can be utilised to extract intra and inter fraction seeds/markers motion. Knowledge of target motion would allow valuable information for many applications in radiotherapy such as determining appropriate margins, individualising treatments and providing location probability distributions for IMRT optimisation.

783 poster

EVALUATION OF SET UP UNCERTAINITY IN HN IMRT TREATMENT USING AN ELECTRONIC PORTAL IMAGING DEVICE

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Purpose/Objectif: To evaluate set up reproducibility and accuracy in HN IMRT treatment and determine margins to add on CTV and OAR (spinal cord).
Materials/Methods: Ten consecutive patients were considered and immobilized with a system consisting of a standard carbon support (Sinmed - Posifix), fixed on the treatment couch, a headrest (5 type of headrest with different conformation), and a personalized mask (Sinmed - Posicast) fixed in 5 points. On line daily portal imaging verifications were acquired, obtaining a total of 515 anterior and lateral portal images (EPIs), an average of 25 images/patient. EPIs were compared with a reference image, a digital radiograph (DRR), reconstructed by the TPS (Elekta PrecisePlan version 2.03) from CT images acquired with a slice thickness 3mm. Set up was verified by only one medical doctor, considering both a laser based positioning and the coordinate of table treatment, in order to minimize inter-observer variability. The quantification of displacement was performed using an home made software, by comparison of bone landmarks delineated on the reference image and reported on the portal image.
Results: Systematic (ES) and random (ER) errors were quantified in all three direction: anterior-posterior (AP), left-right (LL) and craniocaudal from anterior and lateral projection (CCap, CCll). We obtained values ranging 0.6-0.8 mm for the ES (AP 0.7 mm, LL 0.6 mm, CCap 0.6 mm, CCll 0.8 mm) and from 0.9 to 1.1 mm (AP 1 mm, LL 0.9 mm, CCap 1.1 mm, CCll 1 mm) for the ER. PTV-margin and PRV margin for the spinal cord were calculated taking into account the set up error calculated, without consider additional margin for organ motion, negligible in this anatomical region.
Conclusions: Results obtained demonstrate that the procedure adopted for the immobilization and positioning of the patient is of sufficient accuracy and reproducibility and confirm our level of intervention of 3 mm in patient repositioning, suggesting a reduction in the number of controls during the treatment. A comparison with the results obtained from a previously study, performed on 3D-CRT head and neck, demonstrate an improvement of the accuracv in the patient's positioning, due to the technical staff training and to the method for set up verification. PTV and PRV margins calculated are respectively of 3 mm and 2 mm, considering a 3D expansion for the CTV and a 1D expansion for the spinal cord.

784 poster

IMRT IN PROSTATE CANCER. UNCERTAINTIES OF Z (AP) COORDINATE. WHEN IS CORRECTION INDICATED?

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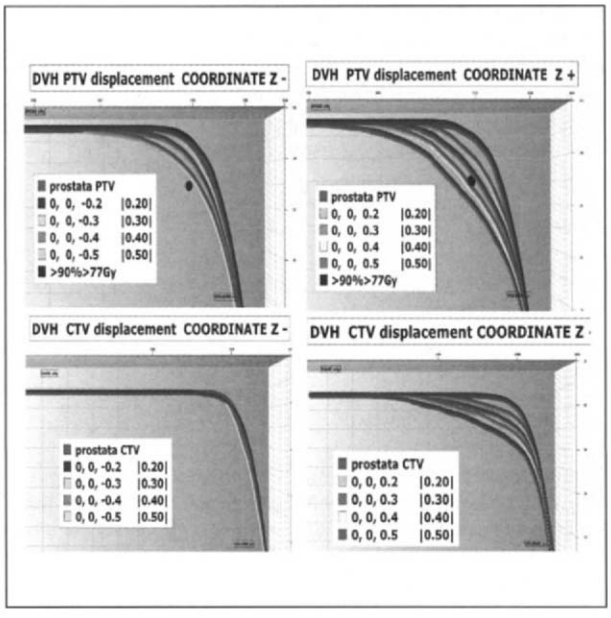
Purpose/Objecti: As radiotherapy requires more and more precision, the geometric uncertainty requires more consideration. There are few publications with data of when and which limits need correction. The purpose of this paper is to present some indications and formulate some questions.
Materials/Methods: From January 2004 to February 2006 22 treatments of prostate cancer with IMRT (sliding windows technique) were studied.
PTV was defined as CTV (prostate) plus a 1 cm margin except 0.6 cm in the posterior margin. The patients were treated with 5 fields isocentric technique (posterior and anterior and posterior oblique). For the optimization process in the Helios (Varian®) planner the parameters published by Memorial Sloan Kettering Cancer Center were used. Criteria from MSKCC were also used in the evaluation plan: maximum dose within PTV < 90Gy and ^{3} 90% of PTV must receive 77Gy. For the rectal wall in the high dose region no more than 30% the rectal wall should receive ^{3} 75.6 Gy. In the intermediate dose region for rectum and bladder no more than 53% should receive 47Gy or higher.
The treatment was delivered with 6MV X-rays to a dose of 81Gy in daily fractions of 1.8 Gy on a Clinac 2100C/D (Varian®) equipped with MLC120.
Daily orthogonal Rx (1980RX) were mandatory in order to determine the 3D movements for field set up related to bony anatomy in coordinates X (R-L), Y (S-I) and Z (A-P), (5940 observations). It wasn't possible to measure organ motion.
Results: In previous observations using simulations in 3D commercial software it was determined that the coordinate Z (AP) in vectorial movement presents more repercussions. Taking into account the published organ motion studies and the field set up movements, the coordinates X (R-L) and Y (S-I) are more stable. Having studied DVH for linear movements of 2,3,4 and 5 mm both in positive and negative magnitudes of the coordinate Z we found that: In PTV the increment in the minimum dose was 4.6%, 8.4%, 12.4% and 16.8% for movements to positive coordinates and 0.6%, 2.7%, 6.85 and 10.8% for movements to negative coordinates.
In the study of the DVH of the CTV (prostate) in the movements to positive coordinates the increase of minimum dose was 3.8%, 5.1%, 6.2% and 7.3%. In the movements to negative coordinates there was no increase in the minimum dose, to the contrary , the minimum dose decreased in 1.6%, 1.5%, 1.1% and 1% in relation to the DVH of the reference treatment(fig). In the PTV of OAR only the movement of -5mm had repercussions on rectal constraints.
Conclusions: The Z coordinate presents more repercussions in 3D movements. According to our results all of the positive movements should be corrected given the implications in the DVH. Why correct the movements -2mm and -3mm if in the PTV there is only a varia-

tion of 0.6% and 2.7% and this movement improves the DVH of the CTV? Further, more extensive studies of movements are needed taking into account both the three coordinates and organ motion.



785 poster

SET-UP IMPROVEMENT IN RECTAL CANCER RADIOTHERAPY USING A 3D OFF-LINE EPID-BASED CORRECTION PROTOCOL

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Purpose/Objectif: In this study an off-line setup correction protocol was applied to minimize systematic errors during pelvic irradiation of patients with rectal cancer. Setup Margin (SM_i) in each direction, where i=medial-lateral (ml), cranial-caudal (cc) and anterior-posterior (ap), was determined, including both systematic and random errors, to establish safety margins between CTV and PTV in our institution for this group.

Materials/Methods: Fifteen rectal patients were arbitrarily chosen. All of them underwent a CT study in prone position. A dosimetric plan including opposing lateral fields and a posterior field was designed. Patients were positioned in the treatment unit (Varian Clinac 2100 C/D) by alignment of lasers with skin tattoos. No immobilization devices were used. A Shrinking Action Level (SAL) protocol was applied using semi-automated matching between DRR and EPID (Varian Portal Vision)images of left lateral and posterior traetment fields. The parameters of SAL were N_{max}=3 and α=9mm. Internal margin was supposed to be negligible, so SM was considered to be the only safety margin between CTV and PTV. The expression proposed by Stroom et al. was then used: $SM_i=2\Sigma_i+0,7\sigma_i$ where Σ_i and σ_i are the standard deviations in each direction of systematic and random error respectively for this group. Mean systematic errors (μ_i) were also calculated. Finally all the measurements were used to stimulate the cases where a single first-day correction and no correction were performed.

Results: Table 1. Mean set-up errors, standard deviations of the set-up errors and set-up margins.

		μ(mm)	Σ(mm)	SM(mm)
Direction	σ (mm)	SAL		
ml	3,1	-0,8	1,6	5,4
cc	1,7	0,0	1,9	5,0
ap	5,0	-0,1	1,5	6,6
		First-day correction		
ml	4,1	-1,5	2,8	7,8
cc	1,7	0,8	2,0	5,2
ap	5,0	1,2	2,1	7,7
		No correction		
ml	3,1	-0,2	3,9	9,9
cc	1,7	1,7	2,4	6,0
ap	5,0	7,6	7,2	17,8

Results are shown in Table 1. No correction was found between any factor and the large mean systematic error and its standard deviation in ap direction when no correction was applied during treatment. Even random errors are significantly larger than those found in the literature in this direction. Results for SAL and for initial correction agree with published ones.

Conclusions: SAL off-line correction protocol improves patient set-up accuracy so that margins between CTV and PTV range from 5 to 7 mm in all directions. Initial correction is sufficient to eliminate large systematic errors, but leads to margins up to 8 mm. Positioning in ap direction should be improved anyway. We have decided to implement the use of belly-board immobilization devices. Further study will be done to compare results with this new technique.

786 poster

SET-UP VERIFICATION FOR LUNG CANCER PATIENTS USING BONE STRUCTURES IN COMPARISON TO TRACHEA AS ANATOMICAL LANDMARKS FOR IMAGES MATCHINGA.

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Purpose/Objectif: The interpretation of information on set-up accuracy obtained by Electronic Portal Imaging Devices (EPID) may pose many problems and lead to inaccurate estimations of errors. The purpose of this study was to assess whether use of bone structures in comparison to trachea as anatomical landmarks in matching of images from simulator and EPID is more accurate for verification of lung cancer patients.

Materials/Methods: The 109 anterior isocentric EPID images from 23 lung cancer patients were compared with the respective anterior isocentric simulator reference images. All patients were treated with the same technique and the same set-up procedure. Manual matching of the images was performed off-line using dedicated software. These images represented treatment field position with respect to the patient body. If the realization of treatment was correct, both images - the reference image and the portal image had to differ on less than 5 mm. The identity meant that the position of the borders of the fields with respect to the internal reference organs was the same on both images. For this study the position of the field borders was determined using two different anatomical landmarks for im-

ages matching. First, the matching was performed using the bone structures - vertebrae, then the matching was done with respiratory tract structures, like trachea and carina. Displacements in the superior-inferior (S-I) and right-left (R-L) directions were measured in millimeters for both types of matching separately. Subsequently, standard deviation (SD) of the random (s) and systematic (S) set-up errors were calculated for both types of matching. Differences of measurements using bones and trachea for particular patients were assessed.

Results: About 61% (75%: R-L, 47%: S-I) of displacements were ≤3mm and 81% (91%: R-L, 72%: S-I) ≤5mm for the vertebrae as anatomical landmark, and respectively 52% (59%: R-L, 45%: S-I) and 78% (90%: R-L, 67%: S-I) for the trachea. The S error was 2.7 mm in the R-L and 4.3 mm in the S-I directions for the vertebrae compared with respective 3.2 mm and 5.2 mm for the trachea as a landmark. The corresponding SDs of the s errors were 4.1, 3.9 and 2.5, 3.1 mm. No significant difference in set-up accuracy for both examined procedures was found for a whole group. On the other hand a direct comparison of measurements using bones and trachea, showed large differences with SD of 5.0 mm (R-L) and 5.1 mm (S -I). The largest relative positions were 11 mm (R-L) and 23 mm (S-I).

Conclusions: Despite no difference found in the magnitude of set-up errors in examined directions for a whole group when matching different anatomical landmarks, the differences in measurement of displacement for trachea and vertebrae may lead to undetected errors in particular patients.

787 poster

THE IMPORTANCE OF IMAGE FUSION OF COMPUTERIZED TOMOGRAPHY AND 18FDG-PET (POSITRON EMISSION TOMOGRAPHY) IN DEFINING TARGET AND CRITICAL ORGANS IN LUNG CANCER PATIENTS

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Purpose/Objectif: Positron Emission Tomography (PET) has been used for the staging, the detection of recurrences and the evaluation of the response to the therapy. As a newly developed modality, PET-CT (Computerized Tomography) is a combination of PET and CT devices and is capable of taking both metabolic (functional) and anatomical images in the same session. Images can be fused and tumor margins can be drawn much more precisely. In cases where normal tissues pathological changes such as, atalectasis, pleural effusion and pneumonitis, tumor contouring is difficult. Therefore, variations in contouring of tumor and nearby critical organs can be seen frequently. The aim of our study is to compare treatment plans performed using PET-CT and CT alone in terms of treatment volumes, maximal and mean doses within both lungs.

Materials/Method: Twenty-five patients, 5 with small cell lung cancer and 20 non-small cell lung cancer, were included in this study and evaluated. Siemens Biograph PET-CT machine was used in our study. Vacuum beds were prepared and patients were positioned as hands over the head before image taking. 18FDG (18 fluorodeoxyglucose) was administered intravenously an hour before the patient was taken into the PET-CT machine. Three small markers were placed onto the points where the lasers crossed each other on the patient skin using A2J Laser System to use as reference points on CT slices. Images of the scanned patient were sent to FocalPro computers in DICOM format. CT and PET images coming separately from the PET-CT machine were then fused in the FocalPro workstation. Gross Tumor Volume (GTV), Clinical Target Volume (CTV) were defined separately, using CT images alone (GTVt - CTVt) and using PET-CT images combined (GTVp - CTVp) in accordance with ICRU Report 62. Planning Tumor Volumes were also defined with 1 cm margin to the both CTVs as PTVt and PTVp.

Results: In 3-dimensional conformal radiation treatment plans in lung cancer patients, GTV, CTV and PTV were 1.3, 1.05 and 1.04 times larger in plans using images from the CT alone when compared to plans using images from the PET-CT. Mean dose to left lung was reduced 20% in plans performed using PET-CT when compared to plans performed using CT images alone while reduction rate was 5% for the right lung. Maximum doses were 2% and 2% lower when PET-CT images used, in left and right lungs, respectively. Reduction rates in volumes receiving >20 Gy were 20% and 2% for left and right lungs, respectively.

Conclusions: Normal tissues and organs can be much more precisely spared from the negative effects of the radiation therapy in plans using PET-CT images when compared to plans using CT images alone.

Posters Geriatric Oncology

788 poster

CURATIVE RADIATION THERAPY FOR ELDERLY HEAD AND NECK CANCER PATIENTS: GERIATRIC ASSESSMENT AND OUTCOME

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Purpose/Objectif: To analyze the geriatric assessment, the cancer characteristics, the treatment type, the patient's treatment compliance and outcome of elderly (≥70 years) patients with head and neck (H&N) cancer referred to our Radiotherapy (RT) Department.

Materials/Methods: From July 2002 to December 2005, 78 consecutive elderly patients with H&N cancer received RT. In the present analysis 53 patients with epithelial carcinomas (86.6% squamous cell carcinoma, SCC) of the laryngo-hypopharyngeal area (19 cases), oral cavity (15), oropharynx (11), nasopharynx (5) paranasal sinuses (3), and 5 patients with parotid gland carcinomas, submitted to curative RT were considered. Mean, median and maximum age were 75, 77 and 94 years. Stage distribution for SCC patients was I in 21%, II in 19%, III in 30% IVA in 22%, IVB in 8%; for parotid carcinoma was II in 40%, IVA in 60% of patients. Comprehensive geriatric assessment (CGA) was performed before RT according to: performance status (PS Karnofsky score), activities of daily living (ADL) independence and instrumental acitivities of daily living (IADL) independence, comorbidities, social aspects, emotional and cognitive status. Fourty-one patients received definitive RT (69%) or adjuvant RT (31%) for locoregional disease. Seventeen patients received radical RT (35%) or adjuvant RT (65%) for local (53%), regional (29%) or locoregional relapse (18%). Median total dose was 70 Gy, 66 Gy, 60 Gy, 66 Gy for definitive, postoperative high risk, postoperative low risk and salvage RT, respectively. In 8 patients platinum-based chemotherapy was given concomitantly to RT. Acute toxicity was recorded in all the patients. The median follow- up was 15 months (range, 2-39 months).

Results: PS range was 80-100; 60-70; ≤ 50 in 65%; 32% and 3% of patients, respectively. ADL independence was observed in 80% of patients, while 60% showed IADL independence. More than 3 co-morbities were detected in 41% of patients. Seventy-one percent of patients lived with their family. In 86% of cases no cognitive disorders were reported. No depression was observed in 55% of patients. Major severe acute effects included: dysphagia (11%); mucositis (10%); xerostomia (19%) and dermatitis (12%). Three patients stopped RT due to toxicity. The 3-years overall survival, disease-free survival and locoregional survival rates were 76,7%, 48,7% and 48,7% respectively.

Conclusions: radiation therapy in elderly patients with HN cancer is a suitable curative therapeutic approach. CGA may be hepful to individualize the treatment strategy according to the single patient's features.

789 poster

DOES AGE INFLUENCE THE RATE AND SEVERITY OF RADIOTHERAPY SIDE EFFECTS IN PATIENTS WITH PROSTATE CANCER ?

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Purpose/Objectif: To evaluate retrospectively if conventional radiation therapy for prostate cancer was well tolerated in patients aged 70 years or older, and if the rate and severity of acute and late side effects were different, compared to younger patients.

Materials/Methods: Between January 2002 and August 2005, 51 patients with prostate cancer were referred to our Department. Three patients were excluded from the study because they ceased treatment for personal reasons. The medical notes of twenty-four patients aged 70 years or older were compared to the notes of twenty-four patients aged less than 70 years. Conventional radiation therapy was carried out through the whole course of radiation therapy. All patients were treated with 6 or 18 MV photons from a linear accelerator via 4 individually shaped fields (4-field box technique). Dose was prescribed respecting the ICRU 50 guidelines. Dose per fraction was 1.8 or 2 Gy. Median dose to prostate was almost similar in both groups. All patients completed their treatment. Acute toxicity was evaluated according to the CTC criteria. Evaluation of late side effects was investigated with RTOG/EORTC scale.

Conclusions: This retrospective study demonstrates that conventional radiotherapy for prostate cancer with doses up to 70 Gy is well tolerated by elderly patients. Acute and late toxicity after conventional radiation therapy was proved to be low and there was no significant difference for elderly patients compared to younger patients. The management of acute and late complications was in all cases successful with pharmaceutical agents. Our study indicates that curative radiation therapy should be offered to elderly patients affected of prostate cancer, considering concomitant diseases and life expectancy. High-dose conformal radiotherapy and IMRT will offer the possibility to reach higher doses in the target volume with optimal tissue sparing, making this therapy well tolerated in patients aged 70 years or older.

790 poster

NEOADJUVANT CHEMORADIOTHERAPY IN ELDERLY PATIENTS WITH LOCALLY ADVANCED RECTAL CANCER. TOXICITY AND RESULTS. ISTITUTO ONCOLOGICO VENETO EXPERIENCE.

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Purpose/Objectif: To evaluate the toxicity and feasibility of neoadjuvant high dose pelvic radiotherapy (RT) in combination with chemotherapy in elderly patients with locally advanced rectal cancer.

Materials/Methods: From June 2000 to June 2005, 36 patients older than 70 years out of a total of 300 consecutive cases with histologically proven locally advanced rectal adenocarcinoma (≤ 12 cm from the anal verge) classified as either T3 or T4, N0 or N1-2 M0 disease, were examined. Comorbidities were evaluated according to Cumulative Illness Rating Scale-Geriatric (CIRS-G) and patients were deemed "fit" if they were otherwise healthy or had one or more comorbidities of only grade 1; "vulnerable" if had one or more comorbidities of grade 2.

Results: Median age was 74 years (range, 70-82). 14 patients (5 healthy, 13.8%, and 9 with slight comorbidities, 25%) were fit and 22 (61.2%) were vulnerable. All the patients received the full course of RT, with a total dose of 50.4 Gy. The mean number of chemotherapy weeks was 5.34 (range, 2-6). 4 out 14 (28.6%) fit patients and 9 out 22 (40.9%) vulnerable patients had to interrupt chemotherapy prematurely because of toxicity (p=0.26). Vulnerable patients did not experience superior toxicity compared to fit patients (8/22 vulnerable and 6/14 fit patients developed toxicities of grade ^{3} 2, p=0.69). With the exception of 2 fit and 2 vulnerable patients who were lost to follow up before surgery, 32 patients (88.9%) were operated. Thirty cases (12/14 fit patients, 85.7%, and 18/22 vulnerable patients, 81.8%) were radically resected without relevant postoperative complications. 13/20 vulnerable and 10/12 fit patients had a pathological downstaging of disease (p=0.24).

Conclusion: Elderly patients with locally advanced rectal cancer can be undergone to a neoadjuvant chemoradiotherapy treatment without important side effects. Surgery is radical in 81.8% of cases. Total toxicity and results are positive.

791 poster

RADIATION THERAPY FOR THE OLDEST-OLD PATIENTS IN JAPAN

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Purpose/Objectif: In Japan, the number of elderly patients with cancer is rapidly increasing, especially the oldest-old (85 years old or older) patients. Radiation therapy is considered to be less toxic than either surgery or chemotherapy. Generally elderly patients need specialized care because they are elderly, often frail and feeble. Therefore, even though it is not strictly a medical problem, undergoing regular irradiation is compromised. To reveal the characteristics of irradiation for elderly patients compared with the all other patients undergoing radiation.

Materials/Methods: We examined 122 cases of 116 the oldest-old patients who underwent radiation therapy for cancer in our department from August 1984 to May 2005. There were 228 patients randomly chosen as a control group from a total of 6559 cancer patients .

Results: We treated 113 cases in the elderly group (6 cases were treated twice). We aimed for a curative therapy in 60 cases, relative curative therapy in 28 cases and palliative therapy in 25 cases. In the control group, our goal was a curative therapy in 104 cases, relative curative therapy in 61 cases and palliative therapy in 52 cases. Performance status (PS) was measured by the WHO criteria : , there were 2, 15, 42, 35, and 6, of PS0-4, respectively, in the elderly group. And in control, there were 28, 47, 73, 41, and 19 of PS0-4, respectively. in the elderly group. And in control, there were 28, 47, 73, 41, and 19 of PS0-4, respectively. There were 17 outpatient cases and 87 cases were of hospitalized patients in the elderly group, and 49 (23%) were outpatients and 160 (73%) patients were hospitalized in the control group. We completed treatment in 90 cases and discontinued treatment in 23 cases during the study period in the elderly group, and in the control group, there were 177 and 40 cases, respectively.

Conclusions: To provide radiation therapy for elderly patients, we have to consider their PS and their transportation support to and from the hospital will have to be improved. Other than age and PS, there is no significant difference in the treatment objective, i.e., curative treatment can be achieved with radiation for patients of any age. Radiation is a noninvasive treatment in the sense that it is a curative or palliative modality, and it often is the only way to provide a curative treatment for the lesion especially in cases for elderly patients. The number of patients who choose radiation will continue to increase in the near future.

792 poster

THE INCREASING PLACE OF CURATIVE-CONSERVATIVE TREATMENT OF RECTAL CACENR IN ELDERLY PATIENTS

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Purpose/Objectif: With ageing of the population the management of rectal cancer in the elderly patients is increasing regularly. In this group of patients conservative treatment is of prime importance, not only to increase sphincter preservation but also to avoid as much as possible open surgery associated with a non negligible risk of morbidity or postoperative death.

Materials/Methods: Between 2001 and 2005, 29 patients presenting primary adenocarcinoma without distant metastasis and aged 80 years or more, have been treated in CAL . A conservative radiotherapy treatment with curative intent was given in 10 patients (5 men, 5 women). Staging performed with endorectal ultrasonography showed T2 = 7pts, T3 = 3. All patients were treated with contact x ray (mean dose = 100 Gy/4 fractions). External beam radiotherapy with 45 Gy/5 weeks was performed in 7 patients. Concurrent chemotherapy (Capecitabine) in 2 patients. One patient underwent local excision.

Results: Median follow-up time was 2 years (1-5 years). Primary local control was achieved in eight patients out of ten. One patient presented a local recurrence. Good anorectal function was preserved in all patients even in 3 patients with locally evolutive disease. No diverting stoma was necessary. All treatments were ambulatory without severe toxicity. Six patients are alive without symptoms (1-5 years). Three died from intecurrent disease, none from rectal cancer.

Conclusions: Elderly patients with rectal cancer deserve a specific approach starting with a comprehensive geriatric evaluation. Overall survival is not a relevant end point and time without symptom or stoma should be more often utilized. The place of open surgery should progressively diminish as radiotherapy if possible with contact x ray (50 kV) can provide long term local control with good anorectal function and moderate toxicity. These results are in agreement with the "Lyon-Papillon" experience (ref 1, 2).

References:

1- Gerard JP, Romestaing P, Chapet O, et al. radiotherapy alone in the curative treatment of rectal carcinoma. The Lancet Oncol 2003; 4:158-66

2- Gerard J.P, Chapet O, Hartweig J, et al. Improved Sphincter Preservation in Lox Rectal Cancer with High-Dose Preoperative Radiotherapy: The Lyon R96-02 Randomized Trial. J Clin Oncol 2004;22:2404-409

Posters Gynaecological Cancer

793 poster

40% PATHOLOGICAL COMPLETE RESPONSE AFTER PREOPERATIVE RADIOCHEMOTHERAPY OF LOCALLY ADVANCED CERVICAL CANCER

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Purpose/Objectif: evaluation of the efficiency and toxicity of preoperative radiochemotherapy in advanced cervical carcinoma

Materials/Methods: retrospective evaluation 2001-2005, n=20, histologically proven squamous cell carcinoma of the cervix, median age 52 years (36-74), tumour stages FIGO IIa (n=2, 10%), IIb (n=8, 40%), IIIb (n=2, 10%), IVa (n=2, 10%), IVb (n=6, 30%, inguinal and paraaortal lymph node metastases). Preoperative radiation of the uterus and pelvic lymph nodes including inguinal and paraaortal lymph nodes in case of macroscopical lymph node metastases at these sites with single doses of 1,8 Gy, overall dose 50,4 Gy, simultaneously weekly chemotherapy with 6 cycles cisplatin (40mg/m²) or carboplatin (auc 3) in case of creatinin clearance < 90ml/min. Chemotherapy was aborted in case of pronounced (ctc III°) hematotoxicity or nephrotoxicity. After completion of radiochemotherapy operative treatment (Wertheim) was performed within 4 to 6 weeks. Toxicity was evaluated following common toxicity criteria.

Results: 19 patients (95%) were treated within time schedule until completion of the planned overall dose. 8 patients (40%) received all six chemotherapy cycles. 3 patients (15%) received 5 cycles, 3 patients (15%) 4 cycles, 2 patients (10%) 3 cycles, 2 patients (10%) received 2 chemotherapy cycles. Reasons for abortion of chemotherapy were hematotoxicity in 7 patients (35%), nephrotoxicity in 3 patients (15%). 2 patients (10%) remained without chemotherapeutic treatment because of initial renal insufficiency. 10 patients (50%) were treated with cisplatin, 1 patient (5%) was initially given cisplatin and changed afterwards to carboplatin, 7 patients (35%) were given carboplatin initially. 1 patient died of hepatic failure before completion of radiation, 1 patient died of heart failure after completion of radiation. 2 patients were not surgically treated because of local inoperability or progress of mediastinal lymph nodes respectively. In total 16 patients were surgically treated, all of these could be treated by r0 resection. Downstaging was reached in all resected patients, in 8 patients (40=%, initially stage IIa n=1, IIb n=3, IIIb n=2, IVa n=1, IVb n=1) a pathologically complete remission (ypT0 ypN0) was reached. Perioperative morbidity was not elevated.

Conclusions: preoperative radiochemotherapy is a well tolerated and highly efficient therapeutic option in locally advanced cervical carcinoma. Even in advanced tumour stages a high rate of complete remissions was reached.

794 poster

A PROSPECTIVE CASE CONTROL STUDY OF TOXICITY IN HIV POSITIVE AND NEGATIVE CERVICAL CANCER PATIENTS

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Purpose/Objectif: Cervical cancer is the most common cancer in women in the developing world. It occurs in association with HIV infection and has been designated as an AIDS defining illness since 1993. There is little published data on the toxicity of radiotherapy treatment in HIV positive women with cervical cancer. Available data suggests that toxicity is increased,[i],[ii] as has been demonstrated with other cancer sites. We prospectively compared toxicity scores in HIV positive and negative patients receiving radical radiotherapy.

[i] HIV infection and invasive cervical cancers, treatment with radiotherapy; toxicity and outcome, Shrivistastava SK, Engineer R, Rajadhyasksha S, Dinshaw KA, Rad & Onc 74(2005)31-35

[ii] HIV impact on acute morbidity and pelvic tumour control following radiotherapy for cervical cancer. Gichangi P, Bwayo J, Benson E et al, Gyne Oncol 100(2006) 405-411

Materials/Methods: All patients with biopsy proven cervical cancer were offered participation in the study. Standard workup included: history and examination, EUA for biopsy and staging, full blood count, renal and liver function tests, HIV test and ultrasound of the abdomen and pelvis. Stage was according to the FIGO system. The following exclusion criteria were applied: Karnovsky performance status <60, FIGO stage IVB, previous abdominal / pelvic radiotherapy.

Treatment in all cases was as follows; external beam radiotherapy consisted of 50Gy in 25 fractions, simulated with anterior and posterior fields, delivered with cobalt machine, and a single brachytherapy insertion of 25Gy delivered using a caesium source.

Patients were reviewed on a weekly basis. Clinical examination, Karnovsky performance score, RTOG toxicity score, and full blood count were recorded at each clinic visit in a standardised format.

Results: The results given are at time of writing; the study is ongoing. 46 HIV negative and 20 HIV positive patients have completed radiotherapy. One patient in the HIV negative group developed acute renal failure and died in the second week of treatment. All other patients completed the prescribed treatment course. 10% of HIV positive patients had KPS <70 recorded during external beam radiotherapy, none of the HIV negative patients had KPS <70 recorded during radiotherapy. Grade 3/4 toxicity is illustrated in table 1.

10% of HIV positive patients required a break in radiotherapy for treatment of toxicity. The planned caesium treatment date was deferred in 10% of the HIV positive group due to slow resolution of skin toxicity. This did not occur in the HIV negative group.

Grade 3 / 4 toxicity		
Organ	HIV positive - no. (%)	HIV negative - no. (%)
Skin	7 (35)	1 (2)
Gastrointestinal	1 (5)	-
Genitourinary	2 (10)	-
White cell count	3 (15)	1 (2)
Platelets	1 (5)	1 (2)
Haemoglobin	3 (15)	8 (17)

Conclusions: HIV positivity is associated with increased acute toxicity during external beam radiotherapy for the treatment of cervical cancer. This resulted in treatment breaks and delay in the administration of brachytherapy, which is known to be associated with adverse outcome in terms of tumour control and survival in the HIV negative population. This confers a further adverse prognostic factor in a group of patients known to have an increased rate of tumour recurrence after radiotherapy.

795 poster

ANAEMIA MANAGEMENT DURING RADICAL PELVIC RADIOTHERAPY OR CHEMO-RADIOTHERAPY FOR CERVIX CANCER: AN AUDIT OF 12% OF UK CANCER POPULATION BY THE SOUTH WEST CANCER INTELLIGENCE SERVICE (SWCIS)

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Purpose/Objectif: To assess compliance with anaemia correction guidelines during radical radiotherapy or chemo-radiotherapy for cervix cancer.

Materials/Methods: Anaemia correction during radical radiotherapy or chemo-radiotherapy for cervix cancer appears to improve control rates in 2 case-control series, 1 randomised control trial (RCT) of transfusion support and 2 RCTs of erythropoietin support. It is advocated in national protocols (US) and regional protocols (UK). The benefits of correcting anaemia are large and appear to exceed 10% improvement in control at 5 years. The SWCIS Gynaecology Audit Database covers 12% of the gynaecological cancer population. The SWCIS protocol mandates weekly blood test and treatment to maintain a target of Hb ≥12g/dl during radical radiotherapy or chemo-radiotherapy for cervix cancer. We audited all cases of non-small cell cervix cancer treated radically during 2002 in our region. Blood counts were retrieved for the weeks of external beam radiotherapy from paper records, haematology records and computer databases in each hospital. The sample size was calculated by the Gehan Method to be able to exclude non-compliance of 10% or worse (to $p \leq 0.05$).

Results: 81 patients were identified. Mean age was 60 years, 47% were FIGO stage II, and 83% have squamous cell cancer. Despite central guidelines, compliance with protocol was poor. In 8/81 cases, no record of blood count could be found. In only 13/81 cases blood tests were available for each week of radiotherapy treatment. Where blood count was recorded on at least one occasion (73/81), the treating teams failed to keep Hb >12 in 51/73 cases (69%) and failed to keep Hb>11 in 27/73 cases (36%). Anaemia correction was by oral iron and transfusion. Erythropoietin was not used.

Conclusions: Despite regional and international guidelines, the compliance with anaemia correction during radical cervical cancer treatment is poor; this suggests that education about this issue is still needed. The lack of regular blood count tests in many patients means that significant anaemia may develop during radiotherapy before it is detected and corrected. Uncorrected anaemia may contribute to poor outcomes in cervix cancer, and is a treatment variable that other audit groups should consider when assessing their treatment results. SWCIS plans to repeat the audit to assess change.

796 poster

COMBINED MODALITY TREATMENT OF CERVICAL CANCER IN A LOW RESOURCE SETTING – INDICATIONS FOR TREATMENT

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Purpose/Objectif: Combined chemo/radiotherapy is well established as the standard treatment for cervical cancer in the developed world. However, the majority of women worldwide with cancer cervix now live in the developing world. In Uganda, cancer of the uterine cervix is the most commonly diagnosed cancer in women with an estimated incidence of 44.1 per 100,000.[1]

Multiple economic, social and geographic factors result in late presentation with advanced disease, which may be associated with HIV infection. These characteristics may preclude the administration of cisplatin based chemotherapy in many cases. We prospectively assessed all cervical cancer patients for suitability for combined modality treatment.

1] Trends in cancer incidence in Kyandondo County, 1960-1997. Wabinga HR, Parkin DM, Wabire-Mangen F, Nambooze S. British J Can (2000) 82(9) 1585-1592.

Materials/Method: All patients referred with biopsy proven cervical cancer over a ten month period were eligible for this study. Standard work up included the following: history and examination, Karnovsky performance score, EUA for staging and biopsy, complete blood count, renal and liver functions tests, HIV test and ultrasound of the abdomen and pelvis. Stage was assigned according to the FIGO staging system. Patients with stage IB, II and III disease were considered potential candidates for combined modality treatment. The following exclusion criteria were applied when considering eligibility for cisplatin based chemotherapy: stage IA, stage IV, HIV positive, Karnovsky performance score <60, age >70 years, hydronephrosis, postoperative recurrence, haemoglobin <8g/dL, total white cell count <2,000/mL, platelets <100,000/mL, creatinine >97mmol/L.

Results: 314 women were referred with cervical cancer during the study period, representing 34.8% of the total caseload in the department. After workup, 40 patients (12.8%) were eligible for combined modality treatment and 190 (60.5%) were not eligible based on the exclusion criteria. Eligibility could not be established in 84 cases (26.7%) as the workup was incomplete. The most frequently encountered exclusion criteria were hydronephrosis and anaemia, as illustrated in the table. 65 (36.3%) of those not suitable for combined modality treatment failed on multiple exclusion criteria.

Exclusion criteria	No. of patients (%)
Stage IA	4 (1.3)
Stage IV	44 (14)
Age >70 yrs	9 (2.9)
Hydronephrosis	91 (29)
HIV positive	36 (11.5)
Postoperative recurrence	40 (12.7)
Haemoglobin <8gm/dL	55 (17.5)
White cell count <2,000/mL	-
Platelets <100,000/mL	-
Creatinine >97mmol/L	15 (4.8)
Patients with: 2 exclusion criteria	51 (16.2)
3 exclusion criteria	14 (4.5)
>3 exclusion criteria	4 (1.3)

Conclusions: Patient characteristics at the time of presentation in our setting preclude administration of combined modality treatment in the majority of cases. While blood transfusion may correct anaemia in a small number, 36.3% of those excluded had multiple risk factors which cannot be reversed. Hydronephrosis was the commonest exclusion criteria. This can be treated by insertion of ureteral stents - however this is not routinely available in Uganda . The commitment of significant resources to combined modality treatment in this setting is questionable. We suggest that measures to encourage early diagnosis and institution of cervical cancer screening represent better interventions.

797 poster

COMPARISON OF ORTHOGONAL RADIOGRAPHY AND 3D CT-BASED TREATMENT PLANNING IN HDR BRACHYTHERAPY OF CERVIX CANCER

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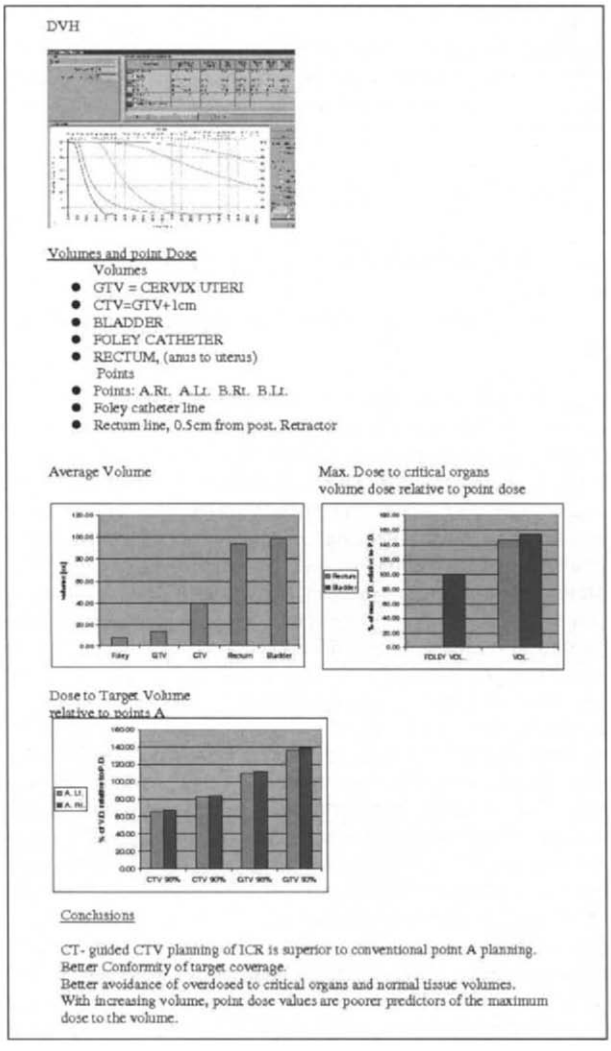
Purpose/Objectif: Intracavitary brachytherapy (ICBT) is a well established treatment modality in the management of cervical cancer. A modern approach in treatment planning for cervical carcinoma is based on a series of computed tomography (CT) sections and 3D dose computation. When these techniques were not yet available, dose evaluation was based on orthogonal radiographs. Radiographic planning is still the standard in many clinics. With this technique geographical misses of tumor or potential tumor spread, as well as overdoses of critical organs, may happen due to insufficient knowledge of the individual anatomical situation. CT-based planning provides information on target and organ volumes and allows calculation of dose-volume histograms (DVHs). The radiography based planning provides only dimensions and doses at selected points. The aim of the current study is to correlate the information obtained with the two approaches for high dose-rate (HDR) brachytherapy of cervix carcinoma.

Materials/Methods: 10 patients with primary cervical carcinoma in Stages I to III receiving overall 25 HDR applications with Ir-192 were investigated. The, BrachyVision (VARIAN) planning system was used. Different aspects of available data, results and inaccuracies regarding quality assurance were looked at.

Results: For CT-based planning, the volume, location and DVHs were calculated for the CTV, rectum and bladder, and compared with point doses as found on the orthogonal radiographs: doses to points A (prescription), B, rectum and bladder (Foley catheter). These two sets of information were compared and the following mean values derived. For a dose prescription of 8 Gy at point A, on average 90% of the clinical target volume (CTV) receives at least 10.5 Gy. The maximum dose at the rectum reference point is 4.1 Gy, the 3D data set show that the maximum dose received at the rectum is 6.1 Gy. The maximum bladder dose is 6.5 Gy, whereas the 3D data set shows a maximum dose of 10.1 Gy. The maximum dose to the rectum is 1.5 times higher than the dose at the 2D reference point, and for the bladder 1.55 times higher. Uncertainties caused by the reconstruction of the applicator and merging of isodoses were evaluated.

Conclusions: Ct-based treatment planning provides detailed anatomical data for both tumor and normal tissue volumes, and allows for true 3D plan optimization. The Dosimetric data provided is significantly different from that obtained based on radiographic planning, and indicates that some plans deliver much higher doses to the rectum and bladder than calculated, when planned only by radiographs. These results could explain complications that occur even when rectal and bladder point doses are within tolerance. Accurate definition and delineation of CTV and critical organs has a direct impact on the BT procedure, especially when it is possible to perform a volumetric optimization.



798 poster

CONCURRENT CHEMORADIOTHERAPY IN PATIENTS WITH CARCINOMA OF UTERINE CERVIX: OUR INSTITUTIONAL EXPERIENCE

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Purpose/Objectif: Carcinoma of uterine cervix is the commonest

malignancy in Indian women and majority of them present in advanced stages. Concurrent chemoradiothetrapy, which is emerging as the new standard of care, is increasingly being used in such patients. Our aim is to study the results of concurrent chemoradiotherapy in patients with carcinoma of uterine cervix at our institute.
Materials/Methods: All patients with cervical carcinoma, FIGO stage IB2-IVA were treated with concurrent chemoradiotherapy. Patients with age more than 70 years, deranged kidney function tests and bilateral hyderonephrosis were excluded. The treatment consisted of external beam radiation therapy (EBRT) to whole pelvis with a dose of 50 Gy in 27 fractions over 5.5 weeks (last 10Gy with midline shield) followed by intracavitary radiotherapy (30 Gy to Point A by LDR or 3 fractions of weekly 7 Gy by HDR). Cisplatin 50 mg was used every week concurrently with EBRT.
Results: A total of 119 patients were treated over a period of 2 years. Age ranged from 25 to 67 years (median 52). Majority (66 patients) had stage IIIB disease. A total of 458 cycles of chemotherapy was used with median of 5 cycles per patient. Acute hematological and GI toxicity was observed in 15 and 11 patients respectively. Pelvic disease control was observed in 54 patients and overall survival at 18 months was 45%.
Conclusions: As per our institutional experience, concurrent chemoradiotherapy is a tolerable treatment in the patients with carcinoma of uterine cervix and results in effective disease control and survival.

799 poster

CONTEMPORARY MANAGEMENT OF CERVIX CANCER

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Purpose/Objectif: Since 1999,the addition of chemotherapy concurrent with radiotherapy (chemoradiation) has been considered standard in the treatment of cervix cancer patient not suitable for surgery. We therefore decided to review the treatment approach and outcomes of cervix cancer patients treated with curative intent at the Ottawa Hospital Regional Cancer Centre since 1999 using radiotherapy +/-chemotherapy .
Materials/Methods: A retrospective chart review of all cervix cancer patients treated with primary radiotherapy +/- chemotherapy from 1999 to 2004 was performed. Survival curves and local control were analyzed using the Kaplan -Meier method and compared via the Log Rank test and Cox regression analysis .
Results: A total of 87 patients were identified and treated during this time period, 78% receiving chemoradiation and 22% receiving radiotherapy alone . The median age was 51.1 years and median follow -up was 20.5 months. The treatment generally consisted of pelvic external beam radiotherapy (4500cGY /25 fractions/ 5 weeks) concurrent with weekly intravenous Cis-platinum chemotherapy (40 mg/m^2) followed by low dose rate intracavitory brachytherapy (3500-4000cGY prescribed to point A).
The overall survival(OS), progression -free survival (PFS) and locoregional control (LC) rates for the entire group at 3 years were 64.9%, 50%,79.3%. The OS,PFS,and LC at 3 years were 66.7%, 48.6%, and 72.2% for those receiving radiotherapy alone and 62.3% ,51.6%,and 81.2%for those receiving chemoradiation. These differences in outcome were not statistically significant . However , patients treated with radiotherapy alone were older,had smaller tumours and were less likely to have lymph node involvement (P<0.05).
Conclusions: Management of cervix cancer with either chemoradiation or radiotherapy alone in appropriately selected patients leads to high rate of local control and surival.

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CORRELATION BETWEEN CYCLOOXYGENASE-2 EXPRESSION AND TUMOR VOLUME RESPONSE IN PATIENTS TREATED WITH RADIOTHERAPY FOR UTERINE CERVICAL CANCER

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Purpose/Objectif: Emerging evidences suggest that both cyclooxygenase-2 (COX-2) status and tumor regression rate (TRR) are potential prognostic factors for cervix cancer. The present study aimed to investigate the correlation between COX-2 expression and TRR in cervix cancer treated with radiotherapy (RT).
Materials/Methods: From 1997 to 2004, 57 patients diagnosed as squamous cell carcinoma of uterine cervix were enrolled who had three serial Magnetic Resonance (MR) examinations within 1 month before the start of RT (pre-RT), at 4 weeks after the start of RT (mid-RT) and at 1 month after treatment completion (post-RT). These patients were treated via external beam RT plus intracavitary brachytherapy. External beam RT was performed with a 15-MV photon in daily 1.8 Gy at 5 fractions per week. Total dose to the pelvis was ranged from 45 Gy to 66.6 Gy (median 50.4 Gy). Intracavitary brachytherapy of 24 Gy was given to point A with 4 Gy per insertion at two weekly insertions per patient using a high-dose-rate remote afterloading system. Twenty-nine patients received cisplatin-based chemotherapy concurrently with RT. Three tumor volumes (pre-RT, mid-RT and post-RT) for each patient were calculated by multiplying the sum of the areas by the slice thickness using T2-weighted MR images. Complete response (CR) was defined as complete disappearance of primary cervical tumor and partial response (PR) as the reduction of 50% or more. Immunohiostochemical staining was performed with a COX-2 monoclonal antibody (Cayman Chemical Company, Ann Arbor, MI). Positive immunoreactivity was defined as the extent of the distribution of immunostaining that exceeded 10% in tumor cells. Fisher's exact test was used to analyze correlation between COX-2 expression and TRR. P £ 0.05 was considered statistically significant.
Results: According to FIGO staging system, stage I, II, III and IVA were 7, 33, 12 and 5 patients, respectively. The mean tumor volumes of all patients at pre-RT, mid-RT, and post-RT were 58 cc (1.1~166.4 cc), 15.6 cc (0~132.6 cc) and 14.2 cc (0~96.8 cc), respectively. At mid-RT, 7 patients (12.3%) achieved CR and 40 patients (70.2%) did PR. At post-RT, 39 patients (68.4%) achieved CR and 16 patients (28.1%) did PR. COX-2 expression was positive in 43 patients (75.4%). CR rates were 28.6% in COX-2 negative patients and 7.0% in COX-2 positive patients at mid-RT (p=0.0541), while CR rates were 64.3% and 69.8% at post-RT (p=0.7472). In patients treated with RT alone, COX-2 status significantly influenced CR rates at mid-RT; 44.4% in COX-2 negative patients and 5.3% in COX-2 positive patients (p=0.0256). But TRR was not different according to COX-2 status when treated with concurrent chemo-radiotherapy.
Conclusions: TRR was more rapid in cervix cancer without COX-2 expression, especially when treated with RT alone. But COX-2 expression couldn't influence on TRR when treated with concurrent chemo-radiotherapy.

801 poster

DO STANDARD FIELDS IN THE EXTERNAL PELVIC RADIOTHERAPY OF CERVICAL CARCINOMA INCLUDE THE COMMON ILIAC LYMPH NODES SUFFICIENTLY?

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Purpose/Objectif: In the external pelvic radiotherapy of cervical carcinoma, the fields are determined with reference to the bony landmarks. A superior border passing through the L5-S1 intervertebral space is considered to cover the hypogastric, obturatory and external iliac lymph nodes. In order for the common iliac nodes to be included in the field, a superior border passing through the L4-L5 intervertebral space is considered to be sufficient. However, studies utilizing surgical clips, intraoperative measurements, or lymphangiograms have shown that the level of L4-L5 might not be sufficient. The aim of the study was to investigate the localization of the common iliac lymph nodes by using abdominopelvic computerized tomography (CT) and to determine whether the common iliac nodes were included in the standard treatment fields.
Materials/Methods: 3-D reconstructions of abdominopelvic CTs obtained from 65 patients were evaluated by an experienced radiologist from the Department of Radiology at the Hacettepe University Faculty of Medicine. Since the common iliac lymph nodes are localized around the common iliac arteries, aortic bifurcation was used as a landmark to assess whether the standard pelvic fields included the common iliac lymph nodes.
Results: While the aortic bifurcation was found to be at the level of L5 in 4 patients (6%), and at L4-L5 interspace in 3 patients (4%), it was at L4 level in 41 (63%), at L3-L4 interspace in 5 (8%), and at L3 level in 12 patients (19%).
Conclusions: Radiation therapies based upon the conventional fields do not include the common iliac lymph nodes sufficiently in the majority of patients. Our suggestion is that, in order to obtain the optimum dose distribution, the upper border of the treatment field should be at the level of aortic bifurcation that can be assessed with the help of CT or MRI.

802 poster

DOES IMPLEMENTATION OF CONFORMAL TELERADIOTHERAPY IMPROVES THERAPEUTIC INDEX IN CERVICAL CANCER PATIENTS?

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Purpose/Objectif: The use of combined modality approach-chemotherapy and radiation therapy for the treatment of patients with cervical cancer is associated with significant toxicity-mainly hematological and gastrointestinal. Conformal radiotherapy (RT) has the potential to deliver adequate dose to the target structures while sparing the normal tissue. Both the radiation dose to the small bowel and the volume are factors known to influence the risk of complications. The aim of this study was to determine whether the implementation of conformal RT can reduce the volume of normal tissue included in the RT field.
Materials/Methods: 14 cervical cancer patients (IIB and IIIB FIGO) treated with conformal RT concurrently with cisplatin (40mg/m^2) once a week were analyzed. According to ICRU 50 recommendations target volumes and the organs at risk were contoured on CT slices. For the GTV the tumor, uterus and cervix were traced. The CTV was defined as the vessels and lymph nodes from the obturator level to the aortic bifurcation, presacral region, and upper 1/3 of the vagina. The margin for PTV was added. Normal tissue region included small bowel, large bowel and bladder. Using 3-D treatment planning system and multileaf collimator, irregularly shaped four field plan was performed for the each patient. Conventional plans with two -and four-field-box techniques were generated as well. Dose-volume histograms of target volumes and organs at risk were calculated and compared. Analyses of variance were performed to compute the statistical significance.
Results: There was no statistical difference between doses received by target volumes - in each plan PTV was covered with 95% isodose.
Significantly different volumes of critical organs were included in the treatment volume:

3-dimensional treatment modality compared to conventional ones prevented geographical miss in 28% of patients.
Conclusions: These preliminary data suggest that implementation of conformal radiotherapy allows adequate target coverage while reducing the irradiated volume of contoured critical organs.

	Rectum		Small bowel		Bladder	
Treatment modality	V (%)	SD	V (%)	SD	V (%)	SD
2 opposite fields AP-PA	96,82	9,11	61,37	10,41	97,27	9,71
4 field-box	58,59	25,38	48,98	19,88	96,06	12,91
4 conformal fields	38,23	25,72	30,79	16,23	80,64	11,65

803 poster

EVALUATION OF RADICAL RADIOTHERAPY (RT) RESULTS AND PROGNOSTIC FACTORS IN CERVIX CARCINOMA - EXPERIENCE OF DOKUZ EYLUL GYNAECOLOGIC ONCOLOGY GROUP (DEJOG) - IZMIR

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Purpose/Objectif: This is a retrospective analysis of 116 patients with histologically proven invasive carcinoma of uterine cervix treated with concomitant chemoradiotherapy according to DEJOG protocol.
Materials/Methods: A hundred sixteen patients with carcinoma of uterine cervix who treated between August 1991 -June 2003 were evaluated. Median age was 54 (28-80). A hundred three patients had squamous cell carcinoma (88%), 3 had adenosquamous cell (3%), whereas 10 had nonsquamous cell histology (%9). The dispersion of stages were IB-IIA 8%, IIB 40%, IIIA 5%, IIIB 39% and IVA-IVB 8%. External RT was performed with megavoltage X-rays (Co 60 or 6 MV-X) to all patients using with anterioposterior (AP/PA) (24%) or pelvic box (76%) fields. Median dose was 54 (50,4-61,2) Gy, including midline bloc in 39,6-45 Gy, in 33 patients who treated before the protocol revision (1995). Median dose was 45 (45-54) Gy in 83 patients who treated after 1995. In 85 patients with parametrial invasion were treated with parametrial boost field (10 Gy). High dose rate intracavitary brachytherapy was applied to all patients as to point A in 3-5 fractions with 6-10 Gy/frx (Manchester system). Median 45 Gy RT was performed in 6 (5%) patients with paraaortic involvement to the paraaortic lymph nodes. Concomitant chemotherapy (Cisplatine, Cisplatine + 5-FU) was administered to 60 (52%) patients. Total treatment time was median 63 (36-121) days.
Results: Median follow up was 30 (2-144) months. The response rates were as follows: Complete 67%, partial 27%, no response 6%. The 5-8 year overall and disease free survival rates were 57.2 %-48.5% and 62.7%-58.5% in respectively in all patients. The 5-8 year disease free survival rates were 76.5%-70.1% fort he patients with complete response. Factors found to be associated with overall survival by Cox regression test were the tumour regression degree (the treatment response rate ($p< 0.001$). The crude moderate and severe rectal and bladder complication rates were 6% and 3% respectively.
Conclusions: The current data showed that the tumour regression rate is an important prognostic factor of cervical cancer treatment results.

804 poster

IGRT FOR CERVICAL CANCER: IS IT LESS TOXIC THAN NON IGRT?

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Purpose/Objectif: We have been used MR images for brachytherapy for cervical cancer with the purpose of getting more conformal dose distribution and reducing late morbidity. We evaluate whether this technique is less toxic than our historical data using Manchester system.

Materials/Methods: Between January 1995 and December 2003, 82 patients with histological confirmed squamous cell carcinoma of the uterine cervix (FIGO Stage Ib: 12, stage IIa:2, stage IIb: 32, stage IIIa:2, stage IIIb: 21, stage IVa: 1, stageIVb:12) were treated with external irradiation and MR image guided intracavitary HDR brachytherapy. Average age of the patients was 61.3 years (range: 33-85 years). Median follow-up duration was 60 months (range: 5-135 months). All patients were treated 30Gy whole pelvic irradiation followed by 20Gy boost to parametrium. Both CT and MRI were performed at the first and third time of brachytherapy under CT-MR compatible applicator insertion. The GTV was defined as high signal intensity region obtained MRI. The PTV was defined as a volume, which include 1cm margin in cranio-caudal directions. We delivered 6Gy/fraction to the PTV, one fraction /week, to a total dose of 24Gy. Until 1994, 332 patients were treated with same external irradiation technique followed by Intracavitary brachytherapy using Manchester system optimization (6Gy /fraction to a total dose of 24Gy to Point A). The 5-year survival rates according to stage, average Point A dose, maximum rectal, bladder dose and late genitourinary morbidity rates were compared between the two groups.

Results: In IGRT group, ten patients have died of their cancer and two died of intercurrent disease without evidence of recurrence. The 5 year overall survival and RFS rates according to stage in IGRT group were as follows; stage Ib: 88%, 91.7%, stage IIb: 92.4%, 96.7%, stage IIIb: 68.7%, 85.2%, stage IVb: 67.5%, 68.8%, respectively. Average point A dose was 496cGy (ranged: 102-710cGy). The average maximum rectal dose was 549cGy±214cGy in IGRT group and 1000cGy±640cGy in non-IGRT group and, respectively. The average maximum bladder dose was 594±180cGy in IGRT group and 1210cGy in non-IGRT group. The 5 year overall survival rate according to stage in non-IGRT group were as follows; stage Ib: 90%, stage IIb: 75%, stage IIIb: 52.3%, respectively. Grade1 late morbidity of bladder was observed in 2/60. Grade 1 and 2 late rectal morbidity was observed in 10/82 and 2/82, respectively. No cases were observed equal to or greater than Grade 3 morbidity at 5 years in IGRT group, whereas late rectal morbidity in non IGRT group was as follows; Grade 1: 21% (70/332), Grade 2: 9.7% (32/332), Grade 3: 5.7% (19/332), respectively.

Conclusions: We have shown that IGRT using MRI for cervical cancer is less toxic than non-IGRT technique and the survival rate using IGRT was equal to or better than non-IGRT.

805 poster

IS THE INCREASED LEVEL OF SERUM NITRIC OXIDE RESPONSIBLE FROM GENITOURINARY COMPLICATIONS OF CHEMORADIOTHERAPY IN CERVIX CANCER ?

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Purpose/Objectif: In this study we aimed to investigate the relationship between serum nitric oxide level (NO) and the complications of chemoradiotherapy in locally advanced cervix cancer patiens.

Materials/Methods: Inoperable, locally advanced FIGO stage 2B-3B cervix cancer patients were included into the study. Patients were treated with 50.4 Gy external-beam pelvic radiotherapy and 14-20 Gy boost dose was delivered intracavitary or externally. Patients were assigned to receive cisplatin (50 mg/m^2) weekly, for six cycles with concurrent pelvic radiotherapy. Every week on the 1st, 6th, 11th, 16th, 21th, 26th days of radiotherapy blood samples were collected from patients 15 minutes before irradiation and 30 minutes after chemotherapy. Once a week patients were physically examined and the complications of the treatments were scored according to Radiation Therapy Oncology Group criteria. NO concentrations were determined indirectly by serum nitrite/nitrate levels.

Results: The changes in the serumlevel of NO during radiotherapy and chemotherapy were not statistically significant. The level of NO before radiotherapy and after chemotherapy was found to be highest at the 2nd week of treatment course. Grade 1-2 genitourinary and lower gastrointestinal complaints were the most frequently encountered side effects. Like the NO concentrations the highest rate of the genitourinary system complications occurred in the second week of the treatment course.

Conclusions: The correlation between the highest serum NO concentration and the highest rate of grade 1-2 genitourinary system complications encountered in the 2nd week of the treatment might be considered as the result of injury of urothelium by increased serum NO.

806 poster

ISOLATED FULL-THICKNESS CERVICAL STROMAL INVASION WARRANTS POST-HYSTERECTOMY PELVIC RADIOTHERAPY IN FIGO STAGE IB-IIA UTERINE CERVICAL CARCINOMA.

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Purpose/Objectif: Full-thickness stromal invasion (FTSI) lies conceptually between microscopic involvement of parametria and deep stromal invasion. To evaluate the potential benefit of postoperative radiotherapy (PORT) to reduce recurrence in women with isolated FTSI as an unfavorable pathological finding after radical hysterectomy and pelvic lymph node dissection (PLND) in FIGO stage IB-IIA cervical carcinoma.

Materials/Methods: A total of 1,868 patients with stage IB-IIA cervical carcinoma underwent type III radical hysterectomy and PLND between January 1982 and December 2002. Seventy-four of these patients had isolated FTSI without any other unfavorable pathological finding, such as, lymph node metastasis, microscopic parametrial involvement, involved resection margin, lympho-vascular space invasion, or large clinical tumor diameter (> 4 cm). FTSI was defined as the microscopic involvement of the cervical-parametrial transition zone on the cervical side without invasion of parametrial tissue. Forty-one of these patients had no adjuvant treatment (S group) and 33 received PORT (PORT group). Patients with isolated FTSI who received chemotherapy were excluded. Treatment outcomes in the PORT and S groups were compared.

Results: Median follow-up duration (range) of all patients was 83 months (15-259). Five-year overall survival (OS) and 5-year cause specific survival of S group vs. PORT group were 91.5% vs. 97.0% (P = 0.612) and 91.5% vs. 97.0% (P = 0.245), respectively. However, 5-year disease free survival (DFS) and 5-year pelvic failure free survival (PFFS) of S group vs. PORT group were 77.2% vs. 97.0% (P = 0.038) and 79.8% vs. 97.0% (P = 0.044), respectively. According to

a Cox proportional hazards model developed by forward, stepwise regression incorporating all prognostic variables, only PORT was marginally significant for DFS (RR 0.234; 95% CI 0.051-1.067; P = 0.061) and significant for PFFS (RR 0.055; 95% CI 0.005-0.620; P = 0.019). Median survival duration and 5-year post-recurrence survival measured from the date of recurrence were 26 months and 36.5%, respectively. A Grade 4 late complication developed in two patients (6%) in PORT group.

Conclusions: PORT administered to patients with isolated FTSI after radical hysterectomy and PLND reduces pelvic recurrence which may lead to poor salvage in FIGO stage IB-IIA cervical carcinoma with acceptable morbidity.

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OUTCOME AFTER IRRADIATION FOR UTERINE CERVICAL CANCER PATIENTS WITH PARA-AORTIC LYMPH NODES METASTASIS

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Purpose/Objectif: The prognosis of patient with uterine cervical cancer is relatively good. For all stage, 5-year survival and disease free survival rates of patients treated with radiation therapy are 61% and 73%, respectively. However, para-aortic lymph node (PALN) metastases at the time of initial diagnosis is poorer than that of PALN negative patients and 5-year survival rate is only 31-48% (ref 11-3,11,12). This study is to evaluate the outcome after extended field radiotherapy in patients with PALN metastases from cervical cancer.

Materials/Methods: Between September 1994 and December 2003, total 16 patients with histologically proven uterine cervical cancer, FIGO stages I-IVA and stage IVB limited to supraclavicular node metastasis, had PALN metastases at initial presentation. They underwent both of external beam radiotherapy and intracavitary brachytherapy. The radiation dose to whole pelvis and PALN was 45 Gy (1.8 Gy/fraction). Midline block was applied at dose of 36~45 Gy depending on reduction of tumor size and was followed by parametrial boost dose of 6-14 Gy in 3~7 fractions. All patients except two received concurrent chemotherapy. The follow-up period after treatment for PALN was 24.5 months (ranging 9-124 months).

Results: Fourteen out of 16 patients had subsequent metastases at following areas; bone, liver, distant lymph node area such as supraclavicular node, or abdominal carcinomatosis. Five patients (31.3%) failed at PALN area inside the radiation field. Median time to recurrence was 11 months (range, 0-67 months). Two patients were followed with disease free status for 54 and 56 months after aggressive treatment to metastatic site, respectively. Median overall survival was 27 months (9-124 months). Overall survival rate was 39.0 % at 5-year. Two patients died from cervical cancer unrelated causes; systemic lupus erythematosus and second malignancy. Disease free survival rate at 5-year was 18.8%, respectively. Five patients were still alive for 12-58 months; alive without disease in 3 and alive with disease in 2.

Conclusions: The results of our study were comparable to previous data shown in literatures although most patients failed at distant sites. Also, two patients were followed with stable disease or no evidence of disease for more than 48 months after re-irradiation and/or chemotherapy to recurrent or metastatic tumor. This suggests that aggressive treatment can increase effectively survival duration even in patients with subsequent recurrence or distant metastasis.

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PET/CT PLANNED IMRT AND BRACHYTHERAPY IN CERVICAL CANCER

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Purpose/Objectif: Introduction of PET/CT scanning is a new method to detect lymph nod metastasis in patient with cervical cancer. This requires more intensive treatment with a higher total dose to a larger volume without changing the treatment of the uterus radically.

Materials/Methods: The modern diagnostic equipment creates a need for more intensive treatment in comparison to the past. As far as cervical cancer is concerned, we have now started to define volumes for IMRT (5 or 7 beams/sliding window technique) up to both 50 Gy and 64 Gy in 32 fractions, where the external treatment of the uterus (50 Gy IMRT) is followed by an intracavitary treatment of 17,5 Gy (10 pulses) x 2 (defined in point A). Both treatments are planned on TPS Eclipse (Helios/BrachyVision - Varian) - the following treatments are given with 18 MV on a Clinac 2300CD/EX (Varian) and Ir-192 PDR microSelectron (Nucletron) respectively. At the TPS we are able to sum both kinds of treatments to prepare the total dose plan.

Results: Since 2003 we have treated 30 patients by IMRT followed by intracavitary brachytherapy. We have chosen to look at the summed plans for patients treated in the last 2 years to get an opportunity to make guidelines for future. Out of these patients half have only been treated in the pelvic region, the rest have been treated in the para aortic region as well.

Conclusions: With these treatment modalities we are able to get higher doses to the PET positive lymph nodes and at the same time obtain the usual dose in uterus. This technique allows combination of IMRT and brachytherapy. We recommend IMRT in order to aim a sufficient dose to positive lymph nodes in the pelvic or para aortic region.

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POST-OPERATIVE RADIOTHERAPY (RT) IN CERVIX CARCINOMA STAGE I-IIA; TREATMENT RESULTS AND PROGNOSTIC FACTORS IN 74 PATIENTS FROM 1994 TO 2000

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3 - In Memoriam

Purpose/Objectif: Based on a retrospective analysis of 188 patients (pts) treated with post-operative RT in our department from 1970-1993 the treatment policy was adapted in 1994. After 2000 chemotherapy was added in some categories of pts. In this analysis results of treatment between 1994 and 2000 are analysed and compared to our historical data.

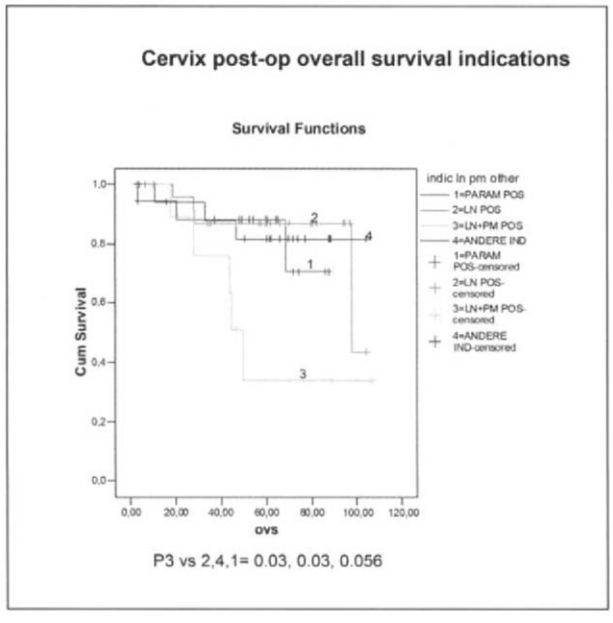
Materials/Methods: Patient characteristics. Seventy-four patients with an early stage cervix cancer, mean age 46 years (range 25-81) were treated with primary surgery, followed by adjuvant radiotherapy; 61 squamous cell carcinomas and 13 adenocarcinomas. Surgery consisted of a radical uterus extirpation (Wertheim-Okabayashi: n=57) or a simple abdominal (n=12) or vaginal (n=5) uterus extirpation. Indications for adjuvant RT were: positive parametrium (n=18), positive lymph nodes (n=28), both positive parametrium and positive lymph nodes (n=10), other (n=18), R1 resection (n=11), R2 resection(n=2). Angio-invasion was present in 23 pts. In 10 pts

a blood transfusion was needed to maintain the haemoglobin level on a minimum of 7.5 mmol/l before or during RT. Treatment characteristics: external beam RT (EBRT) was given in 72 pts (upper limit L4/L5: 63 pts, Th 12/L1: 9 pts), 69 pts received a dose of 45-50.4 Gy. Brachytherapy to the vaginal top was administered in 48 pts.

Results: Actuarial results at 5 years: Overall survival (OS) 78 %, local disease-free survival (LDFS) 85% and distant metastases-free survival (DMFS) 80 %. Prognostic factors: Tumour extension both in lymph nodes and in parametrial tissue had a negative impact on OS, LDFS, DMFS ; angio-invasion and need for transfusion on LDFS; age < 51 yrs had a negative influence on DMFS. No significant influence was seen for pathology, stage, number of nodes, radicality, tumour size , type of surgery, upper field limit, EBRT-dose or administration of brachytherapy. Grade 1-2 or grade 3-4 complications were seen in 17 and 3 pts respectively, the cumulative risk of late grade 3-4 complications at 5 yrs was 6.6 %. OS and LDFS are identical to historical data.

Conclusions: Excellent 5 yrs survival is reached with adjuvant radiotherapy alone after primary surgery for cervix cancer in patients with microscopic tumour extension beyond the uterus.

Morbidity of post-operative radiotherapy is acceptable. Poor prognostic features were 1: presence of tumour both in lymph nodes and parametrium, 2: angio-invasion, 3: age < 51 years. Patients with these features may further benefit from concomitant chemo-radiotherapy (1,2,3) and/or radiation dose escalation by IMRT (1,2).



810 poster

PRIMITIVE UROTHELIAL CELL CARCINOMA OF THE VAGINA: REPORT OF A CASE. TREATMENT AND REVIEW OF THE LITERATURE.

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Purpose/Objectif: Urothelial carcinoma localized outside the urinary tract is uncommon. It has been sporadically reported in the female genital tract with or without concomitant bladder involved. Fertissof was the first one who described in 1990. Up to date, only 6 cases have been published. The urothelial cell carcinoma of the vagina (UCCV) could be primary or metastatic. The pathogenesis of the primary is unclear. The vagina as well as the bladder has its embryological origin in the urogenital sinus, the inestability in their epithelios could explain the tumour development. Nevertheless, other authors believe that they derive from a common pluripotential cell.

Materials/Methods: The case is a 75 years old woman who presented in 1991 grade II papilar urothelial cell carcinoma of bladder. Transurethral resection of the bladder tumour was done and left nefroureterectomy, due to the presence of tumour in left kidney. The findings were: grade II papilar urothelial carcinoma, not infiltrating, multifocal localized in the calyces, distal ureters and bladder.Later, she presented seven local relapses at the bladder that have been treated with transurethral resections plus postoperatives local instillations.In 2004, she presented multiple lesions in the vault and the walls of the vagina; they were excised. Pathological examinations confirmed the presence of transitional cell carcinoma. Metastatic workup was negative for metastases. On May 2004, she underwent abdominal hysterectomy and bilateral salpingo-oophorectomy and vaporization of residual vaginal lesions. She was treated with high-dose-rate brachytherapy.The applicator used was vaginal cylinder, 3 cm diameter was used. The whole length of the vagina was treated, no shielding was used. The treatment was given in 6 fractions, 5.5 Gy/fx, twice a week, to a total dose of 33 Gy, prescribed 5 mm to the vaginal surface.

Results: The treatment was well tolerated. Currently, the patient is alive without evidence of loco-regional recurrence.

Conclusions: Primitive UCCV is a rare tumour with an uncertain pathogenesis. We cannot give any standard treatment recommendation. A close follow-up of the entire urogenital tract should be done given the high risk of local recurrence. After the excision of the vaginal urothelial lesion, adjuvant radiotherapy could be offered as a treatment option in selected patients.

811 poster

PROGNOSTIC FACTORS OF STAGE IIB UTERINE CERVIX CANCER: RESULTS FROM KOREAN PATTERNS OF CARE STUDY 1998-1999

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Purpose/Objectif: The aim of this study is to veryfy prognostic factors in stage IIB cervical cancer who received radical radiotherapy in 1998 and 1999. The data were collected from on-line Korean Patterns of Care Study program.

Materials/Methods: We developed on-line registration format of the Korean Patterns of Care Study (http://www.pcs.re.kr) and conducted a natiowide on-line data entry of uterine cervical cancer by radiation oncologist or trained data manager from 31 institutions out of the whole 42 hospitals operating radiation therapy in Korea at that time. National estimates were made using weights that reflected the relative contribution of each institution and a total of 626 patients record were reviewed from 886 patients selected randomly. A total of 298 patients (47.6%) were stage IIB according to FIGO staging. We analized outcomes of single FIGO stage (IIB) according to various prognostic factors including extent of parametrial involvement.

Results: The median age of the total patients was 61 years old (range 32-86) and 95.0% of the patients received brachytherapy (high dose rate or low dose rate intracavitary radiotherapy) during treatment. Patients with pretreatment anemia (serum hemoglobin level<10g/dl) rate was 16.4% and one half of them received transfusions before treatment. Five year overall survival rate and disease free survival rate (five YDFSR) for all the patients were 80.6% and 57.6%, respectively. Five YDFSR for patients with pretretment anemia was 47.3% compared to 58.2% for patients with hemoglobin levels 10g/dl or more (p=0.261). Serum squamous cell antigen (SCC) level was monitored in 199 patients. Five YDFSR for patientrs with initial SCC higher than 5ng/ml or higher was55.6% compared to 63.1% in patients with lower levels of SCC or normal range and the difference was statistically not significant. About one third (102/298)

of the patients had bilateral parametrial involvement and 5YDFSR for unilateral and bilateral involvement were 58.3%, and 55.3%, respectively (p=0.736). There were no significant survival differences regarding to energy of the treatment machine, methods of brachytherapy. Only tumor size was a significant prognostic factor and 5 YDFSR for patients with tumor size 3cm or less was 67.0% compared to 51.5% for patients with more than 3cm (p=0.010). By multivarate analysis, the tumor size was still a significant prognostic factor in stage IIB cervial cancer.

Conclusions: Extent of parametrial involvement and pretreatment serum squamous cell carcinoma antigen levels were not significant factors. Only tumor size was a significant prognostic factor. More data entry from on-line registration is needed for better evaluation of the prognostic factors.

812 poster

PRONE VS. SUPINE POSITION PELVIC IMRT FOR ENDOMETRIAL CANCER - A DOSIMETRIC AND TOXICITIES COMPARISON STUDY

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Purpose/Objectif: Intensity-modulated radiotherapy (IMRT) has been shown to reduce the radiation dose to small bowel in pelvic RT in gynecology patients. Prone positioning has also been used to decrease small bowel dose by displacement of small bowel from the RT field in these patients. The purpose of this study was to determine the dosimetric and toxicities differences between prone and supine position IMRT in endometrial cancer patients treated with adjuvant radiation

Materials/Methods: Forty seven consecutive patients of endometrial cancer treated with adjuvant RT were analyzed. Patients were non-randomly treated in prone or supine position depending on physicians' discretion. Twenty-one patients were treated in prone position and 26 in supine position. Dose-volume histograms for normal tissue structures and target were compared between the supine and prone IMRT plans using the Matt Whitney test. Similarly acute and chronic toxicities were also compared between the two groups

Results: The demographics, BMI, stage, histology and type of surgery were comparable between the two groups. The V10 (percentage of volume getting 10Gy), V20, V30, V40, V45, V50 for small bowel were 89.5, 69, 33, 12.2, 5, 0 in the prone group and 87.5, 62.7, 26.4, 8, 4.3 and 0 in the supine group. The difference was not statistically different. Similarly the dose volume histograms for bladder and rectum were also comparable except for slight higher V10 (1.5%) and V20 (5%) for the rectum in the supine group which was statistically different. Similarly PTV 95 (percentage of PTV getting 95% of dose), PTV 110 and PTV 120 were 100%, 1.5% and 0% in prone group and 98.5%, 2.5% and 0% in the supine group. The median follow up was 20 months. Acute small bowel toxicities were Grade 1 in 7 pts and grade 2 in14 pts in prone group vs. grade 1 in 6 pts and grade 2 in19 pts in supine group. Similarly chronic toxicity was grade 1 in 7 pts and grade 3 in 1 pt in prone group and grade 1 in 5 pts in supine group. All these toxicities were comparable with no statistically significant difference. No patient had locoregional recurrence in either group.

Conclusions: These preliminary data suggests that there is no difference in normal tissue dosage and toxicities between prone and supine IMRT in endometrial cancer treated with radiation. The supine position is preferred because of less set up uncertainties We need longer follow up and more outcome studies to see if there is any difference in toxicities between the two approaches

813 poster

RADIOTHERAPY AND HYPERTHERMIA FOR CARCINOMA OF THE VAGINA

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Purpose/Objectif: To evaluate the results of radiotherapy in patients with vaginal cancer.

Materials/Methods: A cohort of 44 patients (6 stage I, 23 stage II, 8 stage III and 3 stage IVa) treated between 1990 and 2002 with radiotherapy for primary vaginal cancer was assessed. Radiotherapy was given either alone (n=34), combined with chemotherapy (n=3), or with hyperthermia (n=7). Hyperthermia was added to radiotherapy in case of a tumour size > 4 cm in diameter for FIGO stage III disease. Survival rates and median survival were evaluated.

Results: The calculated overall 5-year survival of primary vaginal cancer was 63 %. High grade tumors had lower OS rates than low grade tumors (25% vs 61%). For FIGO stage II (n=23), 5 yrs OS was 59% and for FIGO stage III (n=8), this was 56%. In the figure, overall survival curves in relation to FIGO stage are shown.

Conclusions: In primary vaginal cancer, tumour stage is the major prognostic factor. In the NCDB report on cancer of the vagina, the 5 yrs overall survival was 58% for stage II tumours, and 36% for stage III-IV tumours [1]. The similar 5 yrs OS rates for stage II and III tumours in the population studied by us may be related to the addition of hyperthermia to radiotherapy in patients with stage III tumours with a diameter larger than 4cm. The supplementary effect of hyperthermia to radiotherapy may be a feasible and beneficial approach to improve the treatment results of vaginal cancer.

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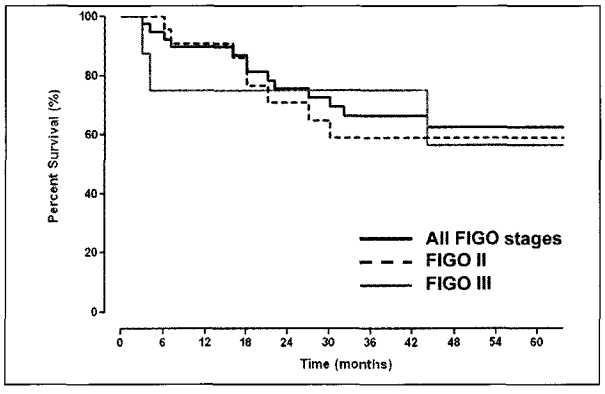

814 poster

RADIOTHERAPY IN THE ADJUVANT SETTING OF CERVICAL CARCINOMA: TREATMENT RESULTS AND PROGNOSTIC FACTORS

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Purpose/Objectif: To evaluate the efficacy of postoperative radiotherapy and to investigate prognostic factors for early stage cervical cancer patients.
Materials/Methods: From December 1993 to December 2001, 157 patients with stage I-II cervical cancer treated by surgery and postoperative radiotherapy were included in this study. Indications for postoperative external radiotherapy were based on pathological findings, including lymph node metastasis, positive surgical margins, parametrial involvement, pT2 tumor and presence of 2 minor risk factors as lymphovascular space involvement, deep stromal invasion and tumor diameter between 2-4 cm. Seventy-two (46%) patients received radiotherapy (RT) alone, whereas 68 (43%) were treated with RT and concomittant chemotherapy (CT) and 17 received neoadjuvan CT. Patients with vaginal margin positivity also received 27.5 Gy HDR brachytherapy in 5 fractions.
Results: Median follow-up time was 50 months. The actuarial 5-year overall (OS), disease free (DFS), local recurrence free (LRFS) and distant metastases free (DMFS) survival rates were 68%, 69%, 77% and 86% respectively. Univariate and multivariate analyses revealed that metastatic lymph node number was the only significant prognostic factor for all end points. While metastatic pelvic LN level was significant for OS, LRFS, DMFS; chemotherapy was found to have significant effect on OS, DFS, LRFS. Moreover RT duration for DFS and LRFS; type of surgery and involvement of endometrium for DFS and DMFS; grade and paraaortic lymph node involvement for DFS and hemoglobin level for OS were the other significant prognostic factors that affect survival rates in multivariate analyses.
Conclusions: Our results indicate that number and level of metastastic LN's, and chemotherapy are the most important prognostic factors determining the survival rates. It seems that current treatment approaches are not adequate.

815 poster

THE BENEFITS OF ADJUVANT EXTRA-FIELD RADIOTHERAPY (EFRT) IN MULTIMODAL TREATMENT OF ADVANCED CERVICAL CANCER.

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Purpose/Objectif: Multimodal therapy, based on neoadjuvant chemotherapy, surgery and RT combination, is one of the most actual variant of advanced cervical cancer treatment, but results are still disappointing and comparable with results of RT alone. Adjuvant EFRT included in post-operative RT programme seems to be the way to improve the results.
Materials/Methods: 57 patients 16-77y.o. with advanced cervical cancer T2a-3bNo-1Mo, after neoadjuvant platinumÃ¥-taxan based chemotherapy and surgery, were included because of metastasis in pelvic lymph nodes (LN) and\or because of 3 and more factors of poor prognosis: tumor volume before treatment more than 50sm^3, tumor embols in lymph and blood vessels, low uterine segment involvement with myometrial invasion, therapeutic pathomorphosis I-II in tumor and metastatic LN. There were no evidence of paraaortic metastasis in any patients before the treatment. All included received the same post-operative pelvic irradiation, and then were randomized in 2 groups with (group 1) or without (group 2) adjuvant EFRT, groups were comparable.
Results: In 27 (47,3%) of patients in group 1 EFRT on para-aortic LN zone was held, in 7 (26%) of them, 0-I ECOG, at the very beginning of post-operative RT course, simultaneously with brachytherapy on vaginal scar and vagina tube, 3-4 hours after vaginal irradiation, in 20 (74%), ECOG II>, GIT II> during neoadjuvant therapy, EFRT was the last step, after pelvic irradiation. Concomitant therapy included gastro protectors, H3-blocators, intravenous infusion of ozone solutions. EFRT programmes were optimized to minimize dose rate in spinal cord, renal, intestine, skin, 2-2,2Gy\fraction, total dose 36-40Gy. No complications grade III-IV RTOG/ EORTC. During the EFRT haematologic toxicity I-II was noticed in 8 (29%), gastro-intestinal toxicity -in 16 (57%), anorexia I- in 10(37%), vomiting - in 6 (22%), gastritis - in 4 (14,8%). 30 (52,6%) patients in group 2 had been observed. 2-year-results in two groups were compared. OS 96,4% vs 85%, DFS 88,6% vs 77,5%, LN progression 12% vs 0% .
Conclusion: Adjuvant extra-field radiotherapy (EFRT) is effective and well tolerated way to improve the results of multimodal treatment in patients with advanced cervical cancer resistant to neoadjuvant chemotherapy.

816 poster

THE ROLE OF PET IN PREDICTION OF TREATMENT RESPONSE OF PATIENTS TREATED BY CURATIVE RADIOTERAPY - EARLY EXPERIENCES AND OBTAINED DATA

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Purpose/Objectif: The carcinoma of the cervix of the uterus is the second most frequent cancer in women in the Czech Republic. The most important prognostic factors are a tumor volume and the involvement of lymph nodes. The nodal status evaluation is very important for the optimal choice of a treatment strategy. The cervix carcinoma metastasizes in a predictable pattern. The involvement of pelvic and para-aortic lymph nodes is the most important prognostic factors. It was proved by many studies that local control in lymph nodes leads to increasing patients' overall survival. Possibilities of CT probe in detecting lymph node metastases are very poor. GOG study has found that CT scans identify only 34% of para-aortic nodal metastases.
Several studies try to find PET prognostic value to increase a treatment effectivity. Some published studies try to use this new diagnostic method in staging and a treatment of the cervix carcinoma. However, most of them are retrospective. PET can be also used for detecting of recurrent or persistent disease. Typical manifestations of recurrent cervical cancer are pelvic masses and lymphadenopathy.
Materials/Methods: Patients are treated with curative radiotherapy. The volume of radiotherapeutic fields will be determined by results of PET and CT scans. Radiotherapy is applied only on the pelvis in the case of negative lymph nodes. The fields are extended to involved lymph nodes in case PET positive scan on lymph nodes.
We plan radiotherapy using planning CT and 3D planning console. Brachyradiotherapy is applied according to the standard recommendation. Concominant is used in indicated cases.
Regularly, patients are followed up in the Department of Radiation Oncology and Gynecology after finishing the therapy. We do new PET and CT scans 3 months and next new PET scan 9 months after the radiotherapy to determine the received results. In our prospective study we observe the local control, DFS, TTP and OS. We will used Cox regression function, log-rank test and Kaplan-Meier sur-

vival function. Another questions we try to find answers on are: Signification of PET imaging in staging of the cervix cancerComparison of PET and CT image before a treatmentSearching for patients in a high riskOptimalization of a treatment strategy Eliminating false positive and false negative resultsEvaluation of a correlation between PET and response rate of the therapy

Conclusions: PET is a new diagnostic method, which is looking for its place in the routine oncological praxis. Its' introduction into staging of cervical carcinoma can change a therapeutic strategy. This trial could identify the patients with a higher relapse risk which have some benefit from a more aggressive therapy and clear up how we can use PET in the conservative treatment of cervix carcinoma. We evaluated 25 patients and this poster will discussed our first experiences and obtained data after first year of ongoing study.

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817 poster

THE VALUE OF TUMOUR VOLUME IN ADVANCED CERVICAL CARCINOMA

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Purpose/Objectif: The value of cervical tumour volume is clearly established in early cervical carcinoma (FIGO stages IB1 and IB2). We have evaluated the effect of the tumour dimension on global survival (SV_3) and local control in advanced cervical cancer (FIGO stages IIB-III).

Materials/Methods: 261 patients were retrospectively evaluated. According to the FIGO stage 93 patients (36%) were in stage IIB, 99 patients (38%) in stage IIIA and 69 patients (26%) in stage IIIB. Regarding the tumour greatest dimension we stratified the patients in two groups: ≤ 4 cm. (135 patients) and > 4 cm. (126 patients). All patients received a four-field "box" external beam radiotherapy (EBRT) with standard fractionation associated with endocavitary utero-vaginal medium dose rate brachytherapy (MDR-BT). In 107 patients a TAHBSO with bilateral pelvic lymphadenectomy was associated: 77 patient from stage IIB (83%), 28 patients in stage IIIA (28%) and two patients in stage IIIB (3%). After a median follow-up of 44 months the SV_3 and LC were evaluated.

Results: The global SV_3 was 86% in patients with tumors ≤ 4 cm. vs. 68% in tumors > 4 cm. in the largest diameter (p=0.01). For stage IIB patients the SV_3=96 % in tumors ≤ 4 cm. vs. 76% for tumors > 4 cm. (p<0.01); in stage IIIA and IIIB we found the same difference between the two groups regarding SV_3, but without statistical significance. The global local control was 73.5% (192 from 262 patients), significant better in patients with tumors ≤ 4 cm.: 81% vs. 66% in patients with tumors > 4 cm. According to FIGO stage the local control was 84% in stage IIB, 73% for stage IIIA and 61% in stage IIIB. Pelvic recurrence ocurred in 33 patients (12.6%): 20 patients with tumors > 4 cm. (16%) vs. 13 patients with tumors ≤ 4 cm. (9%).

Conclusions: We found that in advanced cervical carcinoma the tumour dimension is an important prognostic factor for local control and global SV_3, with the greatest predictive value in stage IIB FIGO.

818 poster

VAGINAL BOOST FOR ENDOMETRIAL CARCINOMA RADIOTHERAPY: BRACHYTHERAPY VS IMRT. A COMPARISON PLANNING STUDY.

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Purpose/Objectif: To evaluate the differences between endocavitary brachytherapy and IMRT in the vaginal boost treatment for endometrial carcinoma, in terms of both vaginal target volume coverage and rectum sparing.

Materials/Methods: Five patients were selected presenting an Endometrial carcinoma. They were treated in our institute with a vaginal intracavitary brachytherapy boost of 2 fractions of 6 Gy, 1 fraction/week, after a pelvic external irradiation. Dose-volume histograms (DVH) of rectum (organ at risk) and vagina (boost target) were analysed, comparing the brachytherapy treatment with Ir-192 HDR (through a cilindrical vaginal applicator), and an intensity modulated treatment (IMRT) with 5 fields of 6 MV and dynamic sliding window delivery. Fractionation was the same for both techniques (2 fractions of 6 Gy, as for actual brachytherapy treatment), and prescription was at the maximum target dose.

Results: Concerning DVHs for rectum, the two techniques were highly comparable and the differences of various parameters between the two techniques were not significant. The rectum was considered only in the portion adjacent to the vagina. The mean dose for this portion of rectum was 30 to 35% independently from the analysed technique. On the contrary, differences were found for the target volume irradiation where Ir-192 HDR brachytherapy reflects the known dose decreasing with depth while IMRT can deliver more homogeneous doses. Mean doses to the vagina were 75% (SD=3%) with brachytherapy and 93% (SD=5%) with IMRT.

Conclusions: The IMRT solution, at planning level, gives the same result as brachytherapy treatment on the organ at risk (rectum), while a great advantage was found for the target (vagina) irradiation.To safely use the advantages of IMRT solution for vaginal boost in Endometrial Carcinoma,it is anyway advisable the association, during treatment, of advanced techniques for patient and organ positioning,like the image guided radiotherapy (IGRT) with ad hoc landmarks.

819 poster

WHOLE ABDOMINAL RADIATION: A CURATIVE TREATMENT OPTION IN A SUBSET OF PATIENTS WITH EPITHELIAL OVARIAN CARCINOMA IRRESPONSIVE TO CHEMOTHERAPY.

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Background: The majority of patients (pts) with advanced ovarian cancer will relapse following initial treatment. Additional therapy for recurrent ovarian cancer is considered palliative with overall survival reported between 0-20% at 5 yr. Debulking surgery is used in a minority of carefully selected pts, the majority will be treated with chemotherapy only. The aim of the present study was to examine if optimal debulking surgery and adjuvant hyperfractionated whole abdominal radiation (WAR) can be justified as a salvage treatment with curative potential to these pts. Disease free survival (DFS) was chosen as primary endpoint.

Materials/Methods: Nineteen pts had a laparotomy preceding WAR to assess tumor extend and to attempt macroscopic complete tumor resection. WAR (AP and PA fields) was delivered using a fraction dose of 0.8 Gy, twice daily, to a total dose of 30.4 Gy. After 8 Gy kidneys were shielded from the PA field. Four pts received a pelvic boost in daily fractions of 1.8 Gy up to 50.2 Gy and 1 pt received a pelvic and paraaortic boost up to 45 Gy. DFS was scored as the time

elapsed since the end of RT and clinical evidence of tumor recurrence or an increase of the tumor marker CA-125.

Results: Mean FU was 1.8 yr (range 0.02 - 5.8). Treatment was completed as planned in 17 pts (90%) and was interrupted after 20.8 Gy in 1 pt because of a durable thrombocytopenia irresponsive to transfusion. Another pt who developed intermitting signs of bowel obstruction did not complete treatment and succumbed 3 weeks following treatment. Median DFS was 0.6 yr. DFS at 5 yr was 24 ± 11%. Histologic type and initial FIGO stage were significant predictors for clinical outcome: DFS at 5 yr was 53 ± 25% vs 13 ± 11% for pts with endometroid ca (n=6) and serous papillary carcinoma (n=13), respectively (p=0.04) and 100% in 3 pts (all endometroid ca) with FIGO stage I vs 10 ± 9% in 16 pts with FIGO stage III (p=0.03). Six pts (31%) developed signs of small bowel obstruction (SBO), mean interval 0.8 yr, range 0.3 - 2.0. At the time of SBO 1 pt was without recurrence and 5 pts had recurrent disease.

Conclusions: Aggressive salvage therapy consisting of debulking surgery followed by WAR seems justifiable as a curative treatment option in a subset of pts. A favorable histological subtype (endometroid ca) and/or limited disease at presentation are predictors for a favorable clinical outcome in our experience. Serious late toxicity (SBO) in pts without recurrent disease is acceptable.

Posters Head & Neck

820 poster

18-F-FDG-PET GUIDED IMRT OF HEAD AND NECK CANCER - FOCAL DOSE ESCALATION PHASE I STUDY

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Purpose/Objectif: To investigate feasibility and to measure acute, late and dose limiting toxicity (DLT) when we performed phase I study of focal dose escalation for IMRT of head and neck cancer. Secondary end-points of the study were response, local control, a site of relapse and survival that will be presented at the ESTRO meeting.

Materials/Methods: Between August 2003 and May 2005, 23 patients with squamous cell carcinoma of the oro-, hypopharynx and larynx were enrolled at dose level I (DL-I) and 18 patients at dose level II (DL-II). Nine patients at DL-I and 14 patients at DL-II received concomitant platinum-based chemotherapy. The dose was escalated to a focal region defined by the 18-F-FDG-PET-positive subvolume within the GTV. The SIB treatment of 25 Gy (DL-I) and 30 Gy (DL-II) in 10 fractions was followed by conventional IMRT applied in 22 fractions that resulted in total dose for the entire treatment of 72.5 (DL-I) and 77.5 Gy (DL-II) to the 18-F-FDG-PET-positive subvolume. The target delineation and treatment planning methodologies have been reported previously [1,2,3]. Acute and late toxicity was scoring using CTC v.2 and LENT-SOMA scale respectively. DLT was defined as any Grade 4 toxicity observed during radiotherapy and up to 4 weeks after treatment end.

Results: A total of 39 patients completed IMRT. A treatment break was required in 2 patients - 1 due to DLT. The most common acute toxic reaction was Grade 2 dermitis - in 21 patients (91%) at DL-I and 13 patients (72%) at DL-II. The most severe acute toxicity fell in dysphagia and mucositis. Twelve (52%) at DL-I and 10 (56%) patients at DL-II developed Grade 3 dysphagia. Five patients (22%) at DL-I and 9 patients (50%) at DL-II had Grade 3 mucositis. There was association between severity of mucositis and dysphagia and concomitant chemotherapy. Percutaneous gastrostomy was performed in 10 patients (43%) at DL-I and 13 patients (72%) at DL-II. None of patients in both groups lost more than 20% of their weight. Six patients (26%) at DL-I and 10 patients (56%) at DL-II required hospitalization secondary to toxicity. One DLT - Grade 4 dermitis was developed at DL-I. There was 1 toxic death at DL-II attributed to sepsis and renal failure that occurred shortly after the end of chemotherapy.

There was no statistically significant relationship between acute and late dysphagia. No patient developed any Grade 4 late toxicity. Ten and 9 patients presented late dysphagia at DL-I and DL-II correspondently; 3 patients had Grade 3 at DL-I and 1 patient at DL-II. One patient presented Grade 3 mucosal toxicity at DL-II. We observed onset of fibrosis in 9 patients in the entire cohort.

Conclusions: 18-F-FDG-PET guided IMRT of head and neck cancer is feasible when dose escalation is limited to the 18-F-FDG PET delineated subvolume within the GTV. Acute toxicity appears tolerable and reversible given a follow-up of 6 months.

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821 poster

A LONGITUDINAL STUDY OF TUMOUR OF THE PAROTID GLAND. A SINGLE CENTRE EXPERIENCE ON RECURRENCE AND SURVIVAL

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Purpose/Objectif: Malignant parotid gland tumours are relatively infrequent in . In this study we establish the overall survival, treatment for malignant parotid gland tumours and the cause of death.

Materials/Methods: Between 1948 and 2004 144 patients, were treated for malignant parotid gland tumours. The patients were treated with surgery and/or radiotherapy or in some advanced cases best supportive care. The time from diagnosis to last follow-up ranged from 2 years to 39.9 years with a median follow-up of 8.1 years.

Results: There were 74 male and 70 female, the mean age was 61.9 (range 16-87) years. Surgery was the primary treatment in 112 (78 %) patients followed by radiotherapy in 81 of these patients. In 25 patients radiotherapy were given as a single treatment. In 7 cases no treatment was possible due to their deteriorated general condition. In our follow-up thirty-eight (26.4%) patients died from cancer of the parotid gland, 4 died of other malignancies, 10 died from cardiovascular or pulmonary disease and another 51 patients of other causes. Younger patients (< 65 years) showed a better prognosis. The total overall 5-year survival was 42% in our material.

Two time periods were compared; 1970-1979 vs 1990-1999, where the 5-year survival was comparable (61% vs 58%). The difference in survival was not significant (p=0.0856).

Conclusions: During the time period, 1948-2004, there have been little change and few improvements in treatment results for this group of mainly elderly patients. The overall 5-year survival was 42 % and is comparable to the results of others.

The two time periods, 1970-1979 vs 1990-1999, did not differ significantly in survival. Fewer patients in the later period might have had an impact on the results. There seem to be a large potential for improvement of treatment results in patients with parotid cancers.

822 poster

A RETROSPECTIVE STUDY OF RADIOTHERAPY AND LASER RESECTION IN EARLY STAGE (T1-T2) GLOTTIC CANCER

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Purpose/Objectif: There is no good evidence that radiotherapy is superior to laser resection in the treatment of early glottic cancer. The aim of this study was to retrospectively evaluate failure rates and laryngectomy-free survival in patients with early glottic cancer treated by a single centre multidisciplinary team of 3 radiation oncologists and 4 surgeons.

Materials/Methods: The study included 124 patients with early glottic cancer seen at the Royal Victoria Hospital Belfast (which serves the population of Northern Ireland) between Jan 00 and Jan 05. There were 78 patients treated with radical radiotherapy as initial treatment. The most common fractionation was 55Gy in 20 fractions in 4 weeks. There were 46 patients who had laser surgery as primary treatment. There was no attempt at randomization, treatment was allocated on a case by case basis and was dependent on clinician preference and patient choice. Age and sex distribution was similar for both groups, however importantly there were more patients with T2 stage in the radiotherapy group 37%(29/78) vs 19%(9/46). There was also a higher proportion of bilateral disease and anterior commissure involvement in the radiotherapy group which is in

keeping with selection bias. Staging investigations were the same for both groups.

Results: There were 9 failures in the laser arm with 5 out of 9 patients with T2 disease failing laser. However 8 out of the 9 failures were successfully salvaged with radical radiotherapy and only one patient required a salvage laryngectomy. There were 10 failures 5 T1 (10%) and 5 T2(17 %) in the radiotherapy arm all of whom went on to total laryngectomy. The failure free survival for the laser group was 80% and for the radiotherapy group was 87%. The laryngectomy free survival was much higher in the laser group 98% versus 87% in the radiotherapy group mainly down to successful salvage with radiotherapy in laser treated patients.

Conclusions: A randomized study is needed to guide clinicians and patients as to the optimal management of early glottic cancer. This study has shown bias in patient selection which will affect all non-randomized studies. Our study has indicated that laser is safe particularly given the high likelihood of salvage of laser failure with radiation. However the inclusion of T2 stage patients in any randomized study must be questioned given the high likelihood of failure with laser surgery.

823 poster

ANALYSIS OF EGFR, VEGF AND P53 IN SERUM OF HEAD AND NECK SQUAMOUS CELL CANCER (HNSCC): PRELIMINARY RESULTS OF THE GORTEC 99-02 RANDOMIZED TRIAL

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Predictive and prognostic markers are warranted in head and cancer.

To assess the potential interest of VEGF, EGFR and p53 serum level,, we designed a prospective study to analyze VEGF, P53, EGFR both in the serum and in the tumor of HNSCC patients included in the GORTEC 99-02 prospective randomized trial, which compared conventional radiotherapy plus 5FU and carboplatin vs radiotherapy with a concomitant boost and 5FU carboplatine vs a very accelerated radiotherapy .This prospective study has been designed to include 820 patients, and we present here the results in a sub group of in 216 patients for whom the biological markers were analyzed. A possible correlation between these markers and TNM staging, age sex, disease progression, and survival was evaluated. Serum analysis was performed for p53 serum auto-antibodies (Immunotech), VEGF (R&D systems), EGFr (Oncogene science). Statistical analyses were performed using Spearman correlation coefficient, Kruskal-Wallis test for quantitative variables, Chi^2 and Fisher exact test for qualitative variables and Logrank test and Cox model for survival analysis. Multivariate analysis of survival took into account T and N status, tumor localisation and the type of treatment.

No correlation was found between the serum levels of VEGF and EGFr, neither between EFGr and p53. There was a non significant trend ($p = 0.07$) towards higher VEGF serum levels in p53 negative, compared to p53 positive patientsNo correlation was found between age, sex, T and N staging and all the tested serum markers. The VEGF serum level was significantly higher in laryngeal and hypopharyngeal primaries and lower in oropharyngeal and buccal primaries ($p = 0.04$). The median follow-up was 2 years. High levels of serum EGFr were associated with better overall survival in univariate and multivariate analysis ($p<0.01$). Overall survival was not significantly higher in positive serum p53 patients than in negative p53 patients ($p=0.11$ in multivariate analysis) and VEGF serum level was not associated with clinical outcome.

These preliminary results suggest that high levels of serum EGFr expression was associated with a better outcome in this series of head and neck cancer patients.

824 poster

AUDIT OF TNM STAGING DATA IN A PROSPECTIVE POINT-OF-CARE DATABASE FOR HEAD AND NECK CANCER

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Purpose/Objectif: As a quality assurance process, the Head and Neck (HN) Radiation Oncology Site Group at Princess Margaret Hospital has established an Anthology system to record outcomes prospectively at point-of-care for all new HN cancer referrals. Clinical data from the electronic medical and radiotherapy treatment records (RR) are entered into the Anthology by a data manager. An audit was conducted of the Anthology TNM stage compared with RR and Cancer Registry (CR) stage.

Materials/Methods: A random sample stratified for radiation oncologist (RO), year of registry and primary treatment modality (surgery versus radiation) included 10% of the Anthology patients registered between July 2003 to Dec 2005. Stage data was retrieved independently from the RR and CR. The TNM staging data in the Anthology were compared with the data from RR and CR in terms of completeness and accuracy. Discrepancies were resolved by the attending RO.

Results: From 1152 cases in the Anthology, 120 (10.4%) cases were audited. Unknown primary cases (5) were excluded from analysis because the cancer registry does not collect TNM staging data. TNM staging was completed in 115 (100%), 102 (89%) and 111 (96%) in the Anthology, RR and CR respectively. For cases with complete staging data, the percentages of discrepancy between the Anthology and RR (n=102) for overall stage, T, N and M category were 4%, 5%, 3% and 0% respectively. A similar comparison between the Anthology and CR (n=111) showed 12%, 13%, 10% and 0% discrepancy. Physician review of discrepant cases indicated inaccuracies in all 3 sources. For T-category, 1 Anthology, 4 RR and 13 CR categorizations were incorrect; for N-category, 4 Anthology, 3 RR and 8 CR categorizations were incorrect; and for overall stage, 3 Anthology, 5 RR and 10 CR stages were incorrect. Suspected reasons for discrepancy included interpretation of clinical data, human error, and failure to update staging for new baseline data.

Conclusions: This audit suggested an approximate 4 to 13% disagreement between the Anthology stage and primary data sources. Physician review suggested a low error rate (< 4 %) in the Anthology staging data. It may be feasible to avoid redundant data entry by linking data from these three systems. The initial two-year experience of the Anthology has also demonstrated the feasibility of real-time outcome recording at point of care. ☒

825 poster

COMPARISON OF INITIAL TREATMENT RESULTS OF CARBON-ION AND PROTON RADIOTHERAPY FOR MUCOSAL MALIGNANT MELANOMA OF THE HEAD AND NECK

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Purpose/Objectif: To compare initial treatment results of two different ion beams (carbon-ions and protons) for mucosal malignant melanoma (MMM) of the head and neck.
Materials/Methods: This study reviewed 25 patients with MMM of the head and neck who were treated with definitive ion beam radiotherapy. Of these 25 patients, 8 received 57.6 GyE/16 Fr of carbon-ions (C) in 2002, and 17 received 65 GyE/26 Fr of protons (P) between 2003 and 2005. There were 5 male and 3 female patients with a median age of 65 in (C), and 5 male and 12 female patients with a median age of 65 in (P). Primary site was nasal cavity/paranasal sinus/oral cavity in 5/2/1 (C) and 12/2/3 (P). Previous treatment was yes/no in 5/3 (C) and 8/9 (P). Corresponding clinical stage was T1/T2/T3/T4 in 1/2/2/3 (C) and 3/6/6/2 (P). Pathologic subtype was melanotic/amelanotic in 6/2 (C) and 16/1 (P). There was no significant difference of characteristics between (C) and (P).
Results: Median follow-up was 24 months (range 5-44) in (C) and 13 months (range 5-26) in (P). Objective tumor response within 6 months was CR/PR/NC in 6/2/0 (C) and 3/9/5 (P) though continuous tumor regression was observed in (P) after 6 months. Local failure was observed in 1 of 8 (C) patients (T3 nasal cavity at 30 months), and in 1 of 17 (P) patients (T4 nasal cavity at 20 months). One-year local control (LC) rates were 100% (C) and 100% (P). Distant failure was observed in 8 of 8 (C) patients at 2-30 months, and 8 of 17 (P) patients at 1-20 months. Of these distantly recurred patients, 8 of 8 (C) and 4 of 8 (P) patients died of disease. One-year progression-free survival (PFS) rates were 25% (C) and 71% (P). One-year overall survival (OS) rates were 75% (C) and 79% (P). There were no significant difference of LC, PFS, OS between (C) and (P). T1 disease and no previous treatment were significant predictors of PFS and OS. Acute skin toxicity of Grade 3 was observed in 0 of 8 (C) and 1 of 15 (P) patients. Acute mucosal toxicity of Grade 3 was observed in 5 of 8 (C) and 5 of 15 (P) patients. All other patients experienced Grade 2 or less acute toxicities. Late skin toxicity of Grade 1 was observed in 3 of 8 (C) and 4 of 15 (P) patients. Late mucosal toxicity of Grade 1 was observed in 5 of 8 (C) and 5 of 15 (P) patients. No severe late toxicity was observed, so far.
Conclusions: Though tumor regression was slower in protons, LC, PFS, and OS showed no statistical difference for initial 2 years between carbon-ion and proton radiotherapy for head and neck MMM. T1 disease with no previous treatment might as well be treated with protons as severe late toxicities are concerned in adjunct normal tissues with carbon-ions. Despite effective local treatment, even early diseases developed distant failure in both carbon-ion and proton patients. The current multidrug chemotherapy has limited effects on distantly recurred patients and good treatment to address this problem is awaited.

826 poster

COMPARISON OF THREE MAJOR SOURCES FOR BRACHYTHERAPY USED IN TREATMENT OF NODE NEGATIVE ORAL TONGUE CANCER AND INFLUENCE OF AGE ON OUTCOME

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Purpose/Objectif: To examine the efficacy of different radioactive sources used in brachytherapy and influence of age.
Materials/Methods: We reviewed 648 patients with node negative oral tongue cancer (T1-3N0M0; 212T1, 352T2, 84T3) treated at Osaka University Hospital between 1967 and 1999. For patients treated with low dose rate (LDR) brachytherapy, the treatment sources consisted of Ir-192 pin for 351 patients (1973-1996; irradiated dose, 61-85 Gy; median, 70Gy), and Ra-226 needle for 217 patients (1967-1986; 55-93 Gy; median, 70Gy). High dose rate brachytherapy using microSelectron-HDR (MS-HDR) was administered to 80 patients (1991-present; 48-60 Gy; median, 60 Gy). The dose rates at the reference point for the LDR group were 0.30 to 0.8 Gy/h, and for the HDR group 1.0 to 3.4 Gy/min.
Results: The 5-year local control rates for patients treated with Ra-226 and Ir-192 were 85%, and 79% for T1, 75% and 73% for T2, 62% and 64% for T3 tumors, respectively, and for those in the MS-HDR group they were 87% for T1, 79% for T2 and 89% for T3. Patients 65 years of age or older attained lower 5-year local control rates (67% for total cases□G72% for T1, 68% for T2 and 59% for T3) than their younger counterparts (79%, 86%, 77□" and 69%; p=0.004).
Conclusions: The three major sources produced the same locoregional results, but age proved to be a factor influencing outcomes for patients with node negative tongue tumor regardless of T category.

827 poster

CONCURRENT WEEKLY CISPLATIN WITH RADICAL RADIOTHERAPY: IN SEARCH OF AN OPTIMAL REGIMEN FOR LOCO-REGIONAL ADVANCED HEAD AND NECK CANCERS

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Purpose/Objectif: Squamous cell carcinoma of the head and neck (SCCHN) affects 500,000 new patients worldwide annually. The dominant pattern of failure for these patients remains loco-regional, although, an increasing number are being diagnosed with distant metastases recently. Radical radiotherapy with chemotherapy is considered standard of care for the non-surgical management of loco-regionally advanced SCCHN. However the most optimal chemo-radiotherapy regimen is yet to be defined.
The aim of this study was to identify prognostic and therapeutic factors affecting outcome (local control, loco-regional control, and disease-free-survival) for patients with loco-regionally advanced SCCHN undergoing definitive concurrent chemo-radiotherapy.
Materials/Method: The medical records of all patients with loco-regionally advanced SCCHN (AJCC stage III & IV), excluding nasopharynx, planned for radical radiotherapy (66-70 Gy) with weekly cisplatin (30 mg/m^2) in a single unit between 1996-2004 were searched electronically. Patients receiving at least 60 Gy and one cycle of concurrent cisplatin were considered eligible for analysis.
Results: A total of 264 patients were identified, with a median age of 54 years. The mean radiotherapy dose was 66 Gy and median number of cisplatin cycles 6. With a mean follow-up of 19 months, the 5-year local control; loco-regional control and disease free survival was 57%; 46%; and 43% respectively for the entire cohort. AJCC stage grouping (III vs IV), Karnofsky performance status (<60 vs 60) , primary site (non-oral vs oral), and intensity of treatment (number of chemotherapy cycles and overall treatment time) were significant predictors of outcome. The acute toxicity of this concurrent weekly chemo-radiation regimen was mildly increased, but acceptable.
Conclusions: Concurrent weekly cisplatin with radical radiotherapy appears to be an optimal regimen in loco-regionally advanced head and neck cancers. Stage grouping, performance status, primary site, and treatment intensity are important determinants of outcome.

828 poster

DELAY IN REFERRAL OF OROPHARYNGEAL SQUAMOUS CARCINOMA TO SECONDARY CARE CORRELATES WITH MORE ADVANCED STAGE AND POORER SURVIVAL

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Purpose/Objectif: Squamous carcinoma of the oropharynx presents with symptoms common to many benign diseases, especially sore throat and neck nodes, and this can cause delay in referral to secondary care. We investigated delay in referral, defining this as the time from symptom-onset to the date of general practitioner's referral letter to secondary care, and the effect of that delay, using a retrospective case notes based study of patients presenting to our institution with oropharyngeal squamous carcinoma between 1995 and 2005.

Materials/Methods: 110 cases were analysed. 17, 19, 4 cases and 1 case were excluded respectively because notes were not available, information insufficient, patient not referred from primary care or disease was recurrent, leaving 69 for analysis.

Results: Using correlation analysis and ordinal regression, we examined relationship between increased referral delay from primary care, clinical stage at presentation and survival. Increasing time from symptom onset to referral to secondary care was positively correlated with more advanced disease at presentation ($r_s = +0.346$, $p = 0.004$). This was confirmed with ordinal regression modelling (delay estimate = 0.045, $p = 0.042$). Patients with delay of less than 6 weeks had significantly improved survival compared to those with a delay of greater than 6 weeks ($p = 0.032$). For every one week of delay in referral, we estimate that the stage of presentation will progress by 0.045 of "a stage".

Conclusions: Previous studies have failed to show a correlation between delay and more advanced stage at presentation, but none have concentrated on the within-patient delay or within-primary care delay, whose sum is often greater than the time from specialist referral to starting treatment.

While other factors such as tumour biology also determine stage at presentation, more national and international efforts should be made to reduce delay in referral.

829 poster

DEMOGRAPHICS AND OUTCOME BY TREATMENT IN PARA-NASAL SINUSES CARCINOMA, A POPULATION BASED STUDY

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Introduction: Cancer of the para-nasal sinuses is a rare disease . It comprise 0.2-0.8% of all human carcinomas. Experience in the management of this disease is limited to retrospective reviews. These tumours usually present late. Symptoms and signs often mimic benign conditions such as chronic sinusitis. 75% of patients present with locally advanced stage III or IV disease. Regional neck disease affects only 7% to 15% of cases and manifests late. Survival is most poor for squamous cell carcinoma (most frequent histology!!!).

Aims of the project:

To report on a single centre experience in a population based cohort of patients. To present outcome by treatment and define the role of combined modality treatment.

Materials/Methods: Computerized data capturing was created in access interrelational database.

All patients' charts seen in the period from 1960 to 2002 were reviewed. All the Head and Neck data base listings were reviewed to ensure that all patients were captured. Data captured included Age at diagnosis, Gender, Presenting Symptoms & Signs, Investigations (findings), Living/disease status at last F/U (+ cause of death), Tumour location, size, Histology, Grade, TNM classification, Treatment modality such as surgery, chemotherapy, radiotherapy, its dose and intent (radical/adj/palliative), Treatment Toxicities, Social Habits (tobacco, EtOH) and occupational exposure Quality assurance audits were carried out on the charts. Data were entered into the computer. A Sass Statistical package was used for analysis.

Result: During that period 231 patients were seen at the cancer centre confirming a percentage of 3.4% of all Head and Neck Cancer during that period. Out of these 88% were in the maxillary, 6% sphenoid and 6% ethmoid sinus. Median age was 62.5 years with a range of 6 to 89. 52% were males and 48% females. Range of follow up varied from 6 to 219 months. 60% of patients treated with surgery and post-op radiation survived longer than 5 years while only 20% of patients treated by radiation alone survived for the same period.

Conclusions: These results are compatible with the literature. The best outcome was achieved by radical surgery and radiation likely reflecting selection biases. This study highlights the need for prospective evaluation in a rare disease such as this one.

830 poster

DIFFERENTIATED THYROID CANCER IN NOVA SCOTIA 1992 - 2001: UPDATED ANALYSIS OF PATTERNS OF CARE AND OUTCOME

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Purpose/Objectif: A preliminary analysis of a convenience sample of 77 cases of Differentiated Thyroid Cancer (DTC) diagnosed in Nova Scotia between 1992 and 2001 was completed in 2003. The purpose of the current review was to update this province-wide assessment of DTC during this time period in regards to the place of surgery and its' relation to place of residence and to review prognostic factors, investigations, staging information, management, and outcome.

Materials/Methods: An existing database was adapted to meet the stated objectives. Patients who had thyroid cancer diagnosed between 1992 and 2001 were identified in the Nova Scotia Tumor Registry. Hospital and cancer centre charts of patients were reviewed to confirm the diagnosis of DTC and the relevant information was entered into the database. The protocol was approved by the hospital Research Ethics Committee.

Results: 248 of 410 cases of potential DTC patients have been reviewed. Of these patients 206 met the inclusion criteria. 42 patients did not meet the inclusion criteria for various reasons, including primary treatment outside of Nova Scotia or histology was other than papillary or follicular thyroid cancer. The majority of the remaining 162 cases of potential DTC as yet unanalyzed will likely not be amenable for detailed review as no charts are available. The updated results validate information from the 2003 preliminary sample analysis. Most surgeries were initiated in either the Capital District or Cape Breton District Health Authorities regardless of place of residence while subsequent radioactive iodine therapy was performed exclusively in Halifax (see Map below). 75% of the DTC cases reviewed were female and with an overall peak age at diagnosis between 30 to 60 years. Important pathologic information was inconsistently and incompletely documented. DFS at 4 years was 92% for papillary cancers and 83% for follicular cancers. OS at 4 years was 93% for

papillary cancers and 79% for follicular cancers. Further information including use of diagnostic procedures and use of external beam radiation will be included in the final presentation.
Conclusions: The age and gender distribution and survival of DTC patients in Nova Scotia is similar to those reported from other areas in North America Critical pathologic information that guides staging, therapy, follow up and prognosis was inadequately documented. Some aspects of therapy, pathologic review and post-treatment follow-up may be improved with centralization of expertise and coordination of patient care. A prospective database for thyroid cancer is needed to optimally review care and outcome.

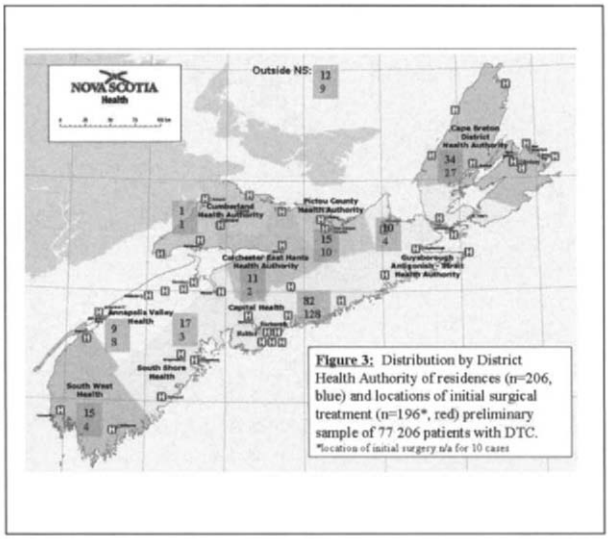

Figure 3: Distribution by District Health Authority of residences (n=206, blue) and locations of initial surgical treatment (n=196*, red) preliminary sample of 77 206 patients with DTC.
*location of initial surgery n/a for 10 cases

831 poster

DOSIMETRIC PREDICTORS OF LARYNGEAL EDEMA

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Purpose/Objectif: To investigate dosimetric predictors of laryngeal edema after radiotherapy (RT).
Materials/Methods: Patients with HN-SCC were selected for the present study if they satisfied all the following criteria: 1. grossly uninvolved larynx at the time of RT; 2. no prior major surgical operation except for neck dissection; 3. treatment planning data available; 4. at least one fiberoptic examination of the larynx within 2 years from RT performed by a single observer.
The larynx was recontoured on each planning CT by one observer as appropriate. Both the mean dose and the cumulative DVH of the larynx were extracted for each patient. Since a variety of fractionation schedules had been used, the dose was transformed into a linear quadratic equivalent one at 2 Gy per fraction assuming a a/b of 3 Gy. No time factor was accounted for. Subacute/late laryngeal edema was prospectively scored at each follow up examination according to the RTOG scale. Endpoint is considered grade 2+ laryngeal edema. Time to endpoint was calculated with log rank test from the date of treatment end. Univariate/multivariate analyses including various patient, tumor and treatment characteristics were run. Median follow up is 12.6 months (range: 0.4-46.7 mths).
Results: 66 patients met all the inclusion criteria. Primary tumor sites were as follows: oropharynx, 54 pts (81.8%); nasopharynx, 7 pts (10.6%); unknown, 5 pts (7.6%). Most patients (N=59, 89.4%) had been treated with whole-field IMRT, otherwise with conformal radiotherapy.
The number of fiberoptic examinations within 2 yrs from RT was 231 for a median number of 3 (range:1-9) per patient. 29 (43.9%) and 3 (4.5%) patients developed grade 2 and grade 3 laryngeal edema, respectively. The actuarial incidence of grade 2+ edema at 13 months is 50.6+7%. 80% of events had been observed by 9 months.
Laryngeal V30, V40, V50, V60 were significantly correlated with grade 2+ edema at univariate analysis. At multivariate analysis, V50 (continuum) and neck stage at RT (N0-x vs N+) were independent predictors of endpoint. V50 was further categorized into 4 groups according to quartile cut-offs. The actuarial incidence of edema at 13 months is 21.5+11%, 32.9+14%, 67.9+13% and 100% if the percentage of larynx receiving 50 Gy at 2 Gy per fraction is <21%, 21-36%, 36.1-77.8% and <77.8%, respectively.
Conclusions: The risk of laryngeal edema is strictly related to the dose to the larynx and possibly to the neck. V50 is the single most important predictor of edema and should be <36%.

832 poster

DYSPHAGIA RELATED QUALITY OF LIFE PATIENTS WITH CANCER IN THE OROPHARYNX IS SIGNIFICANTLY AFFECTED BY THE RADIATION THERAPY DOSE RECEIVED BY THE SUPERIOR- AND MIDDLE CONSTRICTOR MUSCLE: A DOSE-EFFECT RELATIONSHIP

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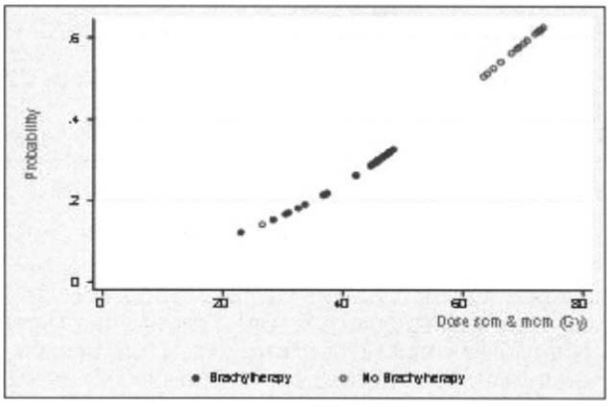
Purpose/Objectif: To assess the correlation between dose received in the swallowing (sw) apparatus and decrement in the quality of life (QOL) of patients with oropharyngeal cancer.
Materials/Methods: Between 2000-2005, 77 patients with scc of the tonsillar fossa and/or soft palate and the base of tongue, were analyzed for dysphagia after having been treated by intensity modulated- (n=37), 3D conformal- (n=22) or CT-based parallel-opposed (n=18) radiotherapy (RT) techniques. In 52% brachytherapy (BT) was used, in 47% radiation was combined with concomitant chemotherapy (cCHT). Five structures, being the superior-, middle-, and inferior constrictor muscles (scm, mcm, and icm, respectively), the cricopharyngeus muscle and the muscular inlet of the esophagus, are of paramount importance for swallowing. The treatment plans of all patients were retrieved; in every axial CT slice the 5 muscular structures were delineated and mean dose calculated (DVHs). Three validated Quality of Life (QOL) questionnaires were used: the Performance Status Scale of List, scoring for "eating in public" and "normalcy of diet", the EORTC H&N 35 items swallowing liquids, pureed food, solid food and aspiration while eating, and the M.D. Anderson Dysphagia Inventory, 20 item - dysphagia specific - QOL questionnaire for Head and Neck cancer (MDADI).Univariate analysis is performed, correlating the mean dose in the 5 sw muscles with the outcome of the questionnaires, using the proportional odds model. In a multivariate analysis the effects of the parameters age, sex, site, T-stage, N-stage, dose, technique, surgery, chemotherapy and brachytherapy were studied.
Results: Out of the 77 patients, 60 were re-examined in 2005 and found to be NED; 5 had previously expired (local failure) and 12 died because of intercurrent disease. Mean FU was 41 mo. (4-72). At 5-yrs the local relapse free survival was 92%, overall survival 65 %. In contrast to parameters 'treatment techniques' and 'CHT', in each QOL instrument, BT seems to project a favorable outcome (p=0.01). In the univariate analysis a significant correlation was observed between dose in the scm & mcm and the outcome of H&N 35 and MDADI. In a multivariate analysis, BT was the only significant factor (p=0.01).
Conclusions: From figure 1, one can appreciate the steep relation-

ship between dose in the scm & mcm and probability of sw complaints. The multivariate analysis shows a significant effect of BT, which suggests less sw complaints with lower doses. Therefore, improving QOL needs further optimization of the dose in the scm & mcm in particular.



833 poster

EFFICACY OF MR-SIALOGRAPHY FOR EVALUATION OF RADIATION-INDUCED XEROSTOMIA

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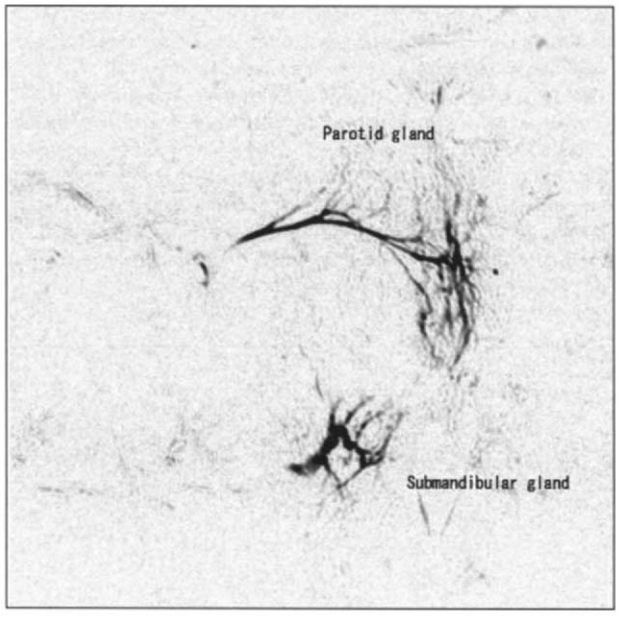
Purpose/Objectif: For head and neck cancer (HNC) patients who receive curative irradiation, radiation-induced xerostomia is one of the frequent and troublesome adverse effects diminishing quality of life. Established objective evaluations of xerostomia are invasive examinations such as catheterization or radioisotope scintigraphy. Therefore, we have adapted a heavy T2-weighted MR-hydrography technique for salivary glands (MR-sialography) to evaluate the salivary secretion function of HNC patient before and following a radiation treatment course.

Materials/Methods: Sixteen patients with HNC (oral cavity: 12; oropharynx: 4; all squamous cell carcinomas) were included in this study. We performed conventional MRI and MR sialography (TR/TE = 10000/1000ms) with a mandibular joint surface coil , prior to and two weeks after radiation treatment course. All patients received greater than 44 Gy to the primary tumor and major salivary glands (median dose to salivary glands: 60 Gy). Fifteen patients were administered oral fluorouracil agent or platinum agent via selective arterial infusion. Salivary secretion responsiveness of MR- sialography to tartaric acid stimulation was evaluated and graded into three categories (good, fair, poor). The severity of xerostomia was evaluated according to CTCAE v 3.0. Subjective symptoms of oral dry sensation were scaled by visual analogue scale (VAS).

Results: No patients complained of any oral dry sensation before the beginning of radiation. Mean VAS of oral dry sensation was 61.8 mm after radiation. Grade 1 xerostomia was noted in 2, Grade 2 in 14, Grade 3 in 0. All patients' parotid glands and submandibular glands on conventional T2 weighted MR images showed atrophy and increase of signal intensity after radiation regardless of severity of xerostomia. MR-sialography after radiation showed a poor response to secretion stimulation, particularly that of the submandibular glands which closely tracked the grade of xerostomia and oral dry sensation VAS.

Conclusions: Our results showed that the poor response on MR-sialography of submandibular glands after radiation correlates levels of radiation-induced xerostomia. More cases and longer follow up are required to confirm the results.



834 poster

EPIDERMAL GROWTH FACTOR RECEPTOR AND CYCLIN D1 EXPRESSION IN PRETREATMENT BIOPSIES AS A PREDICTIVE FACTOR FOR RADIOTHERAPY OF EARLY GLOTTIC CANCER

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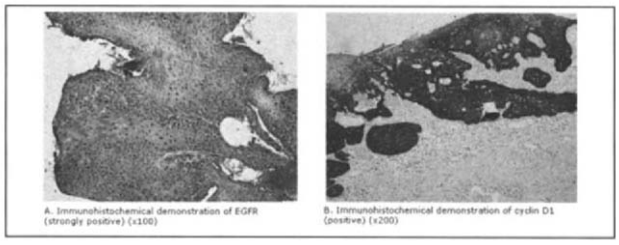
Purpose/Objectif: Traditional clinicopathological features such as tumor stage, histological grade and presence of lymph node metastases do not seem to be sufficient to predict clinical outcome in patients with laryngeal squamous cell carcinoma. This study was done to evaluate the feasibility of expression of epidermal growth factor receptor (EGFR) and/or cyclin D1 as a predictive assay for radiotherapy of early glottic cancer.

Materials/Methods: From 1992 to 2004, 151 patients with T1-2 glottic cancer were treated with radiotherapy at Seoul National University Hospital , and 33 patients developed recurrence. Immunohistochemical staining for EGFR and cyclin D1 were performed for formalin-fixed paraffin-embedded tissues from 25 of 33 patients, whose biopsy specimens were available, and from 25 clinically matched patients who were free from disease.

Results: Both high EGFR ($p = .047$) and high cyclin D1 ($p = .040$) expression were significantly associated with poor outcome in early glottic cancer. There was no association between EGFR and cyclin D1 status ($p = .158$) but the combination of EGFR and cyclin D1 status provided association with local control. Patients with both high EGFR and high cyclin D1 expression had the worst outcome comparing with the others (14 months vs. 29 months of median time to progression).

Conclusions: The molecular biomarkers EGFR and cyclin D1 have a prognostic significance in early glottic cancer. These markers may be used as a predictive assay for radiotherapy of early glottic cancer and dose escalation or extended field radiotherapy may be applied to the patients with high expression of EGFR and/or cyclin D1. Furthermore, the selected patients may benefit from targeted therapy.



835 poster

EPSTEIN-BARR VIRUS DETECTION IN POST-IRRADIATION LOCALLY RECURRENT NASOPHARYNGEAL CARCINOMA

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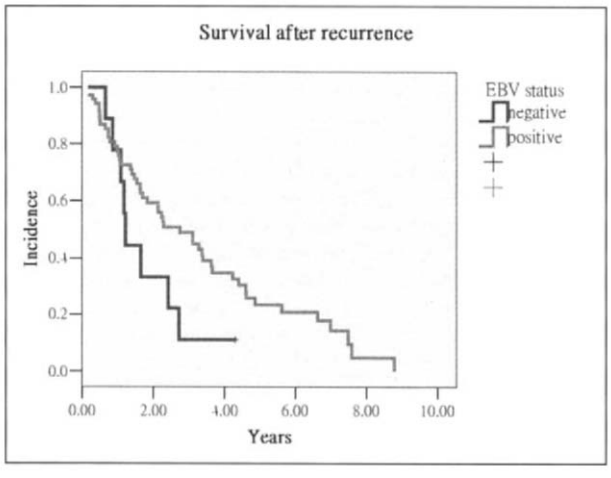
Purpose/Objectif: Epstein-Barr virus (EBV) has been demonstrated to be highly associated with nasopharyngeal carcinoma (NPC). The object of this study is to define the role of the presence of EBV in post-irradiation local recurrent NPC patients.

Materials/Methods: From May 1987 to October 2005 , a total of 95 NPC patients who initially diagnosed to have EBV infection suffered from pathology-proved local recurrence after full-course of radiotherapy (RT dose ¡ù 6480 cGy). Fifteen cases with unknown post-RT EBV status were excluded from this study. Nasopharyngeal swabs or paraffin-embed block were used to detect EBV-derived latent membrane protein-1 (LMP-1) and EBV DNA by polymerase chain reaction (PCR) in these cases.

Results: Of 80 locally recurrent NPC cases entered this study, the distributions of pathology were 19 for WHO type I, 29 for type II, and 32 for type III. There are 19 females and 61 males. Among them, 71 (group A) were EBV positive at the time of recurrence while the others (11.25%, group B) had no detectable EBV LMP-1 or DNA. The median time to recurrence and median overall survival were 1.78 years vs. 1.53 years (p=0.748), and 5.57 years vs. 3.56 years (p=0.526) for group A vs. group B, respectively. However, there seems to be a trend toward longer median survival after recurrence in EBV-expressing patients (2.75 +/- 0.57 years) compared with EBV-negative patients (1.22 +/- 0.06 years) (p=0.1).

Conclusions: After full-course of radiotherapy, some locally recurrent NPC cases were negative for EBV infection. Besides, although the difference failed to reach statistical significance, this study demonstrated longer survival with cases that were positive for EBV infection at the time of recurrence. This may imply that EBV-expressing recurrent carcinomas (most are WHO Type II/III) are more radio- or chemo-sensitive and therefore have better prognosis after salvage treatment compared with EBV-negative ones (most are WHO type I).



836 poster

ERYTHROPOIESIS-STIMULATING AGENTS IN THE TREATMENT OF ANEMIA IN PATIENTS WITH HEAD AND NECK TUMORS ? ANALYSIS OF QUALITY OF LIFE

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Purpose/Objectif: Patients with head and neck tumors frequently present a high grade of anemia as a result of either the malignant process itself or the treatments. Anemia correction using erythropoiesis-stimulating agents (ESA) has been associated to enhanced radiotherapy benefits in cancer control improving patients' survival time and their quality of life (QoL). The purpose of the present study was to evaluate anemia impact in the QoL of these patients.

Materials/Methods: An observational study involving head and neck cancer patients was carried out according to an ESA administration protocol of Radiotherapy Department of Oporto' Instituto Português de Oncologia. Forty five patients with hemoglobin levels that ranged from 10 to 11,5 g/dL (mean=10,4 g/dL) treated with ESA between September 2002 and December 2005 were compared with a control group of 25 patients not treated with ESA. Both groups were previously submitted to cancer treatment. Functional Assessment of Cancer Therapy-Fatigue (FACT-F) and FACT-An (Anemia) scales were used to evaluate patients' QoL on week 1 and week 7 of radiotherapy treatment.

Results: Seventy patients were included in the analysis, 14,3% were female, mean age 57 years old (range 33 to 72). The mean change of hemoglobin levels was -2,5 g/dL for control group and +2,12 g/dL for ESA group (P=0,005). None of the patients in the ESA group received red blood cell transfusions, which occurred in 25% of the control group. Significant differences between patients' QoL within each treatment group were found between week 1 and 7, during radiotherapy (Table 1). QoL scores were significantly greater for ESA group than control group (higher scores in FACT-F and FACT-An scales) while QoL declined in control patients from week 1 to week 7.

Table 1 - Comparing FACT-Fatigue and FACT-An scales' scores between week 1 and 7.

	Week 1	Week 7	P*
ESA Group			
FACT-An	12,5	18,6	<0,001
FACT-Fatigue	39,1	18,0	<0,001
Control Group			
FACT-An	19,6	13,7	<0,001
FACT-Fatigue	17,9	57,1	<0,001
*Wilcoxon Test			

Conclusions: ESA demonstrated to be effective in treating anemia in head and neck tumors and its administration was well tolerated. This study showed that ESA administration clearly has a positive impact in the QoL of these patients.

837 poster

EVALUATION OF TUMOR HYPOXIA DURING RADIOTHERAPY IN HNC WITH FMISO-PET

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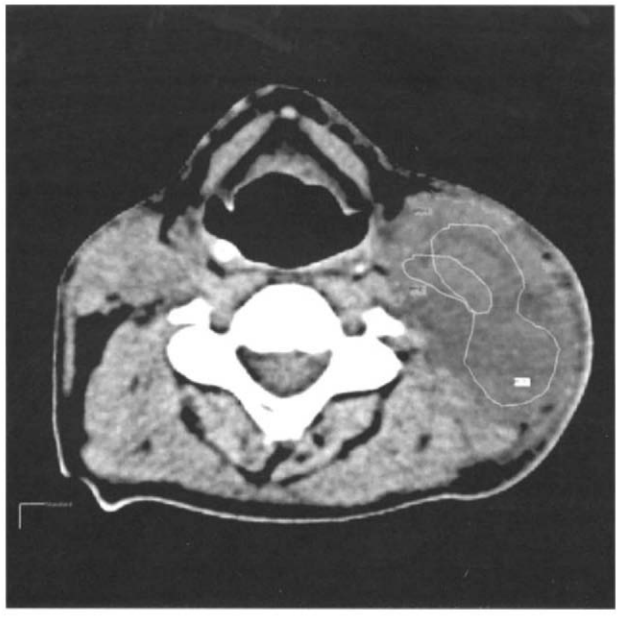
Purpose/Objectif: PET imaging with [^{18}F]-fluoromisonidazole (FMISO) takes advantage of increased tracer retention in hypoxic tissues to non-invasively quantify hypoxia in cancer. We evaluated the use of FMISO-PET to assess changes in tumor oxygenation during fractionated radiotherapy for locally advanced head and neck cancer (HNC).

Materials/Methods: Twenty-one patients with locally advanced SCC of the head and neck have been enrolled in an ongoing PET imaging protocol. FMISO-PET scans were performed at baseline and at week 5 during treatment, consisting of chemotherapy-enhanced radiotherapy (CERT). Three hours after injection of 10 mCi of FMISO, PET-CT images were obtained on a Biograph (Siemens) scanner. Tissue to blood (T:B) FMISO ratio was calculated using venous blood obtained during the emission part of the scan with a cutoff T:B ratio of ≥ 1.2 to signify hypoxia. On the CT scan, both primary tumor and pathologic lymph nodes were delineated as GTV (Gross Tumor Volume). Within every GTV, an Hypoxic Volume (HV) was then determined as the sum of all pixels with a T:B ratio ≥ 1.2. A Fractional Hypoxic Volume (FHV) was calculated as the percentage of HV within the GTV. The scans at the two time-points were automatically co-registered and serial FHVs were compared.

Results: The preliminary results of the first four patients are available. Pretreatment FHVs were 38.3%, 37.1%, 30.6% and 26.7% respectively (mean 33.2%). No correlation between tumor size and FHV was observed. At week 5, the respective FHVs were 37.0%, 31.5%, 34.0% and 29.0% respectively (mean 32.8%). Three patients had significant shrinkage of GTV (reduction of 66.6%, 66.4% and 55.0%) and HV (67.7%, 71.4% and 51.0%), while one patient had only minimal reduction in volume (16.5% for GTV and 7.2% for HV).

When the scans at different time-points were co-registered to compare the location of both HVs within the tumor, there was only partial overlap between the two volumes (Figure). The HV at week 5 was for respectively 48.6%, 43.5%, 39.2% and 38.6% of its volume located within the pretreatment HV (mean 42.5%). Of the pretreatment HV, 21.3%, 18.5%, 15.7% and 11.1% was still hypoxic after 5 weeks of CERT (mean 16.7%).

Conclusions: These preliminary results in a small number of patients suggest that, although there exists a general tendency towards shrinkage of the hypoxic volume within tumors during radiotherapy, the hypoxic fraction stays relatively constant. Both hypoxic volume and tumor volume decrease roughly similar in size, so the percentage of hypoxic cells within the tumor remains the same. Moreover, although there was considerable overlap between the hypoxic regions at the two time-points, the area of hypoxia migrates during treatment. This study is ongoing, results from more patients will hopefully confirm these conclusions and will be presented at the meeting.



838 poster

FATIGUE DURING RADIOTHERAPY (RT) FOR HEAD AND NECK CANCER: PROSPECTIVE STUDY ON 117 CONSECUTIVE PATIENTS

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4 - European Institute of Oncology, *Head & Neck Surgery, Milan, Italy*

Purpose/Objectif: RT related fatigue is an underevaluated cancer- and treatment-related symptom. Our aim was to analyze the fatigue in the head and neck cancer patients (pts) undergoing RT.

Materials/Methods: 117 pts were enrolled (mean age 58 years, F/M 24/93). Primary diagnosis included pharyngeal, laryngeal, oral cancer and other tumors in 42.8%, 20.5%, 24.8% and 7.7% of pts, respectively. 52 pts were treated with exclusive RT, postoperative RT was employed in 65 pts. Chemotherapy (CT) was added before and/or during RT in 61 pts. Mean RT dose was 65 Gy. Pts fulfilled a 20 item questionnaire (Multidimensional Fatigue Inventory, MFI-20) before RT, every RT week, 10 and 40 days after RT. Fatigue could range from 0 (minimum) to 80 (maximum). Evolution of fatigue level was analyzed and the impact of patient-, tumor-, and treatment-related factors was evaluated with uni- and multifactorial tests.

Results: Mean pre-RT fatigue level was 25.8±18.5 (range 0-76). During RT fatigue level was highest at week 6 (36.1±21.8), lowest at week 1 (27.2±19.1). After RT, mean fatigue level was 32.8±21.8. Multivariate stepwise regression analysis showed that the factors correlated with higher pre-RT fatigue level included age (inversely related, $P<0.05$), psychiatric disorders ($P<0.005$) and previous head&neck surgery (inversely related, $P<0.001$). Pulmonary disease, although not statistically significant, seemed to be related to higher pre-RT fatigue level ($0.05<P<0.1$). Factors correlated with higher maximum fatigue level during RT included pre-RT fatigue score ($P<0.0001$), induction CT ($P<0.001$) and cortisone use during RT ($P<0.005$). A remarkable although not statistically significant relationship, involved weight loss<5% and age ($P=0.088$ and $P=0.077$ respectively). Factors correlated with higher fatigue level after RT included pre-RT fatigue score ($P<0.0001$), induction CT ($P<0.001$), cortisone use during RT ($P<0.005$) and age (inversely related, $0.05<P<0.1$). No impact of sex, KPS, comorbidities other than psychiatric, tumor stage/site, RT intent, dose, volume, duration and toxicity was observed.

Conclusions: Fatigue affects the majority of pts undergoing RT for head and neck cancer, reaches maximum score at 6th RT week and slowly decreases after RT. Pre-RT fatigue score, age, CT and cortisone use are correlated with fatigue levels during and after RT. Further studies are warranted to define better the causes, prevention and management of this symptom.

839 poster

HIGH DOSE HYPERFRACTIONATED RE-IRRADIATION OF HEAD AND NECK TUMORS

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Purpose/Objectif: The treatment of a locoregional recurrence or second cancer in the head and neck is a difficult and increasingly important clinical problem. We report our first experiences of a high dose radiation retreatment with curative intend in this group of patients.

Materials/Methods: 24 patients of the Department of Radiation Oncology of the Technische Universität of Dresden were identified who had a second course of high-dose (<60 Gy) radiation therapy to the head and neck region because of local (n=12) or regional (n= 6) recurrence or second cancer (n=6) from 1997 to 2006. 10/24 had surgery before the second course of RT (R1=7, R2=3). Time intervals between the radiation treatments were 13 to 410 months (median 63). Except one patient the dose per fraction was 1.2 Gy b.i.d.. 4 patients had also adjuvant radiation to the neck. Additional chemotherapy (Mitomycin/ 5-FU, Cisplatin w/o 5-FU) was given to 16 patients.

Results: 22/24 patients received the planned dose (60-72 Gy, median 65 Gy), resulting in a total physical dose of 80 to 142 Gy (median 129 Gy). 2 patients stopped their treatment at doses of 46/ 59 Gy. Early or late toxicity (< G2) was observed in 11 patients. 8/11 had confluent mucositis, 1/11 severe pain, 1/11 osteoradionecrosis (but tumor recurrence was found in the same region), 1/11 had tracheotomy for chronic laryngeal edema after a third course of radiation to the hypopharynx. 13/24 patients are alive with a follow up of 2-77 months (median 37), 14/24 had a failure within or at the edge of the treatment volume (42% actuarial local tumor control/ 3 years) and 7/24 had distant metastasis.

Conclusions: A second course of high dose hyperfractionated radiation therapy in combination with chemotherapy is feasible in selected patients with a high probability of local tumor control and acceptable acute and late toxicity.

840 poster

HYPERFRACTIONATED ACCELERATED RADIOTHERAPY IN LOCALLY ADVANCED HEAD AND NECK CANCERS EXCEPT NASOPHARYNGEAL LOCALIZATION: FIVE YEARS RESULTS

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Purpose/Objectif: Head and neck cancers are rapidly proliferating and radiosensitive tumors. While trying to give optimum doses to tumor we must protect the functional neighbourhood normal tissues to keep the morbidity minimum. Increase in number of fractionation daily and decrease in total treatment time give more promising results in clinical practise.

Materials/Methods: Twenty patients diagnosed as head and neck cancer (except nasopharyngeal carcinomas) applied to our center between August 2000-July 2001 were choosen for this trial. Most of them (70 %) were male. Median age was 63 (42 -78) and 40 % of them were above 70 years of age. Performance status of patient were above 70 according to Karnofsky Scale. Almost all of them (95 %) were epidermoid carcinoma in histology. Most of the tumor were located in larynx (40 %) then hypopharynx (25 %). Others were as follows: Base of tongue (20 %), maxillary sinus (10 %), oropharynx (5 %). Most of them (95 %) were in stage IV. A daily dose of 1.5 Gy thrice a day in six hours intervals were given on each day of twelve consecutive day with the exception of weekend (total treatment time was 16 days). Large volume (primary tumor and locoregional lymphatics) was irradiated first nine days with a total dose of 4050 cGy. Then spinal cord was restricted and small volume (primary tumor and involved lymphatics) was irradiated 1350 cGy additionally. Early and late morbidity parameters were scored according to RTOG-EORTC morbidity scale.

Results: Median follow up was 62 months (57-67). Overall response rate were 85 % (35 % of them were complete and 50 % of them were partial response). Five years locoregional recurrence and distant metastasis rates were 55% and 20 % respectively. Two patients were died due to treatment complications. Five patients (25 %) are stil alive as complete responders except one. Grade 3 mucositis and dysphagia were seen 28 % and 20 % respectively. Overall grade 3 toxicity was 24 %. No grade 4 toxicity was seen. Grade 4 late toxicity was seen just in one case (because of his comorbidity). Five years progression free and overall survivals were 20 % and 25 %.

Conclusions: High percentage of late stages and relatively low total dose can be the reason of our locoregional failure. Our schedule was acceptable regarding the toxicity. To decrease locoreginal recurrence we can increase the total dose using conformal techniques, add a chemotherapeutic agents concomitantly and newly delivered targeted therapy agents in addition.

841 poster

HYPOFRACTIONATED RADIOTHERAPY IN OROPHARYNGEAL CANCER: TOXICITY AND EARLY OUTCOMES WHEN GIVEN ALONE OR COMBINED WITH INDUCTION CHEMOTHERAPY

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Purpose/Objectif: Hypofractionated radiotherapy (RT) schedules have routinely been used in the UK for many years in the treatment of oropharyngeal cancer. Addition of chemotherapy (CT) means management of toxicity remains challenging. This small study assesses clinically relevant toxicities and early outcomes with a hypofractionated regime given alone or in combination with induction CT.

Materials/Methods: Retrospective review of patients diagnosed with oropharyngeal squamous cancer between 1st January 2004 and 31st December 2005, treated with induction CT (1-3 cycles cisplatin 80 mg/m^2 or carboplatin d1 and 5-FU 800 mg/m^2 d2-5, 3 weekly) followed by RT (55 Gy in 2.75 Gy/fraction over 28 days, to primary disease and relevant lymph node regions), or RT alone.

Results: 72 patients were diagnosed during this period, 27 (38%) were treated with hypofractionated RT, of these 13 received induction CT. 16 patients required in-patient care for treatment related symptoms, average admission length 16 days (range 5-55 days). Admission was required for 11 of 13 patients given induction CT, and 5 of 14 receiving RT alone ($c2=6.68$, $p£0.01$ 95% CI 41.7-75.5). Enteral nutritional support was required in 16 patients, 10 with prior CT and 6 having RT alone ($c2=3.24$, $p£0.1$), with mean duration of support 85 days (range 12-293 days). The majority had grade 3 (RTOG) mucosa and skin reactions. 9 of 12 patients requiring opiate analgesia received induction CT. There were no treatment related deaths and all patients completed treatment. 6 weeks post treatment complete clinical response was seen in 10 of 13 given induction CT and 7 of 14 who received RT alone. After mean follow-up of 171 days (range 41-590 days) 19 patients have no clinical disease (10 received induction

CT and 9 RT alone), 5 have died of non-responsive disease and 1 has metastatic disease.
Conclusions: 55 Gy in 20 fractions is effective in oropharyngeal cancer, but has significant toxicity. Addition of chemotherapy may increase complete response rate, however increases toxicity and demand on in-patient services . Further follow-up is required to assess long-term outcomes.

842 poster

IMPACT OF NOVEL TECHNOLOGIES ON CANCER TREATMENT: PET/CT WITH IMRT IMPROVES TREATMENT OUTCOME OF PHARYNGEAL CARCINOMA

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3 - Zurich University Hospital, *Nuclear Medicine, Zurich, Switzerland,*
4 - Instituto Oncologico della Svizzera Italiana, *dept, Bellinzona, Switzerland,*
5 - Kantonsspital Chur, *dept, Chur, Switzerland*

Purpose/Objectif: The impact of non-pharmacological innovations in oncology is difficult to assess. The clinical benefit of 2-[18-F]-fluoro-2-deoxyglucose-positron emission tomography and integrated computer tomography (PET/CT) in combination with intensity-modulated radiotherapy (IMRT) for curative treatment of advanced pharyngeal carcinoma is not defined.
Materials/Methods: 45 consecutive patients with AJCC stage IVA carcinoma of the oro- and hypopharynx were staged with a PET/CT and treated with IMRT. In order to estimate the impact of PET/CT with IMRT on definitive RT and outcome, a matched pair analysis was performed. Patients with PET/CT and IMRT were matched with patients without PET/CT and IMRT with respect to gender, age, stage and grade, tumor location (oro-/hyopharynx), 3D-conformal treatment planning, and concomitant chemotherapy with a ratio of 1:2. The 86 control patients were treated from January 1991 to December 2001 and got all 3D conformal RT with curative intent. The median follow-up time was 18 months (range, 6-49 months) for the PET/CT-IMRT group and 28 months (range, 1-168 months) for the controls.
Results: Patients with PET/CT treated with IMRT fared better than patients without access to PET/CT and IMRT. The overall survival of patients with PET/CT-IMRT was 97% and 91% at 1 and 2 years respectively, compared to 74% and 54% for patients without PET/CT (p=0.002). The event-free survival rate of PET/CT-IMRT group was 90% and 80% at 1 and 2 years respectively, compared to 72% and 56% in the control group (p=0.005).
Conclusions: Modern RT with PET/CT and IMRT for pharyngeal carcinoma improves oncological treatment outcome.

843 poster

IMPORTANCE OF PATIENT, TUMOUR AND TREATMENT RELATED FACTORS ON QUALITY OF LIFE IN HEAD AND NECK CANCER PATIENTS AFTER DEFINITIVE TREATMENT

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Purpose/Objectif: Quality of life (QoL) of a cancer patient after definitive treatment for head and neck cancer could be affected by many factors. The aim of this study was to assess the patient, tumour and treatment related factors on quality of life (QoL) outcomes of patients received definitive or postoperative radiotherapy with or without chemotherapy for head and neck cancer.
Materials/Methods: In this cross sectional study, 108 head and neck cancer patients who attended for a scheduled follow-up visit in a 3 months period were evaluated. Patients were asked to fill out the Turkish version of European Organisation for Research and Treatment of Cancer Quality of Life Core Questionnaire (EORTC) as well as the EORTC Head and Neck Module (EORTC QLQ-H&N35). During the visit patients were also graded for their late side effects using EORTC / RTOG scoring system. The QLQ C-30 and QLQ-H&N35 mean scores were compared using ANOVA analysis for these variables: age, gender, occupation, educational status, social security status, place of residence, tumour localization, clinical stage, co-morbidity, karnofsky performance score, treatment modality and presence of grade 3-4 side effects.
Results: Fifty one (47%) patients were treated with adjuvant radiotherapy and 57 (53%) with radical radiotherapy with or without chemotherapy. Median follow up was 26 (2-155) months. Tumour location was a significant factor affecting physical (p=0.03), social (p=0.01) and cognitive (p=0.01) functioning scores. Patients with nasopharyngeal primary had the worst scores. The only significant factor affecting the role functioning was the gender with females having worst scores (p=0.05). Treatment modality also had a significant impact on the physical and cognitive scores with patients receiving chemoradiotherapy having the worst scores (p=0.01). Global quality of life was affected significantly by the clinical stage (p=0.02), the occupation (p=0.01) and the social security status (p=0.009) of the patient. EORTC / RTOG late morbidity scores were grade 0-1 in 46 (43%), grade 2 in 46 (43%) and grade 3 in 16 (14%) patients. The analysis of QLQ-H&N35 symptom scores were found significantly higher in patients with moderate or severe late morbidity such as pain (p=0.01), swallowing (p=0.003), senses (p=0.01), social eating (p=0,03), teeth (p=0.02), open mouth (p =0.001), dry mouth (p=0.005) and sticky saliva (p=0.01).
Conclusions: Tumour location and treatment modality are the most important factors affecting the quality of life of head and neck cancer patients treated definitively however it is very important to consider other patient related factors to be able to understand and support our patients. Patients with higher symptom scores have higher grades of morbidity as expected.

844 poster

IMPROVEMENT IN TARGET COVERAGE AND IN SPARING OF ORGAN AT RISK FOR OROPHARINGEAL CANCER WITH HELICAL TOMOTHERAPY: A PLANNING STUDY

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Purpose/Objectif: The goal of this study was to estimate the ability of Helical Tomotherapy (HT) to optimize the dose distribution in patients with oropharingeal cancer (OPC) using a simultaneous integrated boost (SIB) approach.
Materials/Methods: Four T1-3 N0-2 OPC patients were considered. Two IMRT plans, both in SIB modality, were performed for each case: one with the TomoTherapy Hi·Art2 System® and the remaining with dynamic MLC (Varian 600CD Linac, Millennium™ MLC-80) inversely optimised by the Helios/Eclipse system. The plan prescriptions were 54 Gy, 61.5 Gy and 64.5 Gy delivered in 30 fractions to 95% of PTV1 and at the median dose of PTV2 and PTV3 respectively, where PTV1, 2 and 3 correspond to low-risk nodes, high-risk nodes and tumour respectively. The same optimisation goals were followed for PTV coverage and for parotids, mandible, spinal cord, brain stem and

optical pathways sparing in both modalities. The planner also tried to reduce the dose to other structures: larynx, thyroid, esophagous, sub-mental connective tissue, brain, lung apexes.
The comparison was performed considering a number of dose-volume parameters, like D_mean, D_median, D_max and fractions of volume V receiving at least a dose d (Vd). The conformity index (CI) and the normalized treated volume (TV) were also considered. The first was defined according to ICRU 50; TV was defined as the percentage of body outside to PTV receiving more than a "high" dose level: in this case the 90% and 95% of prescribed dose to PTV1.
Results: Results show a better coverage with HT for all PTVs: the fraction of PTV1, 2 and 3 receiving more than 95% of the prescribed doses (V95%) increased from 98.3% to 99.7%, from 97.7% to 99.7%, from 95.6% to 98.2% respectively; moreover, a better homogeneity of the dose distribution within each PTV was found; for example, D_Max for PTV3 reduced from 70.4 Gy to 67.6 Gy.
Concerning OARs, HT showed a much more efficient sparing: D_median of the parotids decreased from 31.3 Gy to 25.8 Gy and the spinal cord D_Max decreased from 40.4 Gy to 35.5 Gy. For other structures, like thyroid and esophagous, D_mean was reduced on average of about 15 Gy. $(TV90\%)_{HT}/(TV90\%)_{IMRT}$ equal to 0.7 and $(TV95\%)_{HT}/(TV95\%)_{IMRT}$ equal to 0.8 were found, showing that HT significantly decreased the tissues irradiated at high dose outside PTV.
Conclusion: In conclusion, HT significantly improves the homogeneity of dose distribution within PTV and PTV coverage together with a much larger sparing of OARs with respect to conventional IMRT.

845 poster

IMRT FOR SINONASAL CANCER: RESULTS IN 32 PATIENTS AT THE UNIVERSITY HOSPITAL GASTHUISBERG LEUVEN

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Purpose/Objectif: To evaluate acute and late toxicity, as well as efficacy, of IMRT in the treatment of sinonasal cancer.
Materials/Methods: Since January 2003, sinonasal tumors are treated with IMRT at Leuven University Hospital . An inverse-planning IMRT technique (sliding window) is used, based on a non-coplanar 6-field arrangement. When appropriate, the planning CT's were co-registered with pre-operative MRI scans to allow more accurate delineation of the CTV and OARs. A 5-mm isotropic margin was used for the expansion of CTV to PTV. The following structures were contoured as OARs: optic nerves with retina (≤ 60 Gy), optic chiasm (≤ 60 Gy), both lenses, brain (≤ 60 Gy), spinal cord and brainstem (≤ 50 Gy). Acute and late toxicity were prospectively scored for all patients (CTC version 3.0).
Results
Between January 2003 and February 2006, 32 consecutive patients with cancer of the paranasal sinuses (n = 30) or nasal cavity (n = 2) were treated with postoperative (n = 29) or primary (n = 3) IMRT. The histological types were adenocarcinoma (n = 18), SCC (n = 4), sarcoma (n = 3), melanoma (n = 2), mucoepidermoid carcinoma (n = 2), esthesioneuroblastoma (n = 2) and adenoid cystic carcinoma (n = 1). Staging was T2 in 18.8%, T3 in 34.3%, T4a in 28.1% and T4b in 18.8% of patients. None of the patients had evidence of regional or distant metastasis. The total dose ranged between 60 Gy (n = 19), 66 Gy (n = 9) or 70 Gy (n = 4). Median follow-up was 13 months (range, 3 - 34 months). At 1 year, LC was 84%, OS 87% and DFS was 80%.
No Grade III or IV acute toxicity was observed. Most frequent acute toxicities (Grade I and II taken together) were dermatitis (84.4%), xerostomia (81.3%), taste disturbance (84.4%), altered smell (65.6%) and mucositis (59.4%). Ocular and visual morbidity was mild. Conjunctivitis (46.8%), keratitis (71.9%) and tearing (46.9%) were frequent. Patients rarely complained of dry eyes (12.4%), blurred vision (24.9%), double vision (6.2%) or photophobia (6.2%).
Late toxicity was available for 27 patients. No Grade III or IV late toxicity was reported. Most frequent complications at 3 months after RT were fatigue (30.6%), altered taste (25.9%), and headache (16.5%). Regarding eye/vision, 5 patients (18.5%) scored Grade I conjunctivitis; no Grade II was reported. At 6 months after RT, only 2 of those 27 patients still scored Grade I eye toxicity, without decreased vision. For 15 patients, follow-up was available until 2 - 2.5 years after RT. None of those patients developed any severe RT-induced late toxicity, such as retinopathy or optic neuropathy.
Conclusions
IMRT for sinonasal carcinoma resulted in very little acute and late toxicity, while preserving short-term LC. Longer follow-up is necessary to evaluate long-term results. ☒

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846 poster

INDUCTION CHEMOTHERAPY (CT) FOLLOWED BY ALTERNATING CHEMO-RADIOTHERAPY (CT-RT) IN STAGE IV UNDIFFERENTIATED NASOPHARYNGEAL CARCINOMA (UNPC)

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Purpose/Objectif: In locally advanced UNPC concomitant CT-RT is standard treatment. Induction CT followed by alternating CT-RT may improve the results further by enhancing both locoregional and distant control.
Materials/Methods: The treatment protocol for 50 patients (between May 1995 and November 2003) with locoregionally advanced UNPC consisted of 3 courses of induction CT with epidoxorubicin and cisplatin (CDDP) every 3 weeks. After radiological and clinical response assessment patients underwent 3 courses of fluorouracil and CDDP bolus (weeks 1,4,7) alternated with 3 splits course of radiation (weeks 2-3, 5-6, 8-9-10) consisted of 70 Gy delivered as daily single doses of 2 Gy, 5 times a week. 3-D conformal technique with individualized half-fields to cover CTV1 (tumor with surrounding areas at high and low risk pre induction CT), restricted CTV2 (tumor and areas at high risk), CTV3 (lower neck and supraclavicular regions) and GTV (residual tumor and neck nodes after induction CT) were planned.Histology was WHO type 1 in 1 patient (2%), WHO type 2 in 10 patients (20%) and WHO type 3 in 39 patients (78%). All patients had stage IV disease.
Results: All the patients are evaluable for response and toxicity. At the end of induction phase 12% of CRs, 84% of PRs and 4% of SD were recorded. All patients but two had the planned of CT courses in the alternating phase and all but one received the planned RT dose. Grade III-IV mucositis in 28% of patients, grade III-IV haematological toxicity in 24% of patients were observed. At the final response evaluation 86% of CRs and 14% of PRs were observed. At a median follow up of 39 months, 16% of patients had locoregional failure (10% local only , 2% nodal only and 4% local and nodal), 20% had distant failure and 2% both. The 4-year actuarial progression free survival and overall survival rates are 71% and 81%, respectively.
Conclusions: Treatment of locoregionally advanced UNPC with this schema of CT-RT is feasible and patients compliance is optimal; induction CT does not seems increase toxicity. 4-year outcome evidenced excellent locoregional control with an high survival probability.

847 poster

INDUCTION COMBINATION CHEMOTHERAPY WITH GEMCITABINE AND CISPLATIN IN LOCALLY ADVANCED HEAD AND NECK CANCER.

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Purpose/Objectif: The optimum induction chemotherapy for patients with advanced head and neck cancer is controversial. The primary objective of this study was to evaluate the activity and toxicity of combination of cisplatin and gemcitabine in previously untreated patients with locally advanced head and neck cancer.

Materials/Methods: Twenty patients with previously untreated advanced head and neck cancer (AJCC Stage IVB) were treated between August 2005 and January 2006. M:F ratio was 60%:40% with a median age of 50 years. The site of disease was oral cavity 35%, paranasal sinuses 30%, hyopharynx 25%, oropharynx 5% and larynx 5%. Histologically 95% were squamous cell carcinomas and 5% had adenocarcinoma. All patients had good performance status (ECOG 0-1). Staging was based on clinical and MRI findings. The decision on unresectable disease was in conjunction with head and neck surgeon. TNM stage was; T4bN0M0 40%, T4bN1M0 5%, T4bN2M0 45% and T4bN3M0 5%. Two 3 weekly cycles of cisplatin 75 mg/m^2 day 1 and gemcitabine 1000 mg/m^2 day 1 and 8 were given to all patients. Toxicity was scored after each cycle and response assessed following completion of second cycle.

Results: All patients were available for assessment of toxicity and response. No grade 3 - 4 haematological, renal or hepatic toxicity was seen. Response at the primary site was complete (CR) 25%, partial (PR) 60% and no response/progression was seen in 15% of the patients. The overall response at primary site was 85%. In 12 patients with node positive disease complete, partial and no response/progression of lymph nodes was seen in 9%, 58% and 33% respectively. The overall response in cervical lymph nodes was 67%. Patients with complete or partial response went on to receive radical chemoradiation.

Conclusions: Cisplatin and gemcitabine combination is well tolerated with low toxicity and high anti tumour activity in untreated head and neck cancer. Forthcoming studies focusing on induction chemotherapy in head and neck cancer should include arms with cisplatin gemcitabine combination regimens.

848 poster

MASPIN EXPRESSION VALUE IN PREDICTING THE OUTCOME OF PATIENTS WITH SQUAMOUS CELL CARCINOMA OF THE HEAD AND NECK

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Purpose/Objectif: Maspin is a tumor suppressor protein reported to be downregulated in numerous types of cancer. The aim of the present study was to determine the prognostic/predictive value of the expression of this protein in patients with H&N cancers (HNC).

Materials/Methods: We evaluated maspin immunohistochemistry in pretreatment samples of 120 patients with HNSCC using microarray technique. All patients were treated in one institution from 1992 to 2000 with an accelerated RT schedule ± cisplatin based chemotherapy.

Results: Maspin has shown to have a significant association with histology grade (p=0.0074), where low maspin expression is associated with high tumor grade. In multivariate analysis for disease-free survival (DFS), beside N- and T-categories, maspin was found to be of borderline significance (p= 0.06). Tumors showing the combination of loss of maspin/low histological grade had longer DFS (83%) vs. those with high maspin/high histological grade (DFS 42%) (p=0.08).

Conclusions: The present study is the first to determine the value of maspin in HNC in a large series of patients. Maspin seems to have a potential prognostic value in patients with HNC, thought that the results need further confirmation.

849 poster

MODERATE DOSE HYPERFRACTIONATED RADIOTHERAPY AND CONCURRENT CHEMOTHERAPY FOR HEAD AND NECK CANCER

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Purpose/Objectif: Despite advances in therapy, local control and survival for stage III and IV head and neck cancers remains poor. Randomized phase III studies have proved the benefit of hyperfractionated radiation therapy [HRT] over once-daily radiation therapy. Similarly, the superiority of combined chemo-radiotherapy over (once-daily) radiation therapy alone has been demonstrated. Relatively few studies so far have reported on the results of combined chemotherapy and HRT.

Materials/Methods: 34 patients with stage III and IV squamous cell carcinoma of the head and neck were treated by concurrent chemotherapy and HRT between June 2000 and September 2004. Six patients were diagnosed with laryngeal cancer and 28 patients were diagnosed with oropharyngeal cancer. Radiation therapy was given twice daily with < 6 hours between fractions. The total HRT dose to the primary tumor site ranged from 7130cGy to 7590 cGy with median fraction size of 115cGy. Single agent chemotherapy using either carboplatin (AUC=2) or cisplatin (50 mg/m^2) was administered, on a weekly basis, concurrently with HRT. Node positive patients underwent planned neck dissection following completion of treatment. All patients had pre-RT dental oncology evaluation, comprehensive dietary evaluation, and nutritional surveillance including use of feeding gastrostomy tubes.

Results: With median follow-up of 26 months, one patient experienced local recurrence and another patient developed regional relapse as first site of failure corresponding to 2 year actuarial local-regional control rate of 92.2%. One patient developed distant metastasis as the first site of treatment failure and four patients expired from intercurrent illness without evidence of treatment failure. The 2 year overall survival and disease free survival rates were 82.3% and 89% respectively. Median survival had not been reached. All pa-

tients completed planned HRT and 75 % of patients completed the RT course within 7 1/2 weeks.
Conclusions: Concurrent chemotherapy with HRT yielded superior local regional control and overall survival rates for a group of patients with advanced head and neck cancer. Longer follow-up will be necessary to determine the durability of response. This excellent result was achieved with HRT dose that is lower than what has been reported in other studies. The possibility of de-escalation of HRT dose in the setting of concurrent chemotherapy deserves further investigation.

850 poster

ORAL CANDIDIASIS (OC) AND CANDIDA CULTURES EVOLUTION DURING AND AFTER RADIOTHERAPY FOR HEAD AND NECK CANCER (HNC)

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Purpose/Objectif: Prospective analysis of the Candida type in cultures in patients (pts) irradiated for head and neck cancer that develop oral candidosis.
Materials/Methods: 100 pts irradiated for HNC and receiving more than 50 Gy in 75% of the major salivary glands. Candida cultures (Cromagar) were performed before radiotherapy and in those pts that developed OC the cultures were done before antifungal therapy and after irradiation having resolution of OC.
Results: Before radiotherapy: 64/100 (64%) pts exhibited negative cultures (NC) & 36/100 (36%) had positive cultures (PC) for: 29/36 (80%) C. Albicans, 2/36 (5.5%) C. SPP, 2/36 (5.5%) C. Krusei, 1/36 (2.7%) C. Tropicalis, 1/36 (2.7%) C. Parapsilosis, 1/36 (2.7%) C. Glabrata. During radiotherapy: 33/100 (33%) of pts developed OC of which 18/33 (54.5%) had NC and 15/33 (45.5%) had PC. Candida type in cases PC: 9/33 (27.2%) C. Albicans and the rest (72.8%) for C. Pstutzeri (3%), C. Krusei (6%), C. Parapsilosis (6%), C. Tropicalis (6%), C. Glabrata (6%), C. Geotrichum (6%). After radiotherapy: 15/33 (45.5%) had NC and 18/33 (54.5%) had PC. C. Albicans was present in 46.2% of the PC and the rest were C. Krusei (9.9%), C. Guilliermondi (6.6%), C. Lipolytica (3.3%), C. Species (3.3%), C. Tropicalis (3.3%), C. Rugosa 3.3%, C. Kefir (3.3),C. Rhodotorula (3.3%), C. Parapsilosis (22.1 %), C. Glabrata 6.6%, C. Tropicalis (6.6%).
Conclusions: 36% of the pts had PC for Candida before radiotherapy, where C. Albicans was present in the 80% of the cases. Oral candidosis developed in 33% of patients during radiotherapy and it can appear both in cases with previous PC & NC. The incidence of C. Albicans decreases in cases with OC and after radiotherapy in favour of other Candida types.

851 poster

ORGAN PRESERVING TREATMENT OF PATIENTS WITH T1-T2 N0 ORAL CAVITY CANCER USING HDR INTERSTITIAL BRACHYTHERAPY AND IMRT TELERADIOTHERAPY.

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Purpose/Objectif: To present a method of organ and function preserving treatment in patients with floor of the mouth and mobile tongue cancers as well as to evaluate early results of proposed modality.
Materials/Methods: Data charts of 20 - 18 (90%) male and 2 (10%) female patients treated between January 2002 and November 2004 in Brachytherapy Department and I Radiotherapy Clinic of Institue of Oncology In Gliwice were evaluated. Median age was 55 years. There were 15 (75%) patients with lip cancer and 5 (15 %) with oral cavity cancer. There were 12 (60%) patients with T2 and 8(40%) with T1 tumour. In all cases pathological examination revealed squamous cell cancer. Teleradiotherapy was planned to the primary tumour and local lymph nodes (level I and II), to the doses from 50Gy to 60Gy in 25 or 30 fractions. In 2 (10%) patients only unilateral neck nodes were irradiated. All patients were treated using IMRT technique, with 5 to 9 fields, to spare the critical stuctures like parotid gland and spinal cord as well as mucosal membrane of phanynx and larynx. In all cases, up to 10 days after teletherapy interstitial brachytherapy was performed using flexible, afterloading catheters. All applications were performed under general anaesthesia. In all cases IBU simulation was used to control geometry of catheters as well as 3-D planning system (Plato). Median total dose in reference point was 18 Gy (ranged from 15 to 21Gy) and median treatment time was 4 days. Median target volume surrounded by the therapeutic isodose was 30cm^3 (ranged from 18 to 52 cm^3). All patients were treated using hiperfractionation regime with two (3Gy) daily fractions given with at least 6 hour gap. Median follow up was 24 months.
Results: After median follow up of 2 years all patients are alive. 2 (10%) patients, 3 and 6 months after treatment, one with tounge and one with floor of the mouth tumour, had local recurrences. One of them also presented nodal metastases. Both were succesfully salvaged with surgery. No distant metastases were noticed. Medial, maximal acute mucosal reaction during teleradiotherapy according to Dische scale ranged 10 points. During and after brachytherapy acute mucosal reactions, with confluent mucositis in 15 (75%) patients, were noticed, but did not exceed 15 points in Dische scale. No toxicity connected with implatation was noticed. One patient suffered from severe mucositis which retreated after two weeks of local treatment. No cosmetic or functional deficites of treated strucutures were found. During the follow up no severe late reactions were noticed. Only one patient (5%), 12 months after radiotherapy, developed radionecrosis of mandible bone after inadequate teeth extraction.
Conclusions: Results of our analysis suggests that combination of IMRT radiotherapy and interstitial HDR-brachytherapy is an useful method in the treatment of T1-2 tumours of oral cavity and can be considered as an alternative to surgery. Such treatment provides similar to surgery and postoperative radiotherapy results but the function of the tongue and other important structures is preserved. Toxicity of proposed modality is acceptable and well tolerated by the patients. Using conformal teletherapy plannig -IMRT- and 3-D brachytherapy allows to escalate the doses to the tumour and to avoid irradiation of sourounding critical structures.

852 poster

PATTERNS OF RELAPSE AFTER EXTERNAL BEAM RADIOTHERAPY FOR WELL DIFFERENTIATED THYROID CANCER: IMPLICATIONS FOR TARGET VOLUME DELINEATION

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Purpose/Objectif: To determine the pattern of recurrence in patients with well differentiated thyroid cancer who received radiotherapy and radioiodine ablation following surgery or biopsy with a view to optimising target volume delineation.

Materials/Methods: 49 patients with well differentiated thyroid cancer received adjuvant external beam radiotherapy and radioiodine ablation at the Christie Hospital between 1990 and 2000. The thyroid bed and regional nodes (excluding the spinal cord) were irradiated using a lateral tipped down parallel opposed pair of 6 MV photons to a dose of 47.5Gy in 16 fractions over 22 days. There was no attempt to irradiate the superior mediastinum.
Results: Median follow-up was 65 months (range 11-149 months). Patients were staged as follows: T3 - 3, T4 - 41, Tx - 5, N0 - 32, N1 - 16, Nx - 1. Twenty-nine patients had clear or microscopic positive resection margins and 19 had macroscopic residual disease postoperatively. Eight patients had inoperable disease. Local control at 5 years was 89% for those with clear or microscopic positive margins and 69% for those with macroscopic residual disease. 5-year cause specific survival was 60% for patients with macroscopic residual disease and 90% for those with clear or microscopic positive margins. Relapses occurred in the thyroid bed in 6 patients, neck nodes in 8 patients and mediastinum in 4 patients. Distant metastases occurred in 5 patients and biochemical relapse in 3 patients. Mediastinal recurrence did not occur in isolation.
Conclusions: The status of postoperative margins is important for local control and cause specific survival. The majority of recurrences were loco-regional and there were few cases of mediastinal recurrence, which did not occur in isolation. Therefore, we propose the target volume to include the thyroid bed and regional neck nodes and spare the mediastinum, thus facilitating dose escalation to improve loco-regional control. Further studies to define the optimal target volume are needed.

853 poster

PDR INTERSTITIAL BRACHYTHERAPY IN RECURRENT AND PREVIOUSLY IRRADIATED HEAD AND NECK CANCER

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Purpose/Objectif: A large majority of patients with recurrences of head and neck cancers are disqualified from radical treatment and constitute a group of bad prognosis. Some of them can be qualified for salvage surgery and treated mostly with a palliative intent. In some cases brachytherapy can be a treatment of choice after previously applied external beam radiotherapy. The paper is to present results of PDR interstitial brachytherapy in a described group of patients.
Materials/Methods: Thirty two patients with recurrent head and neck cancer were treated with PDR interstitial brachytherapy since October 2000 till October 2005. The age of patients ranged from 41 to 79 years, average 59,2 years. The group consisted of 4 women (12,5%) and 28 men (87,5%). Clinical locations were: tongue and floor of the mouth (5), oropharynx (4), laryngopharynx (1), larynx (16), lip (1), orbit (2), salivary gland (3). 26 patients were previously both operated and irradiated (81,3%), 2 were irradiated (6,3%) and 4 were operated (12,5%) as a single modalities. Primary lesions were irradiated with an average total dose of 56 Gy. Median time between primary tumor and its recurrent appearance was 11,9 months (min. 1 and max. 54 months) and it was longer than 12 months in 10 patients. Recurrences were treated up to total dose of 50 Gy, most commonly with a single fraction of 20 Gy in 25 pulses by 0,80 Gy. The assessment of the results was performed 4 weeks after completion of the treatment and then after 3, 6 and 12 months.
Results: Average observation time was 5 months. 14 patients (43,8%) died within the whole follow-up period. 9 and 12 of them died within 6 and 12 months after brachytherapy, respectively. 4 weeks after the end of the treatment complete remission (CR) was found in 8 (25%), partial remission (PR) in 15 (46,9%) and no remission (NR) in 9 (28,1%) cases. After 3 and 6 months remission (CR + PR) was observed in 16 (50%) and 11 (34,4%) patients, respectively. Recurrences or locoregional dissemination were observed in all patients who survived 12 months or more.
Conclusions: 1. PDR brachytherapy can be a treatment of choice in patients previously irradiated with external beam radiotherapy and/or surgery. 2. It appears to be, that in some cases PDR brachytherapy can prolong overall survival time. 3. To confirm the above a comparative investigation of a larger group of patients is needed.

854 poster

PERFORMANCE OF [18F]FLT-PET FOR THE ASSESSMENT OF LYMPH NODE STATUS IN HEAD AND NECK CANCER PATIENTS

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Purpose/Objectif: Repopulation of clonogenic tumor cells is inversely correlated to radiation therapy treatment outcome in head and neck cancer. Treatment modifications such as accelerated radiotherapy and EGFR inhibition aim at counteracting this phenomenon. A functional imaging tool to assess the proliferative activity of tumors could improve patient selection for these treatments and be used for early treatment response evaluation. The novel PET tracer 3'-deoxy-3'-[^{18}F]fluorothymidine ([^{18}F]FLT) is trapped intracellularly during DNA synthesis and can image tumor cell proliferation prior to and during radiotherapy treatment and may provide biological tumor information useful in radiotherapy planning. In the present study, the value of [^{18}F]FLT-PET in determining lymph node status in squamous cell carcinoma of the head and neck was assessed, with pathology as a gold standard.
Materials/Method: Ten patients with newly diagnosed stage II-IV squamous cell carcinoma of the head and neck underwent [^{18}F]FLT-PET one week prior to surgical resection with lymph node dissection. One hour after injection of 250 MBq [^{18}F]FLT, emission PET and CT images of the head and neck were recorded and fused. Standardized uptake values (SUV) were calculated. Preoperatively, the exogenous proliferation marker iododeoxyuridine (IdUrd) was administered. From all 20 positive lymph nodes on [^{18}F]FLT-PET and from nine negative controls, paraffin embedded sections were stained and analyzed for the endogenous proliferation marker Ki67 and for IdUrd. Sensitivity, specificity, positive predictive value and negative predictive value were calculated for [^{18}F]FLT-PET.
Results: Primary tumor sites were oral cavity (7), larynx (2) and maxillary sinus (1). Nine of the ten patients examined had [^{18}F]FLT-PET positive lymph nodes on the PET images (SUV_{mean}: median 1.1, range 0.8-2.9), but only three of these patients had histologically proven metastases. All metastatic lymph nodes showed Ki67 and IdUrd staining in tumor cells as well as in residual germinal centers if present. The remaining seven patients - including the one negative on [^{18}F]FLT-PET - showed abundant Ki67 and IdUrd staining in germinal centers in both PET positive and negative lymph nodes. Sensitivity, specificity, positive and negative predictive values were 100%, 14.3%, 33.3% and 100%, respectively.
Conclusions: [^{18}F]FLT-PET scan showed uptake in metastatic as well

as in reactive lymph nodes in head and neck cancer patients. Because of the low specificity, [^{18}F]FLT-PET is not suitable for assessment of pretreatment lymph node status and possibly also not for early treatment response evaluation of small metastatic nodes.

855 poster

PROGNOSTIC SIGNIFICANCE OF PLASMA EPSTEIN-BARR VIRUS (EBV) DNA LEVEL IN PATIENTS WITH LOCALLY ADVANCED HEAD AND NECK (HN) CARCINOMA TREATED WITH CONCURRENT CISPLATIN AND CONCOMITANT BOOST RADIOTHERAPY (CBRT)

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Purpose/Objectif: EBV DNA is detectable in the plasma in most patients with lymphoepithelial carcinoma (LECA) and in some patients with squamous cell carcinoma (SCC) of the HN. We investigated the prognostic significance of plasma EBV DNA level in a prospective study of concurrent cisplatin and CBRT for locally advanced HN carcinomas.

Materials/Methods: Eligibility criteria included newly-diagnosed SCC or LECA of non-nasopharyngeal HN sites; stage III or IV disease; ECOG performance status ≤ 1; and age ≤ 70 years. Plasma EBV DNA levels were measured by real-time quantitative PCR in 48 controls, and in patients before treatment and at 6 weeks post-treatment. Pre-treatment gross tumor volume (GTV) was measured on CT, and invasion of bone and cartilage was assessed on CT and MRI. Cisplatin 40-50 mg/m^2 was given on days 1, 8, 15 and 22 of CBRT. Radiotherapy consisted of 54 Gy/30 fractions/6 weeks and a concomitant boost (18 Gy/12 fractions) in the last 12 treatment days. Survival curves were compared by the log-rank test and multivariate analysis was performed with Cox regression.

Results: Between March 2001 and January 2005, 46 patients were recruited (36 with SCC and 10 with LECA). Thirty-four patients had stage III and 12 had stage IV disease. Pre-treatment plasma EBV DNA level was < 0 copy/ml in all patients with LECA (range, 37 - 211737 copies/ml) and in 8 patients with SCC (range, 10 - 48734 copies/ml). The pre-treatment plasma EBV DNA levels in all patients with SCC (range, 0 - 48734 copies/ml) were higher than the levels in controls (range, 0 - 8 copies/ml, $p = 0.01$). Ten patients had plasma EBV DNA level < 0 copy/ml at 6 weeks post-treatment. At a median follow-up of 1.8 years for the whole series, the 1-year overall survival rate was 85%. The 1-year locoregional progression-free survival rate was 82% and 1-year distant metastasis-free survival (DMFS) rate was 78%. On multivariate analysis, stage IVb (HR, 6.1; $p = 0.01$) and plasma EBV DNA < 0 copy/ml at 6 weeks post-treatment (HR, 3.5; $p = 0.05$) were predictive factors of decreased DMFS for the entire group. In the subgroup of patients with SCC, stage IVb (HR, 7.6; $p = 0.02$) and post-treatment EBV DNA < 0 copy/ml (HR, 5.4; $p = 0.05$) were predictive factors of decreased DMFS.

Conclusions: Plasma EBV DNA level may be a prognosticator in patients with locally advanced HN SCC and LECA. Further studies are needed to confirm the finding and to elucidate its biological basis.

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QUALITY OF LIFE OUTCOME AFTER CONCOMITTANT CHEMORADIATION FOR INOPERABLE SQUAMOUS CELL CARCINOMA

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Purpose/Objectif: Concomitant chemoradiation (CHRT) is currently considered standard in inoperable head and neck squamous cell carcinoma (HNSCC). As the prognosis of these patients has improved significantly over the last decade, information regarding quality of life (QoL) outcome becomes increasing important. The purpose of this prospective cohort study was to evaluate QoL among patients that were treated with concomitant CHRT for inoperable HNSCC.

Materials/Methods: For the purpose of this study, 78 patients with inoperable HNSCC treated with CHRT were included. QoL was prospectively assessed using the EORTC QLQ-C30 and EORTC QLQ-H&N35 instruments before radiotherapy, and at 1 and 6 weeks, 6, 12, 18 and 24 months after completion of radiotherapy.

Results: The most frequently reported moderate or severe head and neck symptoms after CHRT were xerostomia (68%), sticky saliva (50%), trismus (42%), and swallowing complaints (38%). Although xerostomia and sticky saliva were the most frequently mentioned head and neck symptoms, swallowing complaints had the most impact on the more general QoL dimensions. In general, local and general symptoms were most pronounced at the end of radiation which was reflected into lower scores for the functioning scales and global QoL. After 6 months, a gradual reduction of symptoms and a gradual improvement of functioning and global QoL was observed. At 24 months, the scores of the more general QoL dimensions returned to a level similar to the normal population. The scores for the more general QoL dimensions were lowest in case of more persisting local symptoms, in particular dysfagia.

Conclusions: The results of this study indicate that CHRT results in a number of local symptoms influencing QoL of which those related to salivary function are the most frequently mentioned. Despite these local symptoms, a gradual recovery of the general QoL dimensions was observed that returned to a level similar to the normal population. However, in particular swallowing complaints had a major impact on QoL. Therefore, besides prevention of radiation-induced xerostomia, more attention should be paid to prevention of radiation-induced dysphagia by improved irradiation techniques.

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QUANTIFICATION OF PLASMA EPSTEIN-BARR VIRUS DNA IN PATIENTS WITH NASOPHARYNGEAL CARCINOMA: PRELIMINARY RESULTS OF A PROSPECTIVE STUDY

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Purpose/Objectif: Recently, quantification of plasma EBV DNA was shown to be useful for monitoring patients with nasopharyngeal carcinoma (NPC) and predicting the outcome of treatment. We designed a prospective study, to investigate the correlation between plasma EBV DNA levels and clinical status of the patients with NPC.

Materials/Methods: A total of 76 patients with NPC and healthy controls were enrolled between February 2004 and July 2005. The levels of circulating EBV DNA were measured in 3 NPC patient groups. Group A (24 patients): non-metastatic patients treated with curative

intent and measurements were made at diagnosis and after treatment. Group B (28 patients): patients in remission with conventional follow-up examinations and measurements were made at follow-up. Group C (5 patients): patients with evident clinical/radiological local and/or distant relapse. Group D: 19 healthy volunteers were selected as control groups.

Results: Group A: EBV DNA was detected quantitatively in plasma samples of 16 (67%) out of 24 patients at diagnosis. The median concentration of plasma EBV DNA at the time of initial diagnosis was 653 copies per milliliter (interquartile range, 153 to 15,599). The median EBV DNA concentration decreased to 0 copies per milliliter (interquartile range, 0 to 7,493) after the completion of treatment in all but two patients. A patient with detectable concentration of plasma EBV DNA at last control (7,493 copies/ml) who is in remission with conventional techniques developed diffuse lung and liver metastases 3 months later. EBV DNA level is decreased however detectable in the plasma of the second patient with remission. During follow-up, a quantitative increase was detected in three patients (two of them with clinical remission and one with distant metastases). A stage IVB patient with the highest plasma EBV DNA value at initial diagnosis developed diffuse bone metastasis after second cycle of neoadjuvant chemotherapy, however plasma EBV DNA was not detected quantitatively. Group B: During follow-up period, a quantitative increase in EBV DNA concentrations was detected (range 0-518 copies/ml) in 2 (11%) out of 28 patients. The PET imaging revealed biopsy confirmed liver, lung and bone metastases in one patient. The other patient is still in remission at last control. Group C: EBV DNA concentrations were measured quantitatively in one (50%) of 2 patients with distant metastases and one (33%) of 3 patients with local relapse. Group D: All healthy individuals have negative plasma EBV DNA.

Conclusions: This study showed that quantitative plasma EBV DNA can be detected approximately in 70% of the NPC patients at diagnosis. The plasma EBV DNA levels were persistently undetectable or low in patients with clinical remission. These results suggest that quantitative analysis of plasma EBV DNA may be a useful clinical tool in the screening and monitoring of NPC patients. However, longer follow-up is needed for mature results.

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RADIATION AND WEEKLY DOCETAXEL FOR ADVANCED HEAD AND NECK CANCER

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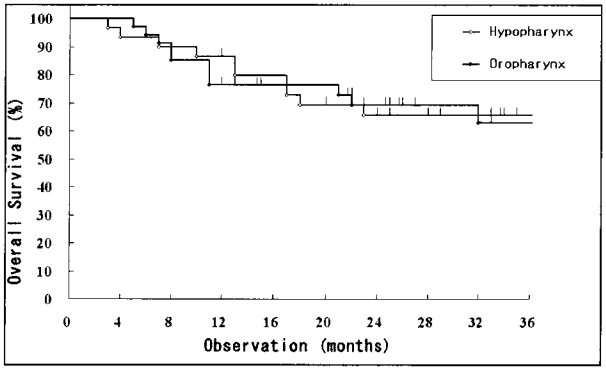
Purpose/Objectif: To evaluate the initial response and toxicity of radiation with weekly docetaxel for advanced head and neck cancer.

Materials/Methods: Between 2001 and 2005, 64 patients with stage ‡V/‡W oropharyngeal or hypopharyngeal carcinoma received radiation with weekly docetaxel. Primary site location and stage were as follows: in the oropharynx, 5 patients had stage III and 29 patients had stage IV, in the hypopharynx 4 patients had stage ‡V and 26 patients had stage ‡W. There were 7 females and 57 males with a median age of 62 years (range 39 to 83 years). Up to 46Gy of radiotherapy was delivered to the whole neck region in daily fractions of 2Gy, 5times/week, and thereafter limited to the involved lesion with a maximum total dose of 60Gy. Concurrent docetaxel 10mg/m^2 was administered once a week during radiation. Toxicity was assessed using the Common Toxicity Criteria, version 3.0. Overall survival and Loco-regional rates were calculated according to Kaplan-Maier method. Neoadjuvant chemotherapy (docetaxel, 5-FU, and CDDP) was done in 27 patients. Adjuvant neck dissection was performed in 8 patients whose primary tumor responded as CR (complete remission) and cervical lymph nodes as PR (partial remission) or NC (no change). Adjuvant chemotherapy was delivered inÅ@6 patients with primary residual tumor. Double cancer was found in 20 patients including 15 patients with esophageal carcinoma.

Results: Fifty-seven patients completed the full course of concurrent chemotherapy. Chemotherapy was terminated in 6 patients with mucositis and 1 patient with renal dysfunction. All patients were followed at least one year or until death, median follow-up period was 25 months (range 3 to 58 months). Initial response of CR, PR, NC and PD (progressive disease) were achieved in 49, 13, 1 and 1 patients, respectively. The actuarial overall survival and loco-regional control rates at 2 years were 69% and 64% in oropharyngeal carcinoma and 66% and 66% in hypopharyngeal carcinoma, respectively. Twenty six patients developed grade ‡V mucositis and 1 patient laryngeal edema (grade ‡W).

Conclusions: Radiation with weekly docetaxel for advanced head and neck cancer provides excellent early response and acceptable toxicity, although longer follow-up is needed.



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RADIATION THERAPY OUTCOME ACCORDING TO FRACTIONATION SCHEME IN EARLY GLOTTIC CANCER

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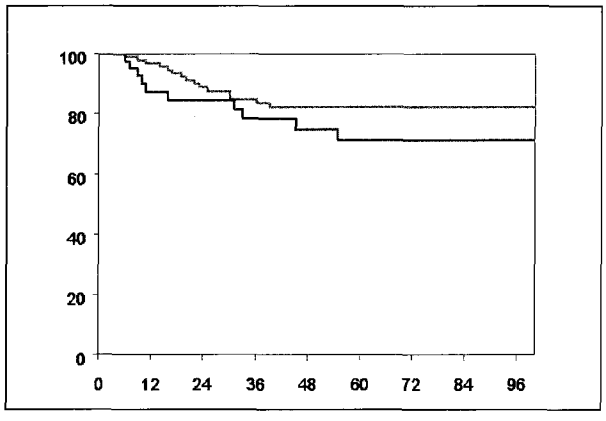
Purpose/Objectif: To evaluate the effect of fractionation scheme of radiation therapy on the outcome of T1-T2 glottic cancers, and to find out prognostic factors potentially influencing local control.

Materials/Methods: From January 1992 to August 2004, 151 patients with histologically confirmed stage T1-2N0 glottic cancer received radical radiation therapy. The distribution of T stage was as follows; T1 100 patients, T2 51 patients. Four patients were treated with chemotherapy followed by radiation therapy. Hypofractionated radiation therapy was performed for 57 of 151 patients (2.5 Gy per fraction to total dose of 60~65 Gy). Conventional radiation therapy was given with 1.8 or 2.0 Gy per fraction to total doses of 58.8~72 Gy. Median duration of treatment was 36 days (30~44 days) in hypofractionated group and 48 days (30~76 days) in conventional fractionated group.

Results: The overall survival rate and disease free survival rate for all patients at 5 year were 93% and 70%. T stage was the only factor influencing local control rate by both of univariate (P=0.04) and multivariate analysis (P=0.0037). Five-year disease free survival for patients with T1 and T2 were 77% and 54%. Five-year disease free survival were 76% and 66% for hypofractionated and conventional fractionated group respectively (P=0.09). Radiation therapy was well tolerated in both of hypofractionated and conventional radiation therapy group. Most common acute reactions were odynophagia and hoarseness and their reactions resolved mostly after radiation therapy. There was 1 case of RTOG grade 3 odynophagia and 3 cases of severe hoarseness. During follow up, total 36 cases of treatment failure were detected. Voice preservation rate after salvage operation was 80.9%. Thirty-four cases were local recurrence, 2 cases were

regional recurrence and 3 cases were distant metastasis.
Conclusions: Radiation therapy showed high survival rate and voice preservation rate for patients with T1-2 glottic cancer. Hypofractionated radiation therapy schedule is effective therapeutic option with benefit of shortening the treatment duration and saving the expenses.



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RADICAL RADIOTHERAPY FOR SQUAMOUS CELL CARCINOMA OF THE ORAL CAVITY

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Purpose/Objectif: To retrospectively evaluate the role of radiotherapy as a primary local modality in patients with squamous cell carcinoma of oral cavity.
Materials/Methods: Ninety-one patients (71 male and 20 female) with squamous cell carcinoma of oral cavity including mobile tongue, floor of mouth, gingival, retromolar trigone, hard palate, and buccal mucosa were treated with radical radiotherapy for curative aim since January 1990 through December 2004. There were 21 patients presented with early stage disease (stage I/II), 53 with advanced disease (stage III/IVA/IVB), and 17 with recurrent disease. Forty-five patients were treated with combined chemotherapy for mainly neoadjuvant aim (42/45). The median radiation dose was 70.2 Gy (range: 57.6~75.0). Conventional dose schedule (77/91) and bilateral opposed field (82/91) was mainly used to treat the primary tumor and regional lymph node.
Results: The objective tumor response consisted of complete remission (CR) in 40% and partial remission (PR) in 38%. After the median follow-up of 16 months (range; 4~107), 16 patients had failed treatment: 12 with local, 1 regional, 1 locoregional, 1 regional plus distant area, and 1 locoregional plus distant area. The median survival duration was 19 months. The 5-years overall survival, disease free survival, local control, and regional control rates were 25%, 18%, 22%, and 48% for all patients; 41%, 11%, 14%, and 84% for stage I/II; 21%, 22%, 27%, and 33% for stage III/IVA/IVB; 11%, 11%, 11% and 33% for recurrent disease, respectively. Regional lymph node involvement was the only prognostic factor in multivariate analysis (p=0.013). Although regional lymph node involvement was significantly more likely in patients treated with combined chemotherapy and radiotherapy (p<0.01), there were not statistically significant differences in survival outcome.
Conclusions: A quarter of patients with squamous cell carcinoma of oral cavity could survive with radiotherapy without surgery. Regional lymph node involvement was the only prognostic factor. Further investigations in other treatment strategies are required considering of poor treatment outcome.

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RADIOCHEMOTHERAPY AND THERMORADIOTHERAPY OF LOCALLY ADVANCED PHARYNX AND LARYNX CANCER.

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Purpose/Objectif: More aggressive treatment regimes improve local tumor control and survival of patients with locally-advanced head and neck cancer. However, combined modality approaches are associated with higher acute toxicity, including hematological one. The purpose of the study was to compare efficiency and toxicity of thermoradiotherapy and radiochemotherapy in patients with stage III-IV of squamous cell cancer of pharynx, hypopharynx and larynx with lymph nodes metastases ($T_{3-4}N_{1-3}$).
Materials/Methods: Two hundred forty patients completed the treatment from January 1995 to December 2005. In the first group, 87 patients underwent a split-course of conventional radiation therapy up to total dose 68-70 Gy. In the second group, 85 patients were performed radiation therapy in combination with local microwave hyperthermia (915 MHz, 60-75 Wt). The treatment protocol in the third group (37 patients) consisted of three courses of chemotherapy (5-FU+cisplatin) given in the first, 5-th and 11-th week and conventional split radiation therapy (6 - 9 and 12 - 14 week), a total dose 68-72 Gy. In the forth group (31 patient), besides, patients were performed 6-8 sessions of local hyperthermia. Heat was delivered for an hour up to 41.5-430C in the tumor after irradiation.
Results: Five-year overall survival in the first and the second group was 7.5% and 18.4%, median survival - 11.5 and 17.1 month, respectively (ò=0.001). Hyperthermia was more effective in patients with larynx cancer (5-year survival - 25.4%, median survival 23.8 month) than pharynx cancer (5-year survival - 14.5%, median survival 17.1 month, ò=0.006). Patients in local hyperthermia group demonstrated non-significant increase of grade 3+4 mucositis, dysphagia, skin and soft tissue toxicity (p=0.067). Hematological toxicity was low and identical in both groups. In the third group (radiochemotherapy), 3-year actuarial survival was 43.3%. Radiochemotherapy was most effective in case of pharynx cancer (3-years survival 58.2%). In case of larynx cancer, 3-year survival was significantly lower (27.1%, p=0.011). Local microwave hyperthermia in combination with radiochemotherapy doesn't improve loco-regional control in patients with advanced pharynx and larynx cancer (34.4%, ò=0.062). Patients treated with radiochemotherapy and hyperthermia more often developed 3+4 grade mucositis (45.5% vs 28%, p=0.02) and dysphagia (41.6% vs 24.1%, p=0.04) compared to those with radiochemotherapy alone. Stage 2-4 anemia developed in 43% and 25% (p=0.004), respectively.
Conclusions:
1. Thermoradiotherapy and radiochemotherapy are of equal efficiency in case of advanced larynx cancer, but thermoradiotherapy possesses less toxicity.
2. Pharynx cancer is the indication for radiochemotherapy.
3. Radiochemotherapy in combination with local hyperthermia significantly increases toxicity of the treatment.

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RADIOTHERAPY DELAYS IN CARCINOMA OF THE HEAD AND NECK AND IMPROVING THERAPEUTIC OUTCOMES

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Background: Over half of all patients in the UK wait longer than the recommended 31 days for radical radiotherapy. Delays adversely affect outcomes for advanced squamous carcinoma (SCC) of the head

and neck where there is rapid tumour proliferation. The aim of this study was to assess compliance to established radiotherapy treatment guidelines: (i) primary radical radiotherapy (RT) to start within 31 days of decision to treat (ii) post-operative radiotherapy (PORT) to start within 42 days of surgery (iii) radiotherapy overall treatment time 49 days or less.

Methods: 156 consecutive patients receiving radical radiotherapy with curative intent from 1 November 2004 to 31 March 2006 were reviewed. There were 110 males and 46 females of median age 62 years (range 26-95). Histologically 70% were squamous carcinomas with overall Stage Groups I, II, III, and IV 6%, 27%, 14% and 53% respectively. Tumour sites included larynx 34; lip and oral cavity 29; oropharynx 30; hypopharynx 7; nasal cavity and para-nasal sinus 11; skin 12; unknown primary 5; parotid 22; thyroid 6. 94 patients received primary RT on a once daily schedule of 54 Gy in 20 fractions or 64 Gy in 30 fractions. 62 patients received PORT on a once daily schedule of 50-54 Gy in 20 fractions or 60-64Gy in 30 fractions.

Results: The prescribed radiotherapy course was completed in 97% of patients. Failure to complete was due to fatal pulmonary embolus in 1; myocardial infarct in 1; chest infection in 1 and widespread metastases in 1. 99% of patients were treated in overall time < 49 days. For RT, 87% started within 31 days of decision to treat (range 10 - 51 days). Non-compliance was due to delays in socket healing following dental extraction in 3; PEG tube placement in 5; transfusion in 3; patient holidays in 2. In contrast, only 22% of all surgical patients started RT within 42 days of surgery (range 26 - 181 days). Of these, only 36% of resected SCC received PORT within 42 days of surgery. Delays were due to post-operative complications including chyle leak in 2; fistula in 2; flap revision in 2; tracheostomy in 2; massive haemorrhage in 2; wound breakdown in 20; wound infection in 10; haemodynamic complications in 2;holiday choice in 2.

Conclusions: Compliance with recommended treatment times was achieved for primary radical radiotherapy but was poor for post-operative radiotherapy. Delays post-operatively were mainly due to prolonged wound healing, placement of PEG tubes and correction of anaemia. Excessive delays post-operatively allow tumour proliferation and may reduce local control and overall survival.

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RECURSIVE PARTITIONING ANALYSIS IN THE POSTOPERATIVE SETTING IN SQUAMOUS CELL HEAD AND NECK CANCER: CONSEQUENCES WITH REGARD TO QUALITY OF LIFE OUTCOME

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Purpose/Objectif: Recently, the VU University Medical Center presented the results of a recursive partitioning analysis (RPA) to define risk groups for recurrence among head and neck squamous cell carcinoma (HNSCC) patients treated with primary surgery and postoperative radiotherapy. This classification scheme was validated in a multicenter setting. The purpose of the present study was to test the hypothesis that the RPA classification system also allowed for prediction of quality of life (QOL) outcome after surgery and postoperative radiotherapy.

Materials/Methods: For the purpose of this study, 213 patients with HNSCC treated with surgery and postoperative radiotherapy were included. There were 56 patients (26%) in class I (intermediate risk), 91 patients (43%) in class II (high risk) and 66 patients (31%) in class III (very high risk). QOL was prospectively assessed using the EORTC QLQ-C30 and EORTC QLQ-H&N35 instruments before radiotherapy, and at 1 and 6 weeks, 6, 12, 18 and 24 months after completion of radiotherapy.

Results: In general, local and general symptoms were most pronounced at the end of radiation which was reflected into lower scores for the functioning scales and global QoL. After 6 months, a gradual reduction of symptoms and a gradual improvement of functioning and global QoL was observed. At 24 months, the scores of the more general QoL dimensions returned to a level similar to the normal population. Patients in class III did significantly worse as compared to class I and II patients regarding local symptoms, including dry mouth, sticky saliva, swallowing and speech and regarding global quality of life. This could be partly explained by the fact that class III patients received bilateral iradiation more often than class I and II patients.

Conclusions: Besides prediction of the classical tumour-related endpoints, the RPA-classification system also allows for prediction of QoL outcome.

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RESULTS OF AN EXTENDED PHASE-II TRIAL USING HYPERFRACTIONATED ACCELERATED RADIATION WITH CONCURRENT CIS-PLATINUM/5-FU (C-HART) IN LOCALLY ADVANCED HEAD AND NECK CANCER

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Purpose/Objectif: To report on a phase I/II study assessing the feasibility, toxicity, and clinical response of C-HART in locally advanced head and neck cancer.

Materials/Methods: From March 2000 to March 2002, 36 consecutive patients with locally advanced, non resectable squamous cell carcinomas of the head and neck received C-HART. Radiotherapy was delivered up to 30 Gy in daily fractions of 2.0 Gy five times per week, thereafter 1.4 Gy b.i.d. five times per week were used up to a total dose of 72 Gy. Concurrent 5-FU 600mg/m^2 over 120 hours continuous infusion and cis-Platinum 30mg/m^2 once weekly for 4-6 courses was administered during radiation. Hematological and local toxicity was assessed using the Common Toxicity Criteria, version 2.0. Loco-regional control (LRC), freedom from metastases (FFM), progression-free survival (PFS) and overall survival (OS) were calculated according to Kaplan Meier.

Results: The median follow-up was 51 months (range: 48 - 67 months). All patients completed the C-HART regimen according to protocol. No severe acute toxicity was noted. 20 patients received six courses of cis-Platinum, 13 patients five, and three patients only four courses, respectively. No grade IV hematologic toxicity was observed. Five patients (13.9%) developed a grade-III anemia and leucocytopenia. Acute grade-III mucositis was recorded in 15 (41.7%), dysphagia in 17 (47.2%), and erythema in 6 (16.7%), respectively. Xerostomia and dysgeusia was observed in one patient each. Complete remissions were observed in 55.5% (n=20) of all patients, partial remissions in 33.3 % (n=12), and tumour progressions in 11.2 % (n=4) of all patients, respectively. The actuarial OS, LRC, PFS and FFM rates at 4 years for the phase-I/II and the subgroup of patients from the Charité treated within the ARO 95-06 study are detailed in table 1:

Survival @ 4yrs	Phase II	ARO 95-06	p value	
	Charité	Phase III	Log-rank	Breslow
OS	55.6 %	25.8%	0.027	0.045
LRC	63.9%	45.5%	0.054	0.039
FFM	70.9%	47.1%	0.154	0.072
PFS	49.2%	24.4%	0.023	0.009

Conclusions: The results of this extended phase II study are promising indicating superiority in terms of LRC, FFM and PFS compared to the ARO 95-06 trial, even for OS. Since OS of the ARO 95-06 trial of the German Clinical Trials Co-operative Group of the Cancer Society was compromised by the high incidence rates of distant metastases of 35% at 2 years, C-HART with concurrent cis-Platinum/5-FU was chosen as alternative experimental arm of phase-III ARO-AHMO 04-01 trial to test the hypothesis that the incidence of distant metastases may be reduced by an optimized chemotherapy schedule.

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RESULTS OF RADIOTHERAPY OF CANCER OF THE BASE OF TONGUE

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Purpose/Objectif: To demonstrate the results of treatment of cancer of the base of tongue treated with exclusive external beam irradiation (EBI) or EBI + high dose rate (HDR) boost brachytherapy (BT) or surgery + postoperative irradiation.

Materials/Methods: 102 patients with biopsy proven carcinoma of the base of tongue (T1-4N0-3M0) treated between 1992 and 2000 were analysed. The mean dose of EBI (group A), HDR boost BT (group B) and surgery + postoperative irradiation (group C) were 60 Gy, 18 Gy and 55 Gy, respectively. The mean follow-up period was 53 months.

Results: The 5-year probability of local-, locoregional tumor control and overall survival for all stages were 36 %, 34 % and 26 % in group A, 60 %, 52 % and 46 % in group B, and 63 %, 52 % and 48 % in group C, respectively. There was not significant difference in the incidence and seriousness of irradiation caused mucositis. More serious swallowing and speech difficulties occurred in consequence of surgical therapy.

Conclusions: HDR boost BT (group B) and surgery + postoperative irradiation (group C) had similar results and had advantage over exclusively EBI (group A), but the irradiation (group A and B) was more favourable regarding the side-effects than surgery + irradiation (group C).

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RESULTS OF RADIOTHERARPY IN LOCALLY ADVANCED HYPOPHARYNGEAL CANCER

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Purpose/Objectif: The purpose of this study is to present the treatment results according to treatment modalities and to identify possible prognostic indicators in patients with locally advanced hypopharyngeal carcinoma.

Materials/Methods: Between October 1985 to December 2000, 127 patients who had locally advanced hypopharyngeal carcinoma were retrospectively studied. Fourteen patients were treated with radiotherapy alone, 94 patients were treated with a combination of chemotherapy and radiotherapy, and 19 patients were treated with surgery and postoperative radiotherapy. Total radiation dose to the primary tumor was from 59.0 to 88.2 Gy (median 71.5Gy) in the RT alone group. In combination of chemotherpay and radiotherapy, most patients (79/94) were treated with neoadjuvant chemotherpay, 14patients were combined with neoajuvant and concurrent chemotherapy, 1 patients was treated with concurrent chemoradiotherpay only. In surgery group, 13 patients had neoadjuvant chemotherpay and 6 patients no chemotherapy. Of 107 patients who had chemotherapy, 76 had ciplatin and 5-fluorouracil, and 27 had cisplatin and pepleomycin. Median follow-up period was 16 months. Kaplan-Meier method was used for survival rate and Cox proportional hazard model for multi-variate analyses of prognostic factors.

Results: The overall 3-year survival rate were 7% for RT alone, 27% for combination of chemotherapy and radiotherapy, and 42% for surgery and postoperative RT group(P=.000). With RT alone, 11 patients achieved more than partial remission (PR); the response rate was 79% (11/14). With neoadjuvant chemotherapy, 4 patients had complete remission (CR) and 23 patients PR. The prognostic factors affecting overall survival were T-stage, nodal stage and local response rate. Surgery and postoperative RT or combination of chemotherapy and RT showed better 3-year survival rate than RT alone (p=0.000).

Conclusions: Surgery and postoperative RT showed better survival rate than combination of chemotherapy and RT in terms of overall survival. The response to neoadjuvant chemotherapy was not statistically significant. In multivariate analysis, T-stage, nodal stage and local response rate were statistically significant.

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RISK OF DISTANT METASTASES AFTER POSTOPERATIVE RADIATION THERAPY FOR LOCALLY ADVANCED LARYNGEAL CANCER.

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Purpose/Objectif: To evaluate the prognostic factors for the risk of distant metastases after postoperative radiotherapy for laryngeal cancer.

Materials/Methods: Medical records of 267 patients cancer treated between 1997 and 2003 were analyzed. All pts had locally advanced squamous cell laryngeal cancer treated with surgery and postoperative radiotherapy. Metastasis Free Survival was analyzed using Kaplan-Meier method. A multivariate Cox proportional hazard model and logistic regression model was used to evaluated influence of the following variables on MFS and the ultimate risk of metastases: age, sex, localization, TN stage, HGB before and at the end radiotherapy, total radiation dose, dose per fraction, overall treatment time, interval surgery-radiation time, pathological margins and positive nodes in surgical specimen.

Results: The crude incidence of distant metastases was 12% (33/267 pts). One year, 3-year, 5- year actuarial metastases free survival were 95%, 85%and 84% respectively. The lungs and bones were the most common sites of metastases (58% and 33% respectively), whereas metastases to liver (6%) and brain (3%) were rare. Localization of cancer (glottic vs. supraglottic) and number of positive lymph nodes at pathological staging significantly and independently affected MFS.

Conclusions: Number of positive lymph nodes in pathological specimen and site of primary cancer (glottic vs. supraglottic) significantly and independently predict a risk of distant metastases in combined modality treatment for laryngeal cancer.

868 poster

SHAPE CHANGES IN H&N RADIOTHERAPY ASSESSED WITH NON-RIGID FEATURE REGISTRATION

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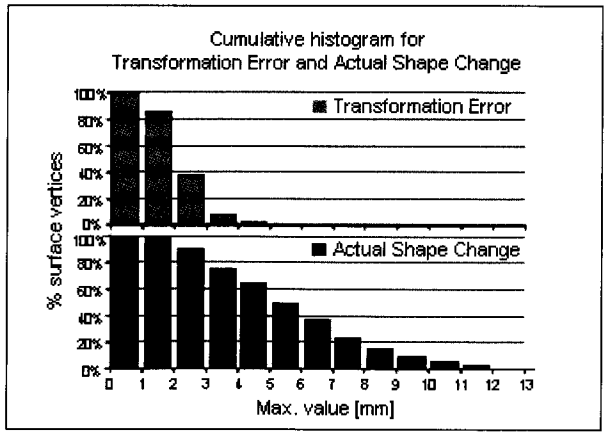
Purpose/Objectif: Patients receiving RT for H&N cancer present anatomic changes during the course of external beam RT (EBRT). To fully understand the clinical impact, theses changes should be quantified on a local scale. A non-rigid registration tool has been developed to quantify local soft tissue changes in H&N cancer patients.

Materials/Methods: We adapted a feature based non-rigid registration method [1], which iteratively optimizes the correspondence and the transformation between two control point sets. The correspondence is fuzzy, allowing noise and outliers in the dataset. The transformation is based on thin plate splines. The method was tested and applied to H&N cancer patients, each receiving a planning and a repeat CT scan after 46 Gy. The CT scans were rigidly pre-registered using bony anatomy. The control point sets were derived from the contoured CTV and OARs. The correspondence-transformation optimization was applied in both directions; from planning to repeat and vice versa. The accuracy of the transformation was determined by measuring the distance between the transformed and reference organ surfaces. On the basis of the transformation results, the shape changes during EBRT were quantified on a local scale.

Results: Results were summarized for the first 7 patients. The transformation was accurate with a mean error of 2±1 mm (1 SD). The error did not depend on the direction of the transformation. Figure 1 shows, as an example, the cumulative histogram of the transformation error for both parotid glands of 1 patient, together with their actual shape change. The volume of the glands reduced on average by 22% (parotid) and 13% (sub-mandibular), where the average was taken over all patients. The most pronounced shape changes of the glands were observed at the lateral sides (7-13 mm for parotid, 6-12 mm for sub-mandibular glands). At the medial sides, which were adjacent to bone, the changes were small (on average 3 mm). The volume of the CTV decreased on average by 24%, where the maximum shape changes were between 7 and 14 mm. These changes were mostly observed in the transverse plane.

Conclusions: The non-rigid registration method was able to model local shape changes that occurred in the H&N region during EBRT. Currently, the non-rigid transformation is applied to the CT images and 3D dose distributions to further validate the method and to determine the dosimetric consequences of the shape changes.

[1] Chui H, Rangarajan A. A new point matching algorithm for non-rigid registration. CVIU 89, 2003



869 poster

SITES OF NECK RECURRENCE IN RELATION TO MIDLINE CORD SHIELD IN HEAD AND NECK SQUAMOUS CELL CARCINOMA (HNSCC): IMPLICATIONS FOR IMRT VOLUME DELINEATION

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Purpose/Objectif: In IMRT planning, medial delineation of neck target volumes results in higher radiation doses to neck midline normal tissues. This region would have been shielded by a midline cord shield (MCS) when used with an anterior or ant-post low neck field. This study was undertaken to examine the pattern of nodal failure in relation to the MCS.

Materials/Methods: From Jan. 2000 to Dec. 2004, 440 patients with oral cavity, oropharynx, larynx, hypopharynx and unknown primary HNSCC underwent curative non-IMRT radiotherapy (RT) that included a low neck field and MCS. Only patients who recurred after a complete response (CR) were included in this analysis. Planning CT or pre-RT diagnostic scans were imported into Pinnacle planning system (version 7.6c, Philips Medical Systems). CT/MRI scans of neck recurrences were registered with the pre-RT images in the region of the MCS. Recurrent (rNODE) and pre-RT nodes were contoured. Multiple nodal levels were recorded when nodes crossed anatomic boundaries. RT fields and MCSs were recreated. The axial distance between rNODE and MCS was measured.

Results: We identified 86 patients with neck recurrences. 25 patients were evaluated after the exclusion of patients with persistent disease or recurrence after neck dissection. Median time to failure was 14.1 months. Primary sites were: 2 oral cavity; 14 oropharynx; 4 larynx; 1 hypopharynx and 4 unknown. TNM 6th edition N-classification at diagnosis was: N0:8/25 (32%); N1:2/25 (8%), N2a:0/25; N2b:5/25 (20%); N2c:6/25 (24%) and N3:4/25 (16%). Recurrence scans were available for 22 (88%) cases. rNODE levels were: Ib:2/22 (9.1%); IIa:8/22 (36.4%); IIb:5/22 (22.7%); III:9/22 (40.9%); IV:4/22 (18.2%); V:5/22 (22.7%); VI:2/22 (9.1%) and retropharynx:1/22 (4.5%). 2 patients had subcutaneous recurrences. MCS width was typically 3 cm at cord depth superiorly overlying the larynx and tapered inferiorly. 6 (24%) patients recurred with disease near (<1cm) the MCS (table). Of these, 2 failures were at original nodal sites. In 2 others, subcentimetre nodes were found in the recurrent nodal level on pre-RT scans. Failure near the MCS was not suspected in the 3 cases without recurrence scans.

Conclusions: For all patients treated with a MCS, recurrence near the MCS was uncommon after CR but was observed. The medial neck recurrence pattern is important to consider when defining neck target and normal tissue sparing volumes for IMRT. Midline normal tissue dose reduction is a feasible planning goal.

Table: Nodal recurrences < 1cm from MCS

Primary	N-Stage	rNODE levels
oral cavity	N1	III, IV
oropharynx	N0	VI
oropharynx	N1	VI
oropharynx	N2c	III
larynx	N1	IIa, III
unknown	N2b	IIa, IIb, III, IV

870 poster

SUBMANDIBULAR SALIVARY GLAND SPARING USING HELICAL TOMOTHERAPY IN POST-OPERATIVE HEAD AND NECK CANCER PATIENTS WITH AND WITHOUT GLAND TRANSFER PROCEDURE.

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Purpose/Objectif: The aim of this planning study is to evaluate the sparing of both submandibular gland (SMG) and parotid glands by combining helical tomotherapy (HT) and surgical SMG transfer procedure in post-operative head and neck cancer (HNC) patients. We also report the results of the attempt to achieve the same goals without SMG transfer using helical tomotherapy in a highly selected cohort of patients.

Materials/Methods: Ten HNC patients (larynx-2, base of tongue-4, tonsil-3, and unknown primary-1; p Stage III-IV) treated with post-operative conventional radiation after SMG transfers to the submental space were selected for the initial phase of this study (HT with SMG transfer). SMG transfer was performed on the side of N0 neck after doing a selective neck dissection (level I-III) to rule out presence of any microscopic disease on the side of the gland transfer. A new plan was generated on Tomotherapy® after contouring the high risk CTV (CTV1), low risk CTV (CTV2) and organs-at-risk which included spinal cord, brainstem, mandible, parotid glands and transferred SMG. The planning objective was to deliver 60 Gy to PTV1 and 54 Gy to PTV2 while maintaining the mean dose to the total parotid volume (TPV) and SMG less than 26 Gy. For the second phase (HT without SMG transfer), 3 post-operative HNC patients (larynx-1, tonsil-2; p Stage III-IV) were selected. HT plans were generated with the same goals using similar dose constraints after contouring the CTVs and organs-at-risk. The only difference in comparison to initial plan was that SMG on the side of N0 neck was contoured as a sensitive organ instead of transferred SMG.

Results: In the plan with HT and SMG transfer, the combined mean values for PTV1 and PTV2 were as follows: PTV1: D_{mean} 61.8 Gy, D_{95} 59.9 Gy, D_{99} 58.2 Gy, V_{100} 94.5 % and V_{110} 0.6 % ; PTV2: D_{mean} 56.9 Gy, D_{95} 54.9 Gy, D_{99} 49.5 Gy and V_{100} 97.5 %. The combined mean and median dose to the TPV and SMG were 25 Gy, 17.5 Gy, 23 Gy and 16.5 Gy respectively. The mean dose to TPV or SMG did not exceed 26 Gy in any patient. The dose profiles for PTV1 and PTV2 in the plan using HT without SMG transfer were as follows: PTV1: D_{mean} 61.8 Gy, D_{95} 59.9 Gy, D_{99} 56.2 Gy, V_{100} 94.9 % and V_{110} 0.9 % ; PTV2: D_{mean} 57.3 Gy, D_{95} 55 Gy, D_{99} 47.7 Gy and V_{100} 97.6 %. The combined mean and median dose to the TPV and SMG were 26.8 Gy, 19.4 Gy, 24 Gy and 18.1Gy respectively. The mean dose to TPV and SMG exceeded 26 Gy in one patient with tonsillar primary. The maximum doses to spinal cord, brain stem and mandible were restricted to 45 Gy, 50 Gy and 65 Gy respectively in all patients in both the plans.

Conclusions: By using a novel combination of the SMG transfer procedure and HT, the mean dose to both parotid glands and transferred SMG could be reduced to less than 26 Gy in HNC patients undergoing post-op radiation. A clinical protocol using this method is ongoing at our center. Sparing both SMG and parotid glands using HT without gland transfer may be possible in highly selected patients with HNC.

871 poster

THE IMPACT OF KU PROTEIN EXPRESSIONS ON RADIOSENSITIVITY AND PROGONOSIS IN NASOPHARYNGEAL CARCINOMA

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Purpose/Objectif: To evaluate the correlationship between the expressions of Ku70/Ku80 protein and the clinical stage, the radiosensitivity, progonosis of nasopharyngeal carcinoma(NPC).

Materials/Methods: The expressions of Ku70/Ku80 protein were detected by immunohistochemical method in tumor tissues of 107 NPC patients. The relationship between the expressions and the clinical stage, the radiosensitivity of tumor, survival rate were analyzed.

Results: The Ku70 and Ku80 protein express in cell nucleus of NPC, none of them was correlates with NPC clinical stage ($P<0.05$).The expressions of Ku70/Ku80 protein had correlation with the tumor regression speed during radiation therapy. The low level expression of Ku70 and Ku80 was more radiosensitive. The exprssion of Ku70 was positively correlated with the expression of Ku80(correlation coefficient=0.772, $P<0.05$). The low level expression of Ku80 protein has the poor progonosis $P=0.042$).

Conclusions: As a possible predictor of tumor radiosensitivity, Ku70/Ku80 may be a useful tumor marker to guide the radiotherapy of NPC. Furthmore, the expression of Ku80 may play an important role in predicting the progonosis of NPC patient.

872 poster

THE LEEDS CANCER CENTRE (LCC) EXPERIENCE OF SPLIT COURSE PALLIATIVE RADIOTHERAPY IN HEAD AND NECK CANCER

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Purpose/Objectif: Uncontrolled head and neck cancer causes distressing symptoms and poor quality of life. Management of these patients, who are medically unfit for radical treatment due to their general frailty and co-morbidity, poses a particular clinical challenge. At the LCC, a split course consisting of 2 weeks of radiotherapy separated by a gap has been used with palliative intent.

Materials/Methods: The patients with head and neck cancer treated with split course radiotherapy between 2000 and 2003 were retrospectively reviewed. Notes were accessed electronically and clinical and pathological data were retrieved. Cases were classified according to disease site and stage; radiotherapy dose, gap duration, response rates and survival were determined.

Results: Twenty-five patients of median age 78 years (range 49 to 95) received this palliative regime. Glottic and oropharyngeal cancers constituted the majority of cases, with most patients presenting with stage 4 disease. 22 out of 25 patients received 20-22.5 Gray in 5 fractions over 7 days for each of the two phases. 22 patients achieved a response, 11 of which had a clinical complete response (cCR). There were no toxicity related admissions. The median overall survival for the group as a whole was 4.5 months (range 0.25-45), but only 3.25 months (range 0.25-6.5) for those with persistent disease. However, in patients who achieved cCR, the median disease free survival was 7 months (range 2-45) and the median overall survival was 9.25 months (range 2-45).

Conclusions: This regime is well tolerated in this clinically challenging population and is effective in achieving local control.

Future work will include prospective assessment of quality of life using validated questionnaires.

873 poster

THE PROGNOSTIC VALUE OF COMORBIDITY IN THE TREATMENT OF SALIVARY GLAND CANCER; RESULTS OF THE DUTCH HEAD AND NECK ONCOLOGY COOPERATIVE GROUP (NWHHT)

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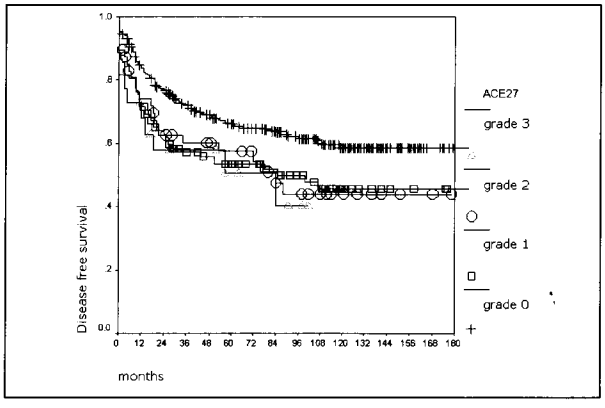
Purpose/Objectif: The importance of the ACE-27 (=Adult Comorbidity Evaluation) as a prognostic factor has been analysed for squamous cell cancer of the head and neck (Piccirillo). However, for patients with salivary gland cancer no results of analysis of the prognostic value of comorbidity, e.g. the ACE-27, have been published.
Materials/Methods: The Dutch Head and Neck Oncology Cooperative Group (NWHHT) conducted a retrospective study in the Netherlands including salivary gland cancer of all sites, excluding paranasal tumors. Mean follow-up was around 10 years. In 487 patients with salivary gland cancer ACE-27 grade was determined. Parotid glands were most involved (52%) followed by minor salivary glands (35%) and submandibular glands (13%). Surgery only was performed in 26%, combined with radiotherapy in 63%. Radiotherapy alone was performed in 8%, and 4% was not treated or treated with chemotherapy.
Results: As expected, mean age strongly correlated with ACE-grade. Comorbidity grade was not correlated with histologic type and complaints. Male patients had a marginally significant higher degree of comorbidity. More advanced disease was more often seen in patients with morbidity, grade 1-3 in 24%, 42%, and 52% for T1, T2, T3-4 respectively. Morbidity was not correlated with site. Grade 3 was associated with lower use of postoperative radiotherapy, and more frequent radiation alone (p=0.003). Delay between radiotherapy and surgery was significant longer (mean of 3 weeks) in grade 3. Comorbidity grade was a strong, independent, prognostic factor for overall survival. Five and ten years overall survival were 70% and 65%, 50% and 30%, 40% and 0%, for grade 0, grade 1, grade 2, grade 3 respectively. In univariate analysis disease free survival was significantly (p=0.01) lower for grade 1-3 vs. grade 0 (see figure). However, in multivariate analysis grade was not an independent prognostic factor for disease free survival.
Conclusions: This is the first study concerning the prognostic factor comorbidity in salivary gland cancer. In salivary gland cancer ACE-27 is correlated with age, T-stage, sex and treatment performed. Overall survival, but not disease free survival depends on comorbidity.



874 poster

THE ROLE OF NECK DISSECTION (ND) IN THE MANAGEMENT OF ADVANCED OROPHARYNGEAL SQUAMOUS CELL CARCINOMA (OPHSCC) TREATED WITH RADICAL CHEMO-RADIOTHERAPY (CRT) ? 10 YEAR EXPERIENCE

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Purpose/Objectif: The role and timing of neck dissection in the management of advanced OPhSCC remains controversial.
We present 10-year results aiming to define the benefit of ND in terms of local control and survival.
Materials/Methods: 155 patients with OPhSCC treated with CRT between 1995 and 2006 were reviewed. There were 130 males and 25 females of mean age 57 years (range 38 - 89). 136 patients had stage III or IV disease, of which 124 were treated with radical intent. ND was performed in 49 patients pre-CRT: in 21 of these, radical excision of the primary site was perfomed in continuity. Median time from surgery to start of radiotherapy was 36 days (range 10- 75). ND was performed in 12 patients within 8 weeks post-CRT. 63 patients were treated with CRT alone. Median follow-up is 26 months (range 4 - 130).
Results: ND pre-CRT: 33/49 patients (67%) are disease free with overall survival 67% & cause- specific survival 79%. Two patients failed to start CRT owing to post-operative complications and died with progressive local disease 3 months post-operatively. Five patients recurred locally: 3 were surgically salvaged but one patient died 20 months following surgical salvage; 2 patients were unfit for salvage and died of progressive local disease. 3 patients died of distant metastatic disease (18%); 3 patients died of unknown causes and 4 patients were lost to follow-up. 7 of the 49 patients (14%) remained PEG-dependent for <12months. 2 patients (9%) experienced delayed wound healing up to 12 months. ND post-RT: 9/12 (75%) remain disease-free with overall survival 83%. 1 patient remains PEG dependent at 18 months. Histology was negative in 7/12 (58%) patients. Of the node-positive patients, 4/12 had extracapsular spread, 1 of whom died of local disease 6 months following ND. 1 patient with completely excised bilateral disease died of pulmonary metastases 6 months later. CRT alone: 43/63 (68%) are disease-free with overall survival 70%. 2 (3%) patients were PEG-dependent for <12months. Overall local control rate is 78%. 3/14 patients who recurred locally were fit for surgical salvage; 10/14 died with progressive local disease and 1 has stable disease. 2 patients have asymptomatic pulmonary metastases (5%). 4 patients have died of unrelated causes.
Conclusions: Overall survival data show a trend towards improved local control and overall survival for ND post-RT (Kaplan-Meier actuarial method). ND prior to CRT is associated with prolonged wound healing and PEG tube feeding. This delays and possibly prevents definitive treatment of the index tumour allowing proliferation and increased risk of distant metastases.

875 poster

TREATMENT RESULTS IN LOCALLY ADVANCED HEAD AND NECK CANCER PATIENTS RADICALLY IRRADIATED.

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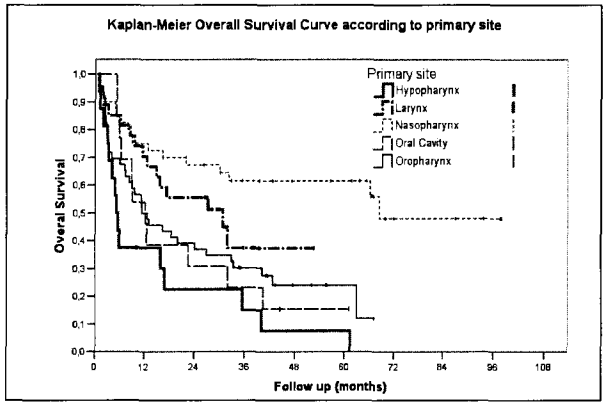
Purpose/Objectif: Radiotherapy is important treatment tool for locally advanced or inoperable head and neck cancer. Concomitant chemoradiotherapy significantly decreased rates of local failure and improves overall survival in comparison with radiotherapy alone. The aim of this study was to evaluate the outcome of radical radiotherapy according to treatment strategy and risk factors.
Materials/Methods: Retrospective clinical study was performed to evaluate 142 patients (16% females and 84% males) with locally advanced or inoperable head and neck squamous cell cancer in the period January 1998-December 2003. There were 46 patients (32%) with oropharyngeal cancer, 40 patients (28%) with nasopharyngeal cancer, 27 patients (19%) with laryngeal cancer, 16 patients (11 %) with hypopharyngeal cancer and 13 patients (10%) with oral cavity tumors. All patients received radical external beam radiation therapy combined in 23% with concomitant chemotherapy. Computed tomography localisation of target volume was used for 3D radiotherapy treatment planning. Patients were treated using linear accelerator. Total dose was 66-72 Gy.
Results: Median follow-up of patients alive is 43 months. Radiotherapy was not completed in 14 patients (9%). The 3-year overall

survival rate was 62% for nasopharyngeal cancer, 37% for larynx, 30% for oropharynx, 23% for oral cavity and 15% for hypopharyngeal cancer (p<0,001). Median survival in nasopharyngeal cancer was 67 months, in laryngeal cancer was 29 months, in oropharyngeal 11 months, in oral cavity 10 months and in hypopharyngeal cancer 5 months. Significant prognostic factors influencing overall survival were concomitant chemoradiotherapy (p=0,041) and stage of the disease (p=0,001). Radiation dose, radiotherapy prolongation, gender, tumor grading or neoadjuvant CHT were not statistically influencing overall survival.

Conclusions: The best prognosis is associated with concomitant chemoradiotherapy and primary site of nasopharynx.



876 poster

TRISMUS RELATED QUALITY OF LIFE OF PATIENTS WITH CANCER IN THE OROPHARYNX IS SIGNIFICANTLY AFFECTED BY THE DOSE RECEIVED BY THE MASSETER-, PTERYGOID-, TEMPORALIS MUSCLES AND THE CORONOID BONE: A DOSE-EFFECT RELATIONSHIP

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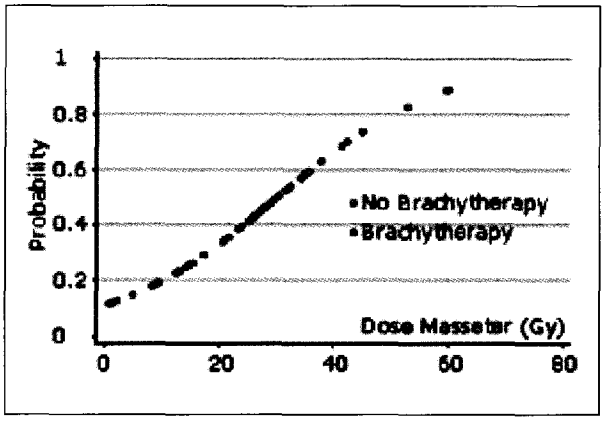
Purpose/Objectif: To assess the correlation between the radiation therapy (RT) dose received by the trismus apparatus and the decrement in the - trismus related - quality of life of patients with oropharyngeal cancer.

Materials/Methods: 77 patients with scc of the tonsillar fossa, soft palate and the base of tongue were analyzed for trismus. Patients were treated by either intensity modulated RT (IMRT: n=37), 3D conformal RT (3DCRT; n=22) and CT-based parallel-opposed fields (P-O; n=18) between 2000-2005 in Erasmus MC. In 52% of the cases, brachytherapy (BT) was used as a boost technique, and in 47% radiation was combined with concomitant chemotherapy (cCHT). The masseter, pterygoid and temporalis muscles and the coronoid process and condyl of the mandible are the 5 components of importance for the jaw movement. These 5 bilateral structures of interest were delineated on axial CT-slices. Dose-volume histograms were computed for these structures. All patients were sent 2 validated Quality of Life (QOL) questionnaires: 1. the Performance Status Scale of List, scoring for "understandability of speech", 2. the EORTC H&N 35 with the item opening mouth. Dose in the 5 trismus-related structures was correlated in a univariate analysis using the proportional odds model with the outcome of the quality of life questionnaires. In a multivariate analysis the effects of the parameters age, sex, site, T-stage, N-stage, dose, technique, surgery, chemotherapy and brachytherapy were studied.

Results: Sixty (NED) out of 77 patients were seen at the outpatient clinic in December 2005; 5 had previously expired due to a local failure and 12 died because of intercurrent disease. Follow-up varied from 16 months (range 4-31) for IMRT, 59 months for 3DCRT (range 41-69), and 48 months for the P-O group (range 24-72). At 5-years a local relapse free survival of 92% and an overall survival of 65 % was observed. The mean QOL in the 3 groups were equal (QOL: 25). Totally 22.9% of the patients scored 3 or 4 on the EORTC list; 21% in the IMRT group and 25% in the 3DCRT and P-O group. TF scores better than BOT (QOL: 22 and 31 respectively). cCHT group scores worse (QOL: 28 and 21). BT group seems to project favorable outcome (QOL: 15 and 43). In the univariate analysis a significant correlation was observed between the dose in the masseter-, pterygoid-, temporalis muscles and the coronoid, BT and T-stadium and the trismus question answer of the H&N 35. In the multivariate analysis, BT was the only significant factor.

Conclusions: The figure shows the steep relationship between mean dose in the masseter muscle and the probability to have trismus complaints. The multivariate analysis shows a significant effect of BT. BT patients receive lower dose in the masseter-, pterygoid-, temporalis muscles and the coronoid bone. Optimizing the dose in the masseter-, pterygoid-, temporalis muscles and the coronoid may improve the ability for mouth opening (trismus).



877 poster

VERIFICATION OF PATIENT POSITION BY DAILY ELECTRONIC PORTAL IMAGING IN PATIENTS WITH HEAD AND NECK CANCER TREATED WITH IMRT VERIFICATION OF PATIENT POSITION BY DAILY ELECTRONIC PORTAL IMAGING IN PATIENTS WITH HEAD AND NECK CANCER TREATED WITH IMRT

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3 - Institut Gustave Roussy, *Statistical Department, Villejuif, France*

Purpose/Objectif: To assess the setup accuracy and reproducibility of daily portal imaging in Head and Neck cancer patients treated with IMRT.

Materials/Methods: Between 2003 and 2005, 20 patients with head and neck cancer treated with dynamic multileaf collimated intensity modulated radiotherapy were included in this study. There were 10 patients with oropharyngeal, 6 with nasopharyngeal, 2 with paranasal sinus, 1 with hypopharyngeal, and 1 with oral cavity cancinoma. There were 4 stage I, 2 stage II, 6 stage III and 8 non-metastatic stage IV patients. The median age was 50 years (range 16-75), and male to female ratio was 14/6. The radiation therapy doses ranged from 46-72 Gy delivered in 23-36 fractions over 5-7 weeks. A five-point fixed mask system was used for immobilization of the head and neck and the shoulders. In all patients, both elective lymph node areas and primary target volumes were irradiated. Target volume definition was performed using planning CT, and a 5 mm margin was used around the CTV determining the PTV. Treatment verifications were

performed using 10×10 cm^2 anterior/posterior and lateral setup fields.
Results: Out of the 20 patients, 625 radiotherapy fractions were given. Before each fraction, a digital portal image was performed in anterior posterior and lateral position. For anterior portal images, a second, third or sometimes a fourth image could be needed (n = 125, mean: 1.22) to match with the reference image. For lateral portal image, film repetition was needed only in 42 patients (mean: 1.09). Before setup correction, mean cranial/caudal displacement was - 2.3 mm (standard deviation [SD]: 2.56 mm), mean medial/lateral displacement was 2.0 mm (SD: 2.20 mm), and anterior/posterior displacement was - 1.4 mm (SD: 1.95 mm). Following setup corrections, mean and SD of the cranial/caudal displacement decreased to - 1.8 and 2.12 mm), mean and SD of the medial/lateral displacement were 1.2 and 2.18 mm), and mean and SD of the anterior/posterior displacement were - 1.2 and 1.78 mm). The correction significantly decreased the random error of cranial/caudal and anterior/posterior positions. As compared to a portal film done every two days, three days, four days or weekly, a daily portal film decreased the random error of cranial/caudal position. In a multivariate logistic regression analysis, no patient related factor (age, gender, stage, anatomical site) influenced the setup errors in all geometrical directions.
Conclusions: Our study strongly suggest that a daily portal imaging is warranted optimize the set-up margin in Head and Neck cancer patients treated with IMRT.

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WEEKLY CISPLATIN AND ACCELERATED RADIOTHERAPY (CISAR) IN LOCALLY ADVANCED HEAD AND NECK SQUAMOUS CELL CARCINOMAS.

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Purpose/Objectif: Both concomitant conventionally fractionated cisplatin-based chemoradiotherapy and accelerated radiotherapy without chemotherapy results in improved local control and survival in head and neck squamous cell carcinoma (HNSCC). Since accelerated radiotherapy for locally advanced HNSCC has been the standard of care in our institution since around 10 years, we decided to add weekly low-dose cisplatin to accelerated radiotherapy (CISAR) for patients with locally advanced HNSCC, in order to improve locoregional control rates with acceptable toxicity.
Materials/Methods: Patients with irresectable stage III-IV-B HNSCC, Karnofsky ≥ 70 and normal renal function were eligible. Cisplatin (40 mg/m^2 i.v. weekly) was given during irradiation (44 Gy in 2 Gy fractions, 5 x per week to the primary tumour and neck, followed by a boost of 24 Gy in 2 Gy fractions 10 x per week to all macroscopic tumor) resulting in an overall time of 5.5 weeks and a total of 5-6 cisplatin gifts. If substantial swallowing problems were expected, a gastrostomy catheter for tubefeeding was placed prior to treatment.
Results: To date, 30 patients with stages III (n=6) and IV(n=24) squamous cell carcinomas of the oral cavity (n=12), oropharynx (n=10), hypopharynx (n=7) and larynx (n=1) were treated. Mean age was 59 years (range 38-73). Mean FU was 81 weeks (range 7-22). Median time to first recurrence was 111 weeks, median time to death was 103 weeks. Relapse free survival and overall survival at 2 years follow-up were 57 % and 48 % respectively. One patient died 4 weeks after start of treatment of septicemia and respiratory failure probably unrelated to treatment and one patient died due tot peritonitis after gastrostomy. Both were recorded as grade 5 toxicity. In 27/30 patients a gastrostomy was performed. Time to gastrostomy removal or death was median 30 weeks (range 1-82 weeks). For 12/30 patients hospital admission was necessary during treatment. One patient died from acute myocardial infarction 9 months after diagnosis without signs of recurrence. In 4 patients grade 3 late toxicity was recorded (3x persistent need for tubefeeding, 1 x osteonecrosis requiring surgery).
Conclusions: The results appear to be in line with what can be expected on the basis of published literature. Longer follow-up in a larger patient group is needed to draw firm conclusions.

Posters Heavy Particle Therapy

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A MONTE CARLO IMPT PLANNING STUDY: ANALYTICAL CALCULATION ERRORS AND INFLUENCE OF GEOMETRY SETUP ERRORS

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Purpose/Objectif: To assess the errors in intensity modulated proton therapy (IMPT) due to analytical dose calculation algorithm and to evaluate the influence of geometry setup errors with help of Monte Carlo.
Materials/Methods: The errors due to an imperfect dose calculation algorithm in IMPT can be divided into systematic algorithm errors (SAE) and convergence algorithm errors (CAE). SAE characterize the difference between real and calculated dose distribution. CAE follow from the SAE since the spot weights are optimized using imperfect dose distribution resulting in a solution different from the optimal one. Most problematic for the widely used analytical dose calculation algorithms in IMPT like pencil beam algorithms are the lateral heterogeneities. To overcome and to assess the errors caused by the analytical algorithm, we use the fast Monte Carlo dose engine VMCpro.Geometry setup errors describe the deviation of the planned and treated patient positioning and are classified as random setup errors (RSE) and systematic setup errors (SSE). If setup errors occur, lateral heterogeneities can cause large errors due to differences in ranges of the repositioned spots. The Monte Carlo dose engine is a straightforward and accurate possibility of studying the effects of setup errors via changing the isocentre position of each individual proton in a spot. A planning study was performed on several head and neck and prostate patient cases.
Results: The CAE show close relation to SAE. In cases, where lateral heterogeneities appear often (head and neck), both the CAE and SAE are significant. For prostate cases, CAE and SAE are smaller. The RSE cause slight underdosage in the planning target volumes, the dose difference in clinical target volumes is very small. IMPT shows large sensitivity to SSE, especially in cases with high heterogeneity level. Here, the prescribed dose area is not only shifted, but can also be largely distorted.
Conclusions: Observed significant CAE and SAE in geometries with high heterogeneity levels give strong reasons for the use of Monte Carlo in IMPT. The influence of RSE on the dose distribution was not critical for the studied cases. Increased attention to diminishing of the SSE is necessary in IMPT.

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ABSORBED AND EFFECTIVE DOSES IN TISSUES EVALUATED FOR HUMAN PHANTOM IRRADIATED WITH HEAVY CHARGED ION BEAMS.

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Purpose/Objectif: Radiation therapy with ions requires careful studies of absorbed dose delivered to the treatment volume and other parts of the patient body with organs exposed to secondary particles produced in heavy charged ion beams. The effective doses to these organs should be evaluated and the risk of induction of secondary tumours discussed. Studies of energy spectra of primary particles and their secondaries as well as spatial distribution of the delivered dose to human organs are of importance for evaluation of biologically equivalent doses delivered to patients. Due to very complex interaction pathways of high energy and heavy charged ions transported in the patient computation methods using three dimensional Monte Carlo particle transport codes provide unique and very useful tool in the prediction of the physical radiation doses to organs. They also provide invaluable information for the development of the other algorithms for physically and biologically optimized ion therapy treatment planning.
Materials/Methods: Calculations of the absorbed and effective doses in specific organs and tissues of human body due to irradiation by heavy charged ion beams were performed using the SHIELD-HIT and MCNPX Monte Carlo codes. SHIELD-HIT simulates the interactions of hadrons and atomic nuclei of arbitrary mass number (Z, A) with complex extended targets, whereas the ion transport capability of MCNPX is limited to projectiles of A=4. In these studies proton, helium, lithium and carbon ion beams in the wide range of energies up to hundreds of MeV/u were transported through the human body phantoms. The mathematical anthropomorphical phantoms ADAM (male) and EVA (female) were applied in the evaluations with MCNPX, whereas in the SHIELD-HIT calculations a simplified body phantom was used.
Results: The incident ion beam was simulated as a quasi-monoenergetic beam with an energy spread, sE, and a Gaussian spatial distribution. The studies were performed also for parallel monoenergetic beams and for a more clinically relevant case with the spread out Bragg peak (SOBP) composed by a non-linear superposition of several Bragg peaks corresponding to ion beams of different energies. The effective doses in specific organs were calculated using the radiation weighting factors and the tissue weighting factors from ICRP Publication 74. The effective doses in the organs calculated by SHIELD-HIT and MCNPX are compared for proton and helium beams.

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ANALYSIS OF TISSUE SUBSTITUTES USING A MONTE CARLO SIMULATION OF HOUNSFIELD UNITS

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Purpose/Objectif: The calculation of carbon ion range in tissue for the purpose of heavy ion treatment is based on a Hounsfield unit look-up table (HULT). The HULT allows a fast and reliable translation of HU to water equivalent depth (WED) provided that the measured HU are correct. However, measured HU values vary with measurement parameters such as X-ray voltage and image reconstruction algorithm. Other parameters influencing the HU values are the size and material of phantoms and substitutes used to develop the database. However, the correlation between the different parameters and HU is known only empirically.
Materials/Methods: In this work, we present an approach to simulate HU taking into consideration the geometry, composition, and physical process behind the measurement of HU values. The approach involves Monte Carlo simulations followed by a simple filtered back projection reconstruction. The Monte Carlo code used is BEAMnrc. The simulations of an X-ray tube including the associated filters and beam shapers of a Siemens Emotion CT were used to generate the initial beam shape and spectra. This was followed by further simulations of the used phantoms and substitutes. The resultant phase space file is analyzed to calculate the projections, taking into account the energy response of the CT-detectors. Then, a simple reconstruction algorithm (FBP using a Ram-Lak filter) is applied to the calculated projections and finally the data is presented in HU format.
Results: Results indicate good agreement between simulated and measured HU values of Gammex tissue substitutes. A maximum deviation of about 100 units larger than measured value was recorded with better agreement in the range 0-500 Hounsfield Units. Moreover, the simulation correctly predicted the behavior of some materials discussed in [1], which did not follow the standard HULT data. Further simulations on the influence of the build-up effect, involving different phantom sizes are discussed.
Conclusions: We have developed an aproach to simulate Honsfield Units preserving thep hysical process behind HU measurement. The calculation results agree with measurements and can correctly predict the effect of composition on HU.
References:
[1] Schardt D, Karger C P and Hartmann G H 2001 Relation between Carbon ion ranges and x-ray CT numbers Med. Phys. 28 701-703

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CARBON ION RADIOTHERAPY FOR LOCALLY ADVANCED ADENOCARCINOMA OF THE UTERINE CERVIX

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Purpose/Objectif: To evaluate the toxicity and efficacy of carbon ion radiotherapy (CIRT) for locally advanced adenocarcinoma of the uterine cervix by a phase I/II dose-escalation study.
Materials/Methods: Between April 1998 and August 2005, 26 patients with adenocarcinoma of the uterine cervix were treated with CIRT. The mean age of the patients was 60 years. Histologically, 19 patients had adenocarcinomas and 7 had adenosquamous cell carcinomas. Seven patients had stage IIB, 17 had stage IIIB, and 2 had stage IVA disease. The median tumor size was 6.0 cm. The treatment consisted of whole pelvic irradiation and local boost. The clinical target volume (CTV) of whole pelvic irradiation included the cervical tumor, uterus, parametrium, at least the upper half of the vagina, and pelvic lymph nodes. The dose of the whole pelvic irradiation was fixed at 36.0 gray equivalent (GyE) in 12 fractions. In local boost irradiation, the CTV was shrunk to the cervical tumor and surrounding tissues. A dose escalation study was performed with an initial dose of 26.4 GyE/8 fractions, and the dose was gradually increased up to 35.2 GyE/8 fractions (total dose: 62.4-71.2 GyE). The dose to the GI tracts was limited to less than 60 GyE. The median follow-up duration for the surviving patients was 34 months (range, 8-74 months).
Results: No patient developed severe acute toxicity. Three patients developed grade 1 late rectal complications and 2 developed grade 1 late bladder complications. One patient who received 68.0 GyE developed rectovaginal fistula 14 months after CIRT. Local tumor control was obtained in 4 of the 7 patients (57%) who received a total of 62.4-64.8 GyE, in 7 of the 9 patients (78%) who received 68.0 GyE, and 9 of the 9 patients (100%) who received 71.2GyE. The 3-year local control rate for all patients was 71%. Three patients who

had developed local recurrence were surgically salvaged. The 3-year overall survival rates for all patients and the 17 patients with stage IIIB or IVA disease were 65% and 58%, respectively.
Conclusions: Although the number of patients was small, the results suggested that CIRT provided favorable local tumor control and overall survival with acceptable rates of late complications in the treatment of locally advanced adenocarcinoma of the uterine cervix.

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CLINICAL IMPLEMENTATION OF MULTIPLE FIELD DOSE OPTIMIZATION IN HEAVY ION TREATMENT PLANNING

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Purpose/Objectif: Evaluate multiple field dose optimization in carbon ion treatment planning in order to establish this technique in clinical routine. The study is performed in cooperation with the biophysics group at the Gesellschaft für Schwerionenforschung (GSI) in Darmstadt, and the radiology department of the university clinic Heidelberg, .Intensity modulated particle therapy (IMPT) evolves into a promising technology in cancer treatment. Heavy ions are superior to proton projectiles e.g. in terms of biological effectiveness and dose conformity. The carbon ion raster scanning technology at the GSI places high demands on treatment planning to obtain a homogeneous dose distribution in the target volume. The treatment planning software TRiP98 used so far for patient treatment optimizes different fields individually. An advanced version developed by the GSI biophysics group, TRiP98BEAM, allows the simultaneous optimization of multiple fields to improve the sparing of organs at risk and to enhance the conformity of the target volume.
Materials/Methods: A planning study is performed using actual patient data of deep seated head tumours close to critical structures. The goal is to derive suitable input parameters for the dose optimization procedure, which are the maximum doses for organs at risk as well as the penalty weights for dose deviations (target volume) and excess (organs at risk). The physical and biological dose distributions are compared for single and multiple field optimization using dose volume statistics like conformity index, homogeneity of the target volume, and maximum dose for organs at risk. Furthermore, the feasibility and the robustness of the application of the treatment plans are investigated concerning beam delivery, dosimetry and patient positioning.
Results: Compared to the currently applied technique multiple field dose optimization yields improved dose conformity, comparable dose homogeneity in the target volume, better sparing of organs at risk, and comparable dose exposure of normal tissue. The improved method is also competitive in terms of treatment plan application and robustness.
Conclusions: The multiple field dose optimization technique as implemented in TRiP98BEAM provides an improved treatment plan while reducing the physicist's time for carbon ion treatment planning. The method is ready to enter the clinical routine of carbon ion therapy.

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CLINICAL RESULTS OF PROTON BEAM THERAPY FOR LOCOREGIONALLY ADVANCED ESOPHAGEAL CANCER

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Purpose/Objectif: Proton beam therapy can deliver higher doses to target tissue with a considerably smaller dose to the adjacent normal tissues compared to that using conventional radiotherapy. The aim of this study is to evaluate the clinical outcomes of proton beam therapy for locoregionally advanced esophageal cancer.
Materials/Methods: Forty-two esophageal cancer patients who were irradiated with protons with or without x-rays between 1985 and 2004 were reviewed. All patients had locoregionally advanced disease with at least T2, N1 or M1a, and had squamous cell carcinoma. Of the 42 patients, 4 had T1 tumors, 8 T2, 19 T3 and 10 T4. The median cephalo-caudal tumor diameter was 6.0 cm (2.0-15.0). Seven patients received combined irradiation with x-rays (median 41.4 Gy) and protons (median 36.8 Gy) over 44-52 days using accelerated fractionation. Twenty-three patients received combined irradiation with x-rays (median 40.0 Gy) and protons (median 37.0 Gy) over 44 - 92 days using conventional fractionation. The remaining 12 patients received a median 75.5 Gy (60.0-89.5 Gy) of protons alone in 33 - 63 days. The median follow-up period was 43 months (4-143). We measured the tumor response, survival rates, patterns of failure and treatment related morbidity.
Results: Thirty-four patients (81%) showed complete response within 4 months after completion of treatment. The overall 5-year actuarial survival rates for all 42 patients, the 32 with cT1-3, and the 10 with cT4 were 18%, 20%, and 10%, respectively. The corresponding 5-year cause-specific survival rates were 37%, 39%, and 35%, respectively. The 5-year local control rates for all 42 patients, the 32 with T1-3, and the 10 with T4 were 36%, 38%, and 36%, respectively. The 5-year local control rates for 7 patients irradiated using accelerated fractionation and 35 irradiated using conventional fractionation were 71% and 29%, respectively. 27 patients (64%) developed disease recurrence. The patterns of treatment failure were persistent disease in 8 patients, local relapse in the esophagus in 10, regional lymph nodes metastasis in 4 and distant metastasis in 5. Of the 10 patients with local relapse in the esophagus, 8 showed relapse within the irradiated volume, 2 at the boundary of the irradiated volume. Four patients (10%) developed grade 3 acute esophagitis according to the EORTC acute radiation morbidity scoring criteria. Late complications in the esophagus included grade 3 for 4 patients (10%) and grade 5 for 1 patients (2%).
Conclusions: The results suggest that proton radiation therapy is an effective modality for patients with locoregionally advanced esophageal cancer. Further studies are needed to determine the role of accelerated fractionation, optimal fractionation regimens, and optimal combinations of protons and x-rays in the treatment of esophageal carcinoma with protons.

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COMPARATIVE TREATMENT PLANNING FOR RADIOTHERAPY OF HEAD AND NECK TUMOURS BY PHOTONS, PROTONS AND CARBON IONS

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Purpose/Objectif: To compare dose distribution of different radiotherapy modalities for head and tumours: photon IMRT, protons with passive scattering (PPS) and active scanning (PAS), carbon ions with raster scanning (CIRS).
Materials/Methods: The analysis was performed on 4 cases: a maxillary sinus adenocarcinoma, an orbital meningioma, a skull base fibrosarcoma and an occipital glioblastoma (GBM). Target and non-target structures were drawn on planning CT: GTV, CTV, PTV, brain, brainstem, optic nerves and chiasm, pituitary gland, retina, lens, cochlea, temporo-mandibular joint, parotid and lacrimal glands. Dose to PTV was 74 Gy for maxillary sinus carcinoma, 56 Gy for orbital meningioma, 76 Gy for skull base fibrosarcoma and 80 Gy for GBM. Dose constraints for non-target structures were established based on literature data. Photon IMRT was planned by TPS Pinnacle (Philips), PPS was planned by Helax-TMS planning system, PAS by PSI-Plan developed at Paul Scherrer Institut () and CIRS by TPS TRiP developed at GSI-DKFZ (Darmstadt-Heidelberg,). Isodoses and DVHs for target and non-target structures were calculated and compared for the different treatment modalities.
Results: The PTV was always quite well covered by all techniques. The integral dose to the whole brain was higher using IMRT than the other techniques in all cases. In maxillary sinus adenocarcinoma, the dose-limiting critical structures were better spared by PAS and CIRS whereas PPS and even more photon IMRT delivered a relevant dose the brainstem and optic pathway. In orbital meningioma, CIRS and PAS delivered minimal dose to pituitary and optic pathway whereas photon IMRT and PPS delivered higher dose to a relevant volume of such structures. In skull base fibrosarcoma, CIRS delivered the lowest dose to pituitary, cochlea, optic pathway and retina. PAS achieved a dose distribution similar to that of CIRS for optic pathway. IMRT delivered the highest dose to most non-target structures. In GBM, CIRS, PAS and PPS achieved a very satisfactory dose distribution whereas photon IMRT delivered a relatively higher dose to non-target structures such as brainstem and cochlea.
Conclusions: A satisfactory coverage of PTV was achieved by all techniques. CIRS and PAS allowed to minimize the irradiation of most non-target structures. Photon IMRT delivered the highest dose to non-target structures and the highest integral dose to the whole brain tissue.

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COMPARISON OF MONTE CARLO AND ANALYTICAL MODELS FOR LIGHT ION SECONDARY PARTICLE PRODUCTION

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Purpose/Objectif: The unique physical and biological properties of light ion beams make them ideal for radiation therapy, particularly in the treatment of intractable cancers that are resistant to conventional low LET beams. The therapeutic interest in ^{7}Li therapy, especially for paediatric patients, has recently been demonstrated. In order to increase the accuracy for biological optimized light ion treatment planning maximum knowledge about the fluence and energy deposition of both primary ions and fragmentation produced secondaries is required. The present work focuses on an analytic description of the fluence of the main secondary fragments ,^{1}H and ^{4}He, that are generated in therapeutic ^{7}Li ion beams.
Materials/Methods: The Monte Carlo code SHIELD-HIT was used for comparison with analytical depth fluence distributions. The depth fluence curve of the secondary ^{1}H can be approximated by assuming simple exponential fluence attenuation of primaries and secondaries according to

$$(1)\quad \Phi^s(z) = -\int_0^\infty \left(\frac{d\Phi^p}{ds}\right) e^{-\mu_s(z-s)} ds$$

$$(2)\quad \Phi^s(z) = \frac{\mu_p \Phi_0^p e^{-\mu_s z}}{(\mu_p - \mu_s)} \left(1 - e^{-z(\mu_p - \mu_s)}\right)$$

where $z = R_p$ (the primary particles projected range) in the last parenthesis beyond $z \geq R_p$.
The μ_p and Φ^p describes the exponential attenuation of the primary Li ions in water and μ_s and Φ^s the absorption of the secondary protons.

Results: Fig 1 illustrates the depth dependence of the secondary ^{1}H fluence along the central axis in a broad ^{7}Li in a water phantom, calculated with the analytical model as well as with Monte Carlo simulations.

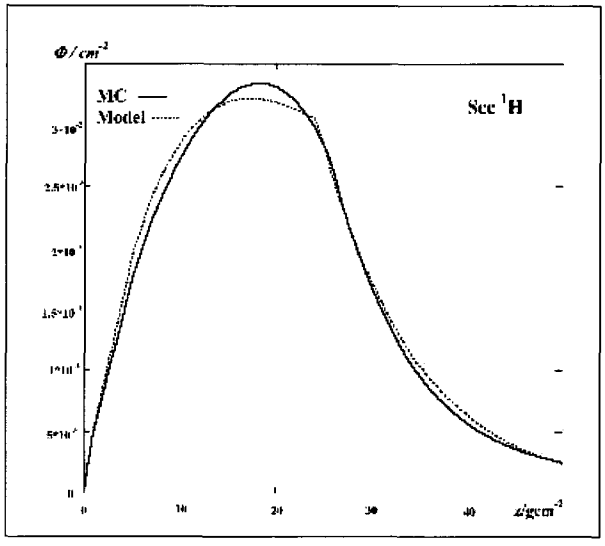

Fig.1 Analytical depth fluence curve of secondary ^{1}H in a 234 MeV/u ^{7}Li ion beam in water(dotted curve) compared with MC data from SHIELD-HIT (solid curve).
Conclusions/ The analytical expression was found to be in good agreement with MC data as seen in the figure. The present model contributes to fast calculations of the dose of the fragments generated in a high energy ^{7}Li beam. This is of greatest importance in treatment planning, where especially a correct description of the fragmentation tail beyond the Bragg peak is often needed.

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EFFECTS OF METAL ARTEFACTS FOR PROTON DOSE DISTRIBUTION AND POSSIBLE SOLUTIONS

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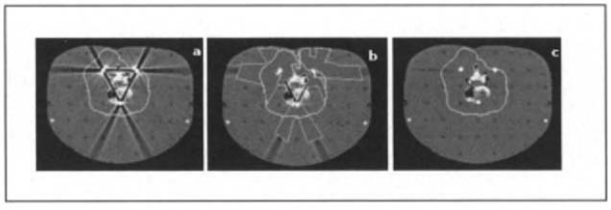
Purpose/Objectif: To investigate the effect of CT metal artifacts on proton dose distributions and to exploit the potential use of MVCT for proton planning
Materials/Methods: Many patients with chordoma or chondrosarcoma along the spinal axis are referred for proton therapy after the surgical removal of one or more vertebrae and insertion of stabilizing titanium rods. Even if the titanium stopping power is known to better than 1%, the presence of metal itself causes reconstruction artefacts in the CT data, which perturb the range calculations. To investigate the magnitude of this problem, we analysed 2 CT's of

an Alderson phantom which had 3 titanium rods inserted: the nominal CT acquired with artifacts (CT_art) and a modified CT (CT_corr), where artifacts were outlined and defined with an average soft tissue value. Finally, a 'free artifacts' CT (CT_ref) was generated, obtained by acquiring a CT without the metal implants, and artificially setting the relevant voxels at the position of the implants to that of titanium (see fig). Plans were calculated and optimized on CT_art and compared with the one re-calculated on CT_ref. The same comparison was performed for CT_corr. To study the possibility of using a MVCT system for proton planning (where artifacts are minimised), we have also calculated a calibration curve wich relates proton stopping power with MVCT.

Results: While DVH comparison between plans on CT_art and CT_ref showed differences below 2% in the PTV, local differences as high as 40 % were found. This is a consequence of range differences, which in the PTV were up to 3.3 cm. For CT_corr, the differences reduced somewhat (2.7 cm maximum). 'Free artifacts' images were also obtained with a MVCT system: a linear correlation between MVCT values and proton stopping power has been found and images of patients are under investigation to better understand the effect of metal artifacts.

Conclusions: For patients with metal implants, the range uncertainties due to artifacts can cause locally large effects. A correction for these, assigning an average HU value to a manually defined 'soft-tissue' volume, shows some improvements. However, a further improvement could be achieved by using a MVCT system that potentially allows to calculate the dose on an 'artifact-free' volume.

Fig a)CT_art:no artifacts correction. The yellow line outline PTV;b)CT_corr:artifacts outlined(green line)and defined as soft tissue;c)CT_ref: presence of metal implants and lack of artifacts



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INTERACTION OF HIGH-LET HEAVY-ION IRRADIATION AND CHEMOTHERAPEUTIC AGENTS ON TWO CELL LINES WITH DIFFERENT RADIOSENSITIVITIES AND DIFFERENT P53 STATUS IN VITRO

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Purpose/Objectif: It is known that relative biological effectiveness (RBE) of high-LET heavy-ion irradiation is higher than that of low-LET radiation such as X-ray. We investigate the differences between two rat yolk sac tumor cell lines with different radiosensitivities in sensitivity to high-LET heavy ion beam and in sensitizing effect of cisplatin and etoposide in combination with heavy-ion beam.

Materials/Methods: NMT-1 (wild-type p53 cell) is a parent radiosensitive cell line and NMT-1R (mutant-type p53 cell) is a variant radioresistant cell line. Heavy-ion (carbon ion) was accelerated to 290MeV/u by a heavy-ion medical accerelator in Chiba at National Institute of Radiological Sciences. The dose average LET value in the samples was 80 keV/μm. The effects of carbon ion irradiation were assessed by clonogenic assay. The concentration of etoposide required to reduce colony formation by 50% at 1-hour treatment (IC50 of etoposide) was selected for heavy ion irradiation pretreatment for each cell line. The RBE of the carbon ion beams to X-rays was calculated for D10 (10% survival dose).

Results: There was no significant difference between NMT-1 cells and NMT-1R cells in sensitivity to high-LET heavy ion irradiation (LET;80keV/μm) and no shoulder in dose-response curve. The RBE was 1.41 for NMT-1 and 2.16 for NMT-1R, respectively. The RBE of carbon beam was larger in mutant-type p53 cells than in wild-type p53 cells. Etoposide showed a synergistic effect in combination with carbon beam irradiation in NMT-1R cells. Etoposide potentiation in NMT-1R cells was manifested by the decrease in the slope of the radiation dose-response curve. However, there was no enhancement effect in radiosensitive NMT-1 cells. On the other hand, cisplatin had no enhancement in both cell lines. Etoposide and cisplatin did not have an effect on the frequency of apoptosis in both cell lines.

Conclusions: Our findings suggested that high-LET radiotherapy is expected to be effective for patients carrying radioresistant tumors and mutated p53 tumor cells. Etoposide might be effective for radioresistant tumors in combination with heavy ion beam irradiation. The mechanism of enhancing effect on NMT-1R (mutant p53 cells) treated with heavy-ion irradiation and etoposide might be independent of apoptosis.

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PERFORMANCES OF A MONITOR SYSTEM USED IN CLINICAL ROUTINE FOR THE TREATMENT OF UVEAL MELANOMA AT CATANA

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Purpose/Objectif: Ocular patologies have been treated since spring 2002 in Catania at Centro di AdroTerapia ed Applicazioni Nucleari Avanzate (CATANA) which was set up by the collaboration between Istituto Nazionale di Fisica Nucleare (INFN) - Laboratori Nazionali del Sud (LNS), Physics Department, Ophthalmology Institute and Radiology Institute of Catania University and CSFNSM Catania. The main goal of CATANA is the study and application of proton therapy for treatment of shallow tumours (4 cm max) like uveal melanomas and subfoveal macular degenerations. In a proton therapy centre, one of the main issues is to assure a correct delivery of the dose to the patient. The beam has to be monitored in a non-invasive way downstream of the spreading system and its position, shape and intensity have to be measured just upstream the target. This in order to feedback the upstream elements of the beam line or to prevent against any possible failure. For this reason a detector system has been developed in collaboration with INFN and Torino University to be used as real time beam monitor.

Materials/Methods: A proton beam of 62 MeV is delivered by a superconducting cyclotron with passive delivery system. The detector, placed upstream of the patient collimator, consist of two parallel plate strip segmented ionisation chambers with vertical and horizontal strip orientation. Each anode consists of 256 strips with 12.8

x 12.8 cm^2 sensitive area. Each strip is 0.4 mm wide with 0.1 mm of interspace. The use of two strip detectors allows the measurement of relevant beam parameters during treatment such as integrated fluence, centre of gravity and asymmetry. These parameters are measured at a rate of about 1 Hz, with no dead time.
Results: At CATANA, the detector has been characterised with different beam conditions and it is used in clinical practice. Beam shape and integrated fluence as measured with this detector will be discussed and compared with those obtained with other reference detectors. The value of skewness and centre of gravity have been tested in different beam settings both online and offline. Limits have been set on the allowed range of values for the beam centre of gravity and skewness. During treatment these parameters are evaluated in real-time and checked against the set limits to ensure the correct delivery of the dose.
Conclusions: In this paper we present the performances of a transmission ionisation chamber with the anode segmented in strips. We report the use of the detector as online beam monitor to measure the beam characteristics. The beam is monitored with frequency of the order of one Hertz and it can be stopped in case of misbehaviour.
The work has been partially supported by the European Integrated Project MAESTRO, granted by the European Commission (N° LSHC-CT-2004-503564).

890 poster

PROTON RADIOTHERAPY FOR ADENOID CYSTIC CARCINOMA OF THE HEAD AND NECK

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Purpose/Objectif: To evaluate preliminary results of proton radiotherapy for adenoid cystic carcinomas (ACC) of the head and neck.
Materials/Methods: Between July 2003 and November 2005, 16 patients with histopathologically proven ACC of the head and neck were treated with proton radiotherapy. The prescribed dose was 65GyE/26fr/5.2wks. Median follow-up time was 6 months (3-27 months) at the time of analysis. There were 6 male and 10 female patients. Median age was 56 years (range, 33 to 81 years). Thirteen of 16 patients had stage ‡W disease and there were no other effective treatment methods at the time of proton radiotherapy. Primary tumors were located in the maxillary sinus in 4 patients, sphenoid sinus in 3, pterygopalatine fossa in 3, major salivary glands in 2,nasopharynx in 2, ethmoid sinus in 1, and lacrimal gland in 1. Nine patients showed a cribriform subtype, 6 a solid subtype and ,Pa histopathological subtype unknown.
Results: Probabilities of overall survival, progression free survival and local control were calculated from the first day of proton radiotherapy using the Kaplan-Meier method. They were 88.9%, 67.3% and 83.3% at 1 year, respectively. Tumor response was classified according to WHO criteria and evaluated at 2.5-3 months. Complete response was not achieved in any patient so far, but all of the tumors showed reduction in volume. Seven patients resulted in partial response, 9 in no change, and there was no progression disease. There observed 1 local recurrence within the PTV whose disease was located in the lacrimal gland, and occurred at 8 months from the beginning of the treatment. One patient developed metastases in the bone at 5 months and another one developed metastases in the bone, meninges and brain at 6 months. All of these 3 patients had solid type disease. Acute side effects Common Toxicity Criteria Grade 3 were observed in 6 patients. Four of them developed mucositis, 1 dermatitis and 1 otitis externa. All of them were limited in the area where received relatively high doses. There observed no acute or late toxicity greater than Grade 3 so far.
Conclusions: Although the follow up period is too short to give any definite conclusion, our clinical results of proton radiotherapy for locally advanced adenoid cystic carcinoma of the head and neck seem to be encouraging.

891 poster

RANGE ADAPTATION FOR PATIENTS TREATED WITH IMPT, AFTER ANATOMICAL CHANGES DURING THERAPY

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Purpose/Objectif: The precision of proton radiotherapy strongly depends on the precision of range in the patient. Changes in the patient weight and anatomy can affect the range and consequently the dose distribution (i.e. under dosage in the target volume and over dosage in critical organs). We investigated the possibility offered by the spot scanning technique to adapt the range to those changes. With this technique, Bragg peaks are delivered at the correct depth in the body using pencil beam specific numbers of computer controlled range shifter (RS) plates. Consequently, a correction of range errors due to anatomical changes during treatment could potentially be obtained by varying the number of plates inserted.
Materials/Methods: We considered two patients with paraspinal tumors treateds with Intensity Modulated Proton Therapy (IMPT) in which significant weight gain and loss had been observed during the treatment course. In both cases, the IMPT plans delivered a 'hole' around the spinal cord which was mainly formed through the modulation of the Bragg peaks in depth. Any anatomical variation can thus cause a difference in the spot positions along the beam direction, which affects the resulting dose distribution. As a consequence of these weight changes, new CT scans had been acquired, and the patient re-planned. In order to assess the potential for range adaptation, range differences between the nominal and repeated CT's were calculated for all Bragg peak positions in each field for both patients. From these calculations, the actual Bragg peak positions delivered in the repeated CT could be 'corrected' through adding or removing RS plates. The effectiveness of this method was assessed by visual and DVH comparison of the corrected dose distribution with the nominal plan.
Results: The mean range differences for the two cases were 4.6 and 5.7mm, corresponding to mean changes of 1.0 and 1.2 RS plates respectively. After range adaptation in the weight loss case, homogeneity in the PTV could be regained (same mean dose and V90) and the maximum dose to the spinal cord increased by only 1% in relation to the nominal plan. For the weight gain patient, the same parameters showed differences below 2.5%.
Conclusions: No significant differences in the dose distributions were detected between the nominal plans and the plans corrected with this method, indicating that the spot scanning technique potentially allows for the on-line correction of range changes without the need for redrawing of the VOIs or re-planning.

892 poster

REACTOR FISSION NEUTRON BEAM FOR RADIOTHERAPY

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Purpose/Objectif: Reactor Fission Neutron Beam Therapy was applied to more than 600 patients from 1985 to 2000 at the research reactor FRM. Clinical data showed good results for treatment of

tumor lesions close to the surface of the patient. The reactor was shut down in 2000. At the New Research Reactor FRM II in Garching / Munich which is in operation since 2004 a new treatment facility for reactor neutron therapy was built.
Materials/Methods: The new facility offers a neutron beam with mean energy 1,6 MeV. The total dose rate is 0,74 Gy/min (0,54 from neutrons, 0,20 from gamma). The half value depth for the neutrons is about 5 cm. This restricts the treatment to superficial tumours.
A 2 x 20-leaf-collimator allows the individual conformation of the field to the tumour size up to the maximum field size 30 x 20 cm^2. For patient's security a patient-verification-System (Risska) was implemented.
Results: The beam characterization for both the neutron and gamma component for all field sizes has been done. The facility has been examined according to the Medical Devices Act, MPG, with respect to the functional, mechanical and electrical safety, with external experts in order to furnish it with the CE safety mark according to the MDD 93/42/EWG. The completion of this procedure is a precondition for the official application to start with treatment. We hope to get the permission for patient treatment still during this year.
Conclusions: In collaboration with MRI, Klinik für Strahlentherapie und Radioonkologie, treatments with the fission neutron beam will start soon at FRM II. Indications for neutrons radiotherapy are various histology, even hypoxic tumours, especially salivary gland neoplasm (adenoid cystic carcinomas, recurrent polymorphic adenomas), sarcomas, melanomas, superficial lymph node metastasis and superficial tumour recurrences of breast cancer. All patients' personal data and radiotherapy data will be served in the patient-verification-system "RISSKA". This program allows also statistical analysis.

893 poster

RESPONSE OF A TRANSPLANTABLE MOUSE MAMMARY CARCINOMA TO SINGLE DOSES OF ACCELERATED CARBON IONS

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Purpose/Objectif: A novel energy-modulated raster scan beam of accelerated carbon ions is available at GSI for patient treatment. The present study was designed to quantitate RBE values of this modality in a transplantable mouse tumour.
Materials/Methods: Mouse mammary carcinoma AT17 transplanted subcutaneously to the flank of isogenic C3H mice was submitted to single dose irradiation in a 2cm SOBP, under either ambient conditions or temporary tumour anoxia (clamp). Reference experiments of identical design were conducted with 300 kV X-rays. RBE measurements were derived from both local tumour control and from a modified regrowth delay assay that utilized the reciprocal delay time.
Results: Well defined dose responses for both endpoints were obtained in the experiments, but due to the slow tumour growth rate observation periods greater than 4 months were required to obtain conclusive results. RBE values measured at 8 months by regrowth delay were about 2.7 both for clamp and ambient conditions, and for local tumour control were 2.1 and 2.2, respectively.
Conclusions: RBE values measured in vivo for the carbon ion beam at GSI were equal to or slightly higher than those reported for other beams of accelerated ions with passive modulation, suggesting a high therapeutic potential.

894 poster

SIMULTANEOUS MULTIFIELD OPTIMIZATION OF THE BIOLOGICAL EFFECT IN RADIOTHERAPY WITH CARBON IONS

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Purpose/Objectif: Simultaneous multifield optimization is a standard technique in treatment planning for IMRT with photons. This is different in radiotherapy with carbon ions, where the optimization has to be done in terms of the biological effect instead of the dose. Up to now, clinical treatment planning for carbon ion therapy was only done by optimizing each field separately ("single field optimization"). We propose a new method for fast multifield optimization of the biological effect for intensity modulated radiotherapy with ion beams and investigate its clinical potential.
Materials/Methods: The calculation of the biological effect is based on the mixed irradiation formalism of the standard linear-quadratic (LQ) model using dose averaged mean values for the LQ parameters alpha and the square root of beta to account for variations of the relative biological effectiveness (RBE). We employ a novel objective function to directly optimize the biological effect (i.e. RBE times dose) rather than the physical dose. It is based on objectives in terms of the biological effect for targets and organs at risk in close analogy to inverse planning for photons. The required biological input data are completely independent from the optimization itself. They are reduced to minimum and can be derived from any radiobiological model or even from directly measured data. The new optimization method was fully integrated into a research version of the inverse treatment planning tool KonRad.
Results: Multifield optimization was compared to single field optimization for a variety of examples from simple spread-out Bragg peaks (SOBPs) for two opposing beams to more complex plans with up to five intensity modulated fields. In all cases it was evident that multifield optimization adds more degrees of freedom that can be exploited to improve the sparing of critical structures and normal tissue while maintaining the same target coverage. For scanned ion beams, multifield optimization also offers the possibility of special scanning techniques like multi-layer distal edge tracking, which can provide the advantages of a multifield plan with a moderate number of beam spots for time-efficient optimization. Depending on the number of beam spots used, typical optimization times are between 10 and 60 minutes.
Conclusions: In conclusion, simultaneous multifield optimization of the biological effect can considerably enhance the resulting treatment plans compared to single field optimization since it makes the best use of all possible degrees of freedom.

895 poster

STOICHIOMETRIC CALCULATION OF THE RELATION BETWEEN CARBON ION RANGES AND X-RAY CT NUMBERS

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Purpose/Objectif: For accurate consideration of tissue-inhomogeneities in hadron-therapy, mainly Hounsfieldunit-Lookuptables (HLUT) are used. This HLUT give a relationship between CT units (HU) and ion ranges, normalized to water as water equivalent path length (WEPL). The purpose of this work is to establish a stoichiometric calculated HLUT as suggested by Schneider U. et. al. (1996), using simulated WEPL, and to compare the results with the existing empirical data.
Materials/Methods: For CT number measurements, tissue substitutes were placed in a Plexiglas phantom and positioned at the im-

age plane centre of a Siemens Sensation 4 CT. With the measured HU and the given composition of each substitute, a parametrization of the CT in terms of absorption processes can be obtained by a fitting procedure. Stoichiometric CT numbers HU_{st} of substitutes and various real tissue compositions were calculated by using the resulting fitting parameters. SHIELD-HIT was used to simulate the WEPL for the same real tissues. The initial energy of the ion beam was 184 MeV/u. In order to double-check the results, a SRIM2003 calculation was carried out. For this WEPL calculation, only the stopping power of carbon ions at various energies (50-250 MeV/u) in the single tissue elements relative to water was calculated. Bragg's rule was then used to calculate the stopping power ratio for the whole tissue composition. numbers HU of substitutes and various real tissue compositions were calculated by using the resulting fitting parameters. SHIELD-HIT was used to simulate the WEPL for the same real tissues. The initial energy of the ion beam was 184 MeV/u. In order to double-check the results, a SRIM2003 calculation was carried out. For this WEPL calculation, only the stopping power of carbon ions at various energies (50-250 MeV/u) in the single tissue elements relative to water was calculated. Bragg's rule was then used to calculate the stopping power ratio for the whole tissue composition.

Results: Measured and stoichiometric calculated CT numbers of the substitutes were compared to evaluate the fitting procedure and showed a maximum deviation of 28 HU. The maximum variation of the WEPL calculated with SRIM2003 for different energies amounts to 1%. The highest discrepancy between the SRIM2003 calculation and the SHIELD-HIT simulation is less than 1%. Apart from the lung tissue, the biggest difference in percent between the calculated WEPL of a tissue and the WEPL suggested by its stoichiometric CT number and the empirical HLUT amounts to 2.5%.

Conclusions: With the accurate data of the SHIELD-HIT simulation and the SRIM2003 calculation, the stoichiometric calibration yields a usefull tool to compare and verify the empirical HLUT. While SRIM2003 calculations indicate very constant stopping power ratios in a wide range of ion beam energy, these ratios have only been compared with an SHIELD-HIT simulation using an initial energy of 184 MeV/u. Additional simulations or measurements with lower energy are needed for further comparison with the SRIM2003 results.

Posters Hypoxia and Angiogenesis

896 poster

RADIOTHERAPY- INDUCED CHANGES ON ANGIOGENESIS AND LEUCOCYTE INFILTRATION IN RECTAL CANCER.

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Purpose/Objectif: We and others have shown that angiogenesis and leukocyte infiltration are important prognostic factors in rectal cancer. However, little is known about its possible changes in response to radiotherapy, which is frequently given to rectal tumors as a neoadjuvant treatment. We therefore investigated the biological effects of radiotherapy on these parameters using fresh frozen biopsies from tumor and normal mucosa tissue before and after radiotherapy.

Materials/Methods: Biopsies were taken from a total of 34 patients prior to and after either a short course or long course of radiotherapy combined with chemotherapy. The following parameters were analyzed by either immunohistochemistry, flow cytometry or qRT-PCR: Microvessel density, leukocyte infiltration, proliferating epithelial and tumor cells, proliferating endothelial cells, adhesion molecule expression on endothelial cells and the angiogenic mRNA profile.

Results: The tumor biopsies taken after radiotherapy treatment demonstrated a significant decrease in microvessel density, the number of proliferating tumor cells and proliferating endothelial cells ($p<0.001$). In contrast, the leukocyte infiltration, the levels of bFGF in carcinoma tissue and the adhesion molecule expression on endothelial cells in normal as well as carcinoma tissue significantly increased ($p<0.05$).

Conclusions: Our data show that together with an overall decrease in tumor cell and endothelial cell proliferation, radiotherapy results in an increase in the expression of adhesion molecules that stimulate leukocyte infiltration. This suggests the possibility that in addition to its direct cytotoxic effect, radiation may also stimulate an immunological tumor response which could contribute to the documented improvement in local tumor control and distal failure rate of rectal cancers.

Posters IMRT

897 poster

2D DOSIMETRY WITH GAFCHROMIC EBT: IMRT PLANNING VERIFICATION

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Purpose/Objectif: Intensity modulated radiation therapy in external beam radiation therapy is one of the latest conformal therapy techniques used in tumour treatments. IMRT employs non-uniform, individual optimised, beam intensity in order to delivery high conformal radiations to the target while minimising doses to normal tissue and critical organs. Individual patient plan QA for IMRT is usually performed with films dosimetry to provide spatial information. Radiographic film often doesn't give a good result in absolute dose verification, especially for the high response at low energy and scatter radiation. A good alternative are the gafchromic films that have an independent energy response; for a right use of these films in 2D-dosimetry verification is, however, necessary a correction for the inhomogeneity introduced by the scanner.

Materials/Methods: To delivery IMRT we use a Elekta LINAC with energy 6 MV and 10 MV in steep and shoot technique. The planning is perform with TPS Precise plan (Elekta). To verify the planning in trasverse and coronal plane we use EBT gafchromic film scanned with an Epson scanner 1680 pro, in the only red channel (bit depth 16bit/channel), due to the optical property of the film. This method has the disadvantage to increase the film's inhomogeneity response in the direction perpendicular to the scanning direction. Moreover, this inhomogeneity response increases with the film darkening (i.e. dose). The dependency on film darkening was determined through the irradiation of 5 gafchromic films with a 35X35 cm^2 field of 6 MV photon beam with different dose level, starting from 1 Gy to 7 Gy. Because of the different response, from the central to the outer region of the scan, of the scanned film and the dependency on dose, we have conclude that dosimetry with gafchromic film can be done in two ways: by using only the central part of the scanner (about 10x20 cm from the centre) or by correcting the inhomogeneity introduced from the scanner. We chose the second solution: we noticed that the complementary representation of the scanned film (i.e. the "negative images"), shows horizontal profile with a minimal inhomogeneity dependency from film darkening (dose). So we are able to correct the scanner artefact, with a the method independent

of the film's darkening.
Results: The correction matrix of the data can be obtained by divided pixel by pixel the original negative image with the pre-acquired background negative image (correction matrix is calculated through an average of multiple scans of a not-irradiated film (background film), in order to reduce the CCD electronic noise, than spatial filtering was used to minimize artefacts related to the manipulation of the gafchromic film) and then multiple the image data with the average pixel in a select central ROI of the background images. We have applied this procedure in QA of IMRT exposure and results are very excellent. In this way is possible to use the gafchromic in 2D-dosimetry verification. An estimate of the relative error introduced by this procedure, shows that it is of the order of 10^{-3} and can be neglected if compared with the other errors, like 3% of the reproducibility of the gafchromic film estimated from our centre.
Conclusions: The analysis performed on 20 patients, treated in head and neck region with IMRT, demonstrates that our method, to correct the gafchromic film, is necessary to prevent errors in dosimetric plan evaluation.

898 poster

3D PORTAL IMAGE-BASED DOSE RECONSTRUCTION IN A PHANTOM GEOMETRY FOR RAPID IMRT PLAN VALIDATION

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Purpose/Objectif: IMRT plan verification can be a very time-consuming task. Presented here is a new method for rapid evaluation of IMRT plans by acquisition of portal images, and subsequent reconstruction of the dose delivered to a virtual 3D phantom. This technique can replace a number of less complete but more labour-intensive measurements such as point doses, 2D composite films, and fluence comparisons on individual fields.
Materials/Methods: A reference dose calculation is first created by transferring a clinical IMRT plan to a cylindrical phantom, retaining the treatment gantry angles. The isocentre of the fields is placed on or near the phantom axis. This geometry preserves the relative locations of high and low dose regions and has the required symmetry for a simple dose reconstruction. For each field, an Electronic Portal Image (EPI) is acquired in an integrating mode, which represents the dose through the mid-plane of a virtual phantom. The image is convolved with an experimentally-derived kernel to replicate the effect of the cylindrical phantom surrounding the dose plane. A dose calibration factor is obtained from a portal image of a reference field that delivers a known dose at the isocentre of the phantom. Off-axis correction is achieved through division by a flood-field image to ensure uniform pixel response, and multiplication by a corresponding dose flood field that has been calculated at the midplane of the phantom. The 3D dose matrix is reconstructed by attenuation and divergence corrections, and summed to create a dose matrix (EPI-dose) on the same grid spacing as the reference calculation. Comparison of the two distributions is performed with a gradient-weighted 3D dose difference based on dose and position tolerances. The values for this work were 3 % of isocentre dose and 3 mm, respectively.
Results: A retrospective three-way comparison (EPI-dose, conventional QA and calculation) was performed for 20 IMRT plans. EPI isocentre doses were in good agreement with ionization chamber point doses (mean difference δ = -1.0 %, standard deviation σ = 1.2 %), and with calculated doses (δ = -0.8 %, σ = 1.5 %). EPI-dose plane differences from calculated dose had significantly less variance than conventional film plane differences (δ = 1.1 % and 2.1 % respectively). 22 further cases have been evaluated using 3D EPI-dosimetry alone. The mean weighted difference over high-dose volumes (doses above 80% of the isocentre value) was -0.3%, and standard deviations of the distributions ranged from 1.0 % to 2.0 %. Verification time per plan, from initial calculation, delivery, dose reconstruction to evaluation, took on average less than 1.5 hours and was more than four times faster than conventional QA.
Conclusions: A technique has been developed and validated that has resulted in a dramatic reduction in the time required for IMRT plan QA. Because of its inherent simplicity, the technique is optimally suited for detecting clinically-significant variances from a planned dose distribution, rather than for use in the validation of IMRT algorithms.

899 poster

A ROBUST AND SIMPLE IMRT APPROACH REDUCING DOSE TO THE HEART IN LEFT SIDED BREAST CANCER

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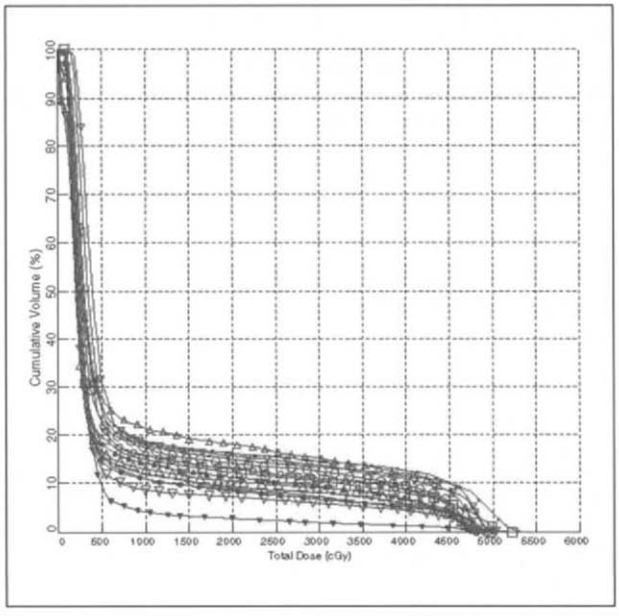
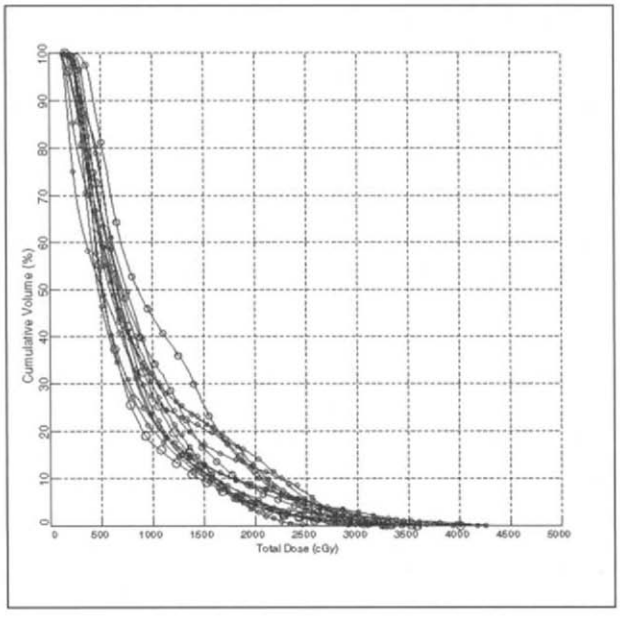
Purpose/Objectif: Although 3D-treatment-planning reduced cardiac dose in postoperative breast radiotherapy, overall cardiac toxicity increased due to the more widespread use of anthracyclines in the adjuvant treatment. Modelling of toxicity based on data from patient series treated for breast cancer and for Hodgkin's disease suggests that reduction of the maximal dose to the left heart might be particularly beneficial.We compared treatment plans created with an aperture based IMRT-approach (an approach that offers some advantages over fully inverse treatment planning) to three-dimensionally planned tangent fields with regard to physical and biological optimisation of the dose distribution, its robustness to positioning errors and its treatment time requirements.
Materials/Methods: CT- and structure data of 14 patients that had been treated postoperatively with external beam irradiation for early breast cancer at our department formed the basis of our plan comparison study. For each patient data set, a conventional 3D treatment plan and an IMRT plan were created on ELEKTA Precise-Plan. Dose Volume Histograms (DVH) were evaluated with regard to target coverage, dose homogeneity, and dose to organs at risk (heart, lung, contralateral breast). Normal tissue complication probability (NTCP) for cardiac mortality as the endpoint was calculated for both approaches based on a relative seriality model. For a representative patient, the influence of positioning errors on the DVH was simulated by moving the isocenter in various directions.
Results: IMRT reduced the maximum dose to the left ventricle from a mean of 49 Gy to a mean of 34 Gy. Heart volume that was exposed to <30 Gy was reduced from a mean of 45 ccm^3 to a mean of 5.8 ccm^3. Mean dose to the heart was increased by an average of 15 %. The change in DVH characteristics translated into a projected reduction of the probability for therapy associated long term cardiac death from 6 % (conventional 3D) to 2.5 % (IMRT) with the relative seriality model. On average, mean dose to the contralateral (right) breast was increased from 1.15 Gy to 5.4 Gy.Coverage of the ventral portion of the breast was robust to positioning errors, coverage of the posterior portion was not as a consequence of steep dose gradients towards the lung/heart.Monitor units, segment numbers and treatment time (<15 min) were within acceptable limits
Conclusions: Aperture based IMRT for left sided breast cancer significantly reduces maximum dose to the left ventricle. This reduction may translate into reduced cardiac mortality based on an appropriate NTCP model. The clinical significance of increased exposure to the right breast is as of now unclear but may be less relevant than cardiac toxicity. As for any conformal technique, patient positioning has to be improved in the direction of the steep gradients (e.g. at the thoracic wall)





900 poster

ACCURACY OF PATIENT DOSE CALCULATIONS FOR IMRT TREATMENT OF LUNG CANCER

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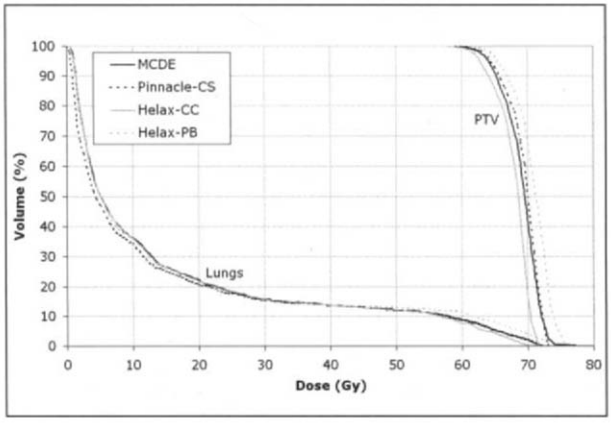
Purpose/Objectif: The accuracy of dose computation within the lungs depends strongly on the performance of the calculation algorithm in regions of electronic disequilibrium. There is a lack of data comparing highly developed analytical dose calculation algorithms to Monte Carlo (MC) computations in a clinical setting.

Materials/Methods: We compared full MC calculations (performed by our MC Dose Engine MCDE) with two different commercial convolution/superposition (CS) implementations (Pinnacle-CS and Helax-TMS's collapsed cone model Helax-CC) and one pencil beam algorithm (Helax-TMS's pencil beam model Helax-PB) for 10 IMRT lung cancer patients. Treatment plans were created for 6 and 18 MV photon beam qualities. The following set of clinically relevant dose-volume values was reported: D_{min}, D_{50} and D_{max} for the GTV and PTV; V_{20} and V_{30} of the lungs and the mean lung dose; D_{33} and D_{max} delivered to the heart and the expanded oesophagus; and D_{max} for the expanded spinal cord.

Results: Statistical analysis was performed. Pinnacle-CS showed an excellent agreement with MCDE within the target structures, whereas the best correspondence for the OARs was found between Helax-CC and MCDE. Results from Helax-PB were unsatisfying both for targets and OARs. Additionally, individual patient results were analyzed. Within the target structures deviations >5% were found in 1 patient for the comparison of MCDE and Helax-CC, while all differences between MCDE and Pinnacle-CS were <=5%. Both for Pinnacle-CS and Helax-CC, deviations from MCDE >5% were found within the OARs: within the lungs for two (6 MV) and six (18 MV) patients for Pinnacle-CS, and within other OARs for two patients for Helax-CC (for heart-D_{max} and expanded oesophagus-D_{33}) but only for 6 MV. The figure shows the DVHs of the PTV and of the lungs of patient no. 4 for 6 MV. For this patient all 4 algorithms were used to recompute the dose after replacing all CT voxels within the patient's skin contour by water. As a result all differences >5% between MCDE and the other dose calculation algorithms disappeared. Thus, the observed deviations mainly arose from differences in particle transport modelling within the lungs.

Conclusions: In conclusion, not one pair of the dose calculation algorithms we investigated could provide results that were consistent within 5% for all 10 patients for the set of clinically relevant dose-volume indices studied. Full MC provides a great benchmarking tool for evaluating the performance of other algorithms for patient dose computations.



901 poster

ALANINE DOSIMETRY IN DOSE VERIFICATION FOR IMRT

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Because of its dynamic character, the use of small leaflets and the high dose gradients which are inherent to IMRT, verification of the integral delivered dose is challenging.

Dose determination with Alanine/EPR is done in a simple way: no correction factors are needed (no angular dependent response and essentially independent of energy). Dose to water is obtained by measuring the peak-to-peak height of the central line of the powder absorption spectrum. Our alanine pellets with diameter of 4.9 mm and 4 mm length provide the accuracy required for medical dosimetry if irradiated at a dose of at least 6 Gy. In this contribution we

report dose measurements compared to dose calculations using the "copy to phantom" methodology. This method allows experimental verification of delivered dose at all locations of clinical interest. Measurements were done in an antropomorphic phantom loaded with alanine pellets and irradiated in just the same way as the patient would be treated. As a result the integral dose is verified as it is delivered by the whole process (dose optimisation, positioning and dose delivering).
Results of dose measurements will be presented for IMRT treatments of the prostate, brain tumours and head&neck tumours. Preliminary evaluation of the data indicates that discrepancies between measured and calculated dose seems to increase with the number of segments (IMRT complexity). Measured dose can be critically dependent on positional accuracy of the patient (2 mm level).
In conclusion, the absorbed dose to water measurements made with the alanine/EPR system offered us the opportunity to evaluate in a simple way highly complicated IMRT treatments. The switch from conventional treatments to IMRT could be done with confidence in a short time. Positional accuracy of the patient explains most of the observed discrepancies between measured and calculated dose.

902 poster

ANALYSIS OF THE EFFECT OF PATIENT POSITIONING IN HEAD & NECK IMRT FOR LARYNGEAL CARCINOMA

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Purpose/Objectif: In general, radiotherapy of laryngeal carcinoma using 3D-CRT is typically performed using lateral opposed beams for coverage of the cranial parts of the PTV's. Thus, shielding the oral cavity and posterior fossa is easy but both parotid glands receive a high dose. When using IMRT for the preservation of salivary gland function, often a 7-9 co-planar beam arrangement is used. This results in an increased integral dose deposition in the oral cavity and posterior fossa when compared to 3D-CRT.
The classical treatment position for laryngeal carcinoma is supine with (hyper-) extension of the neck with caudal positioning of the shoulders to allow for the lateral portals to cover the entire larynx. The optimal treatment position for IMRT for laryngeal carcinoma is ill defined and in most cases identical with that used in 3D-CRT.
The purpose of this study was to investigate whether an optimal treatment position for IMRT in laryngeal carcinoma could be defined.
Materials/Methods: In patients with laryngeal carcinoma referred for radiotherapy, CT-scans were obtained in neutral, extended and hyperextended treatment positions and IMRT-plans using a co-planar 7-beam setup were generated. Both parotid glands, the oral cavity and posterior fossa were considered OAR's and given dose-volume constraints in the optimization process. The final IMRT plans were compared for PTV coverage and dose outside the PTV.
Results: The neutral position resulted in a markedly higher maximal and mean dose in the oral cavity when compared to the extended and hyperextended treatment positions. However (hyper) extension leads to a higher maximum dose to the posterior fossa (Table 1)

	Neutral	Extended	Hyperextended
L Parotid	22 (60)	22 (59)	20 (60)
R Parotid	23 (67)	23 (60)	21 (56)
Oral Cavity	25 (73)	20 (63)	20 (56)
Posterior Fossa	4 (27)	7 (42)	7 (38)

Table 1. Mean and (Maximum) dose in Gy for the different OAR's with the corresponding treatment positions .
Conclusions: The IMRT optimization process cannot fully compensate for differences in treatment position. (Hyper-) Extension seems to remain the preferred treatment position for laryngeal carcinoma because it allows for better sparing of the oral cavity.

903 poster

APERTURE-BASED IMRT FOR RESECTED ENDOMETRIAL CANCER : CLINICAL RESULTS WITH TREATMENT DELIVERY IMPROVEMENT

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Purpose/Objectif: To describe our clinical experience with aperture-based IMRT for post-operative pelvic irradiation of endometrial cancer.
Materials/Methods: Between January and July 2005, 15 patients received 45 Gy to the pelvis after resection of endometrial malignancies using an aperture-based IMRT technique. All patients received vaginal HDR brachytherapy to a minimum of 4Gy X 3 @ 5 mm. None had chemotherapy. Target volume (upper vagina, parametrial tissues, regional lymph nodes) and Organs At Risk (OAR) were delineated. Our aperture-based IMRT class solution was generated with the assistance of an in-house optimization tool named Ballista coupled to Pinnacle[3] . It consisted of 7 coplanar and 2 noncoplanar incidences of 23 MV beams. For each patient treatment, Ballista plans were chosen after comparison to 3 other plans: conventional 4-field, enlarged 4-field (aperture shaped to Planning Target Volume - PTV) and beamlet-based IMRT plans. Acute and late toxicities were prospectively recorded using the RTOG toxicity scales. The toxicity results were compared to retrospective data from 30 patients with similar disease and treatment except for the use of a conventional 4-field technique.
Results: Median follow-up for patients treated with Ballista was 7.6 months. Groups were comparable except for mean body mass index (25.6 vs 30.2, $p = 0.01$, Ballista vs control) and timing of brachytherapy. Ballista plans showed significant advantages for target coverage (only 77.5±1.9% (mean ± SEM) of PTV would have been treated with conventional 4-field, $p<0.001$) and OAR sparing. Genitourinary toxicity was the same in both groups. Although there was more grade 2 acute gastrointestinal (GI) toxicity with Ballista (85.7 vs 53.3%, $p=0.04$), this difference disappeared 2 weeks after the end of treatments. Put aside that data were recorded differently for each group (prospectively vs retrospectively), this difference in per-treatment GI toxicity could result from larger bowel volume irradiated to low doses, higher peak dose and/or time effects related to early brachytherapy. This aperture-based technique offers treatment delivery advantages of reduced treatment time and scattered irradiation as well as easier quality assurance, with 55% less Monitor Units (MU) and 75% less segments compared to beamlet-based IMRT.
Conclusions: Aperture-based IMRT allows better PTV coverage after hysterectomy for endometrial cancer. This technique provides interesting treatment delivery advantages. While dosimetry showed better organ sparing, higher per-treatment GI toxicity was noticed. Actual equivalent late toxicity results remain interesting with the aim of therapeutic ratio optimization, but longer follow-up and a larger randomized trial are essential.

904 poster

CLINICAL RESULTS OF PAROTID-SPARING INTENSITY MODULATED RADIATION THERAPY (IMRT) FOR NASOPHARYNGEAL CANCER (NPC)

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Purpose/Objectif: To analyze clinical results of IMRT for NPC focusing on the local control rate, overall survival rate, and degree of xerostomia.

Materials/Method: Between 2000 and 2005, 22 consecutive patients with NPC were treated at our institution. Excluding two patients with stage IVc disease, 20 patients treated by IMRT were included. The disease was stage‡Tin 3 patients, stage II in 4, stage III in 2, stage IVa in 8, and stage IVb in 3. T-factor was T1 in 4 patients, T2 in 6, T3 in 2, and T4 in 8. N-factor was N0 in 8 patients, N1 in 5, N2 in 4, and N3 in 3. Nineteen patients were treated with whole-neck radiotherapy to 46-50 Gy / 23-25 fr. by IMRT, followed by boost IMRT to the high risk clinical target volume to a total dose of 60-70 Gy / 28-35 fr. (median 68 Gy). The remaining one patient was treated with whole-neck radiotherapy to 44 Gy / 22 fr. by conventional method, followed by IMRT to total dose of 70G / 35fr. Concurrent chemotherapy (cisplatin 80 mg/m^2×1-3 courses) was given for 17 patients. In addition, one or two courses of adjuvant chemotherapy (cisplatin 70mg/m^2, 5-FU 700mg/m^2 x 4 days) were given for 11 patients.

Results: For the 20 patients, median follow-up time was 30 months (6 to 60 month). The 2 year loco-regional control rate and overall survival rate were 83% and 93%, respectively. According to T factors, these values were 60% and 86% for T4 tumors, and 100% and 100% for T1-3 tumors. PTV delineation for the involved nodes was insufficient for 2 patients, resulted in one recurrence in the posterior neck lymph node and one recurrence near the parotid gland. The mean dose to the contralateral and ipsilateral parotid glands for 19 patients treated by IMRT alone was 23.0 Gy and 31.4 Gy, respectively. Among the 19 patients, xerostomia scores were G0;1, G1;6, G2;10, and G3;2 at 3-4 months, and G0;4, G1;6, and G2;5 at 1-2 years.

Conclusions: Excellent survival rate and local control rate were obtained by IMRT for NPC with T1-3 tumors, although the local control rate and overall survival rate for T4 tumors were standard. IMRT could reduce the radiation dose to the parotid glands, which resulted in the low incidence of xerostomia.

905 poster

COMPARISON OF GAFCHROMIC EBT AND BANG (R) GEL FOR THE VERIFICATION OF IMRT AND INTESITY MODULATED ARC THERAPY (AMOA)

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4 - MGS Research Inc, dept, Madison, CT, USA

Purpose/Objectif: The capability of commercial BANG® gel (MGS Research, Inc., Madison, CT, USA) for external beam dose verification like IMRT and AMOA is investigated in this paper. Compared to films, BANG gel provides true 3D dose distributions in a tissue-equivalent medium. New techniques like IMRT and especially AMOA require a high accuracy of dose calculation and delivery. To verify the accuracy of delivery we compared the results of the BANG gel measurements read out with commercial OCTOPUS™ laser CT scanner (MGS Research, Inc., Madison, CT, USA) to those obtained using the established GafChromic EBT films (two-dimensional). The dose distributions were provided by the treatment planning system ERGO (3DLine Medical Systems, Milano).

Materials/Methods: IMRT and AMOA treatment planing for a typical head and neck case was performed. The verification measurements were done using a µMLC manufactured by 3DLine in combination with a Siemens Primus. The BANG gel was placed in a cubic phantom with the same dimensions like our multi-purpose Phantom (EasyCube, Euromechanics) used for the film measurements. The read out of the BANG gel was done using the OCTOPUS scanner. The Scanner is designed for imaging 3D distributions of optical attenuation coefficient distributions in BANG gel for use in 3D dose distribution measurements. After irradiation the GafChromic EBT films were scanned using a flat-bed scanner (MicroTek) and compared with the data provided by the BANG gel using self written MatLab routines. A voxel-by-voxel comparison of measured (BANG gel) and calculated (ERGO) dose distribution was done using MatLab.

Results: The use of polymer gel for verification of IMRT and intensity modulated arc therapy was validated. The results for both treatment types will be presented. As the GafChromic EBT is the established method for IMRT verification in our department, we first compared the 2D dose distributions derived from the GafChromic EBT with the BANG gel measurements. In the second step, we compared the calculated dose distributions (IMRT and AMOA) with the true 3D data derived from the BANG gel. The gel measured dose distributions will be presented in comparison with the calculated plans.

Conclusions: We found BANG gel dosimetry to be suitable for IMRT and AMOA. The results obtained with BANG gel dosimetry (without the use of MRI) compare favorably to the measurements from GafChromic films. The combination of Bang Gel and the OCTOPUS laser-based CT scanner is a very promising approach to the verification of true 3D dose distributions.

906 poster

COMPARISON OF THREE DIFFERENT MEDIASTINAL RADIOTHERAPY TECHNIQUES IN FEMALE PATIENTS: OPPOSED AP-PA VS. 3-D 4-FIELD AND 7-FIELD IMRT

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Purpose/Objectif: To study different radiotherapy techniques for female patients with mediastinal target volumes. Especially in highly curable diseases such as lymphoma, female long-term survivors might develop late cardiac damage and radiation-induced breast cancer.

Materials/Methods: Planning CT scans in standard supine position were obtained in 8 cases. We contoured the clinical target volume (bilateral paraclavicular and upper mediastinal lymph nodes, median size 658 ccm), lungs, esophagus, spinal cord, heart, left ventricle, left coronary artery and breasts. In addition, expanded target volumes also including a. the lower mediastinum (median size 929 ccm) and b. the lower mediastinum and both hilar regions (median size 1047 ccm) were examined. We compared standard 6 MV ap-pa opposed fields to a coplanar 3D conformal 4-field technique and a 7-field step-and-shoot IMRT technique and evaluated DVH's for each structure. The gantry angles remained unchanged for all 8 cases, i.e. no individual optimization was attempted. The planning system was BrainSCAN 5.21 (BrainLAB, Heimstetten, Germany).

Results: Target volume coverage did not improve significantly with 4-field or IMRT techniques. However, IMRT resulted in better dose reduction to the heart, left ventricle and coronary artery than any other technique without an increased risk of lung or esophageal toxicity. For a planned total radiation dose of 30 Gy, the portion of the heart receiving more than 20 Gy was 60-90% (median 78%) with ap-pa fields, 26-61% (median 38%) with the 4-field technique and 26-42% (median 34%) with IMRT ($p<0.05$). Better heart sparing

was achieved when looking at the median dose and all dose levels down to the 15% isodose. The heart volume receiving 10% or less of the prescribed dose was similar for all techniques. The median breast volume was 335 ccm (175-672 ccm). The maximum dose to the breasts was 0.1-2.22 Gy (median 1.9 Gy) per fraction for ap-pa, 1.04-1.22 Gy (median 1.18 Gy) per fraction for the 4-field technique and 0.5-0.76 Gy (median 0.56 Gy) per fraction for IMRT ($p<0.05$). The breast volume receiving 4 Gy or less was higher with IMRT than the other techniques.

Conclusions: Advanced planning and delivery techniques might result in reduced complication risks and therefore a better therapeutic ratio. Such strategies can be pursued to counteract current trends of omitting involved-field radiotherapy in multimodal treatment of lymphoma patients. The best technique for a given patient depends on breast size and the individual risk estimates for breast cancer and cardiac morbidity, respectively.

907 poster

DEFINING AGREEMENT CRITERIA BETWEEN EXPECTED AND MEASURED FIELD FLUENCES IN IMRT OF HEAD AND NECK CANCER

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Purpose/Objectif: A 5-fields IMRT technique with a 10 intensity level step-and-shoot Varian modality is routinely performed at HSR to treat patients affected by head-and-neck (HN) cancer since September 2004. Aim of this study was to analyse our pre-treatment QA data in order to establish uniquely defined operator independent agreement criteria between planned and delivered dose distribution for clinical QA practice.

Materials/Methods: Pre-irradiation QA dosimetry using films in combination with ionisation chambers is routinely evaluated for each patient by comparing planned and irradiated dose distributions in terms of absolute point dose measurements, planar dose verification and gamma function analysis (Wellhofer-Scanditronix OmniPro 1.2 Software). In a previous study a statistical investigation of gamma distribution histograms led to the decision of performing this pre-treatment verification on each field separately and using 4%/3mm values as acceptance criteria. In current investigation, gamma histograms, calculated on dose levels higher than 10% of the prescription dose, were further analysed by considering mean values, gamma values corresponding to D = Mean + 1.5 SD (named as $gamma_D$), the % of points with gamma<1, <1.5 and <2. When considering the patient population, the average values of all these parameters and their confidence limits (mean value + or - 1.5 SD) were calculated. The results here presented refer to 48 HN patients treated on two different Varian machines in the period Sept 04 - Apr 06.

Results: Better results were found for treatments performed with our newly installed Linac (average $gamma_D$: 0.78 vs 0.97 for the old one), due to a more accurate dosimetric configuration, using diodes for dose profiles/pencil beam modelling). Globally, the confidence limits for the % of points with gamma<1, <1.5 and <2 resulted to be 87%, 95% and 2% respectively while the average values of these parameters were 91%, 97% and 1% respectively. Our analyses also highlights a statistical symmetry between complementary fields, suggesting that the dosimetric evaluation of just one of them might be sufficient.

Conclusions: Statistical analyses of gamma evaluation of QA pre-treatment dosimetry are useful to properly define confidence limits of the agreement between expected and measured fluences based on our own experience.

Our results confirm that the dosimetry configuration of the beam may significantly affect the agreement between planned and measured IMRT beam fluences.

908 poster

DMLC USED TO COMPENSATE HIGH-Z MATERIALS IN RADIOTHERAPY

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Introduction: An increasing number of patients referred for radiotherapy presents with implants made of high Z-values and high densities and considerable special variation density. This will produce problems in both CT scanning and radiotherapy dose planning. This study presents a new technique which makes use of dynamic multi leave collimator (DMLC) to compensate for the increased attenuation within implants.

Materials/Methods: A primary fixed radiation field is used to cover an implant. An electronic portal image verifies the primary field. Information for determination of the fluence to compensate for the attenuation in the implant is extracted from the image. An iterative process for fluence projection through absorptions material will be presented. The total compensation fluence is imported to the treatment planning system (Varian Eclipse) and is run trough the planning systems Leaf Motion Calculator (LMC) to calculate a boost DMLC field. The DMLC field is delivered on top of a treatment field to compensate for under dosage behind the implant.

Results: A number of different Hip prostheses had been tested. Compensation field had been added to the primary field. The result shows dose in homogeneity behind the implants less than 9 %.

Conclusions: The method shows the possibility for compensation of under dosage behind implants. This provides the opportunity for making field arrangement which covers implants. The method is independent of the limited range in CT value and treatment planning system. The whole process can be performed online, while the patient is on the couch to avoid any deterioration of the compensation from patient setup error.

909 poster

DOSIMETRIC COMPARISON OF ELECTRON ARC (EA) AND INTENSITY MODULATED RADIOTHERAPY (IMRT) FOR PNET OF CHEST WALL

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Purpose/Objectif: Inhomogenity of chest wall thickness, large curved PTV's, & proximity to critical structures makes treatment planning for chest wall tumors a complex process. A comparative dosimetric analysis of treatment plans generated using EA vs. IMRT was carried out.

Materials/Methods: Five patients of PNET of the chest wall treated with EA were included in this study. Patients were immobilized using thermoplastic moulds followed by treatment planning CT scans using the CT simulator (Somatom Emotion: Siemens). Target volumes and Organs at Risk (OAR) were drawn in accordance with ICRU 50. Both EA and IMRT plans were generated using the PLATO planning system (The Nucletron, Netherlands). For EA plans the aim was to cover the entire PTV with the 85% isodose line. For IMRT, 5-7 equally spaced coplanar isocentric beams were used. Constraints were set depending on the location of the tumor and OARs (Heart, Lung, & Spine). Dose Volume Histograms (DVH) were calculated for PTV and OARs and compared between EA & IMRT. For PTV the following parameters were evaluated: V95, V107 i.e. percentage volume covering 95% and 107% of the prescription isodose respectively. Dmax, Dmin & Dmean (Maximum, minimum, & mean dose). Dmin & Dmax being the volume receiving 99% and 1% of the dose respectively. For OARs

the following parameters were evaluated; Dmax, Dmin, Dmean, V50, V30, i.e. Maximum, minimum and mean dose, percentage volume receiving 50% and 30% of the prescription isodose respectively. For normal tissue irradiation, low dose regions V10 and V30, volume receiving 10% and 30% of the prescription isodose respectively were evaluated.

Results: IMRT resulted in superior PTV coverage, Dmin was 71%(±12%) for EA and 89%(±9%) for IMRT; Dmax was 118% (±11%) for EA and 111%(±10%) for IMRT. However there was not significant difference in V95%; 92%(±5%) and 94.5(±4%) for EA and IMRT respectively. V107, which represents the hot spot within the PTV was more in EA compared to IMRT; 17%(±12%) and 9%(±7%). For Ipsilateral lung (ILL), mean of Dmax, Dmin, Dmean, V50, V30 for EA vs. IMRT were 48.54 vs. 47.8Gy, 0 vs. 0.45Gy, 17.19 vs. 13.8Gy, 14.59 vs. 9.7%, & 25.49 vs. 17.7% respectively. For Contra lateral lung (CLL), Dmax, Dmean, V50, V30 were 47.87 vs. 12.08Gy, 6.04 vs. 0.73Gy, 3.43 vs. 0.3%, & 6.53 vs. 0.5% respectively. Plans with PTV extending close to the midline resulted in higher dose to CLL with EA while the dose to CLL was lesser with EA for latereally placed PTV. The cardiac dose profile followed a similar pattern. Dmax for spinal cord was 50.93 vs. 30Gy for EA vs. IMRT respectively. Normal tissue irradiation V30, V10 were 19.8 vs. 11.3, 40.8 vs. 32% for EA vs. IMRT respectively.

Conclusions: IMRT resulted in comparable tumour volume coverage & superior dose homogeneity compared to EA. Dose profiles for OARs and normal tissues were superior in IMRT compared to EA.

910 poster

DYNAMIC INTENSITY-MODULATED NON-COPLANAR ARC RADIOTHERAPY (INCA) FOR HEAD AND NECK CANCER

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Purpose/Objectif: Improvement has been done on the dose conformity from 3D-conformal radiotherapy (3D-CRT) to intensity modulated radiotherapy (IMRT). We hypothesized, that the dose distribution may be further improved if additional degrees of freedom could be implemented. Therefore, we evaluated the possibility of using dynamic arcs beams that are intensity modulated combined with a non-coplanar beam arrangement while maintaining the arc-like dose delivery.

Materials/Methods: External beam radiotherapy (EBRT) was planned in ten patients with head and neck cancer using coplanar IMRT and non-coplanar arc techniques, termed intensity modulated non-coplanar arc EBRT (INCA). Planning target volumes (PTV) of first order covered the gross tumor volume and surrounding clinical target volume treated with 68-70 Gy, whereas PTV2 covered the elective lymph nodes with 54-55 Gy using a simultaneous internal boost. Treatment plan comparison between IMRT and INCA were carried out using dose-volume histogram and "equivalent uniform dose" (EUD).

Results: INCA resulted in better dose coverage and homogeneity of the PTV1, PTV2, and reduced dose delivered to most of the organs at risk (OAR). For the parotid glands, a reduction of the mean dose of 2.9 (± 2.0) Gy was observed ($p = 0.002$), the mean dose to the larynx was reduced by 6.9 (± 2.9) Gy ($p = 0.003$), the oral mucosa by 2.4 (± 1.1) Gy ($p < 0.001$), and the maximal dose to the spinal cord by 3.2 (± 1.7) Gy ($p = 0.004$). The mean dose to the brain was increased by 3.0 (± 1.4) Gy ($p = 0.002$) and the mean lung dose increased by 0.2 (± 0.4) Gy ($p = 0.9$). The EUD suggested better avoidance of the OAR, except for the lung, and better coverage and dose uniformity was achieved with INCA compared to IMRT.

Conclusions: Dynamic non-coplanar arc IMRT potentially improves the treatment of head and neck cancer.

911 poster

EVALUATION OF COMMISSIONING DOSIMETRY IN HELICAL TOMOTHERAPY

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Purpose/Objectif: We installed the tomotherapy for the first time in, the Our Lady of Merey Hospital, the Catholic university of Korea. We performed the commissiong procedure about the energy fluence modeling. The energy fluence is modeled from static beam measurements and verified by helical delivery measurements early in the commissioning process.

Materials/Methods: In static measurements, the spectrum along the central axis must be quantified first. Transverse dose profiles were recorded on the film. The longitudinal dose profiles had to be measured as well for accurate dose modeling. The film-measured longitudinal profile was compared to a longitudinal profile measured by an ion chamber via a topographic scan. In helical verfication, a series of measurements was recorded in a specially fabricated cylindrically symmetric VirtualWater phantom (Med-Cal). EDR2 film was placed between the phantom halves. Next, the A14SL ion chamber measured the longitudinal dose profile topographically in the cylindrically symmetric Virtual Water phantom. The longitudinal dose profile for the 6-rotation delivery was measured, over multiple treatment deliveries, by the A14SL ion chamber.

Results: For the energy fluence modeling, the convolution-predicted dose values in the center of each helical delivery are compared to all those measured by film and by ion chamber. There was excellent agreement between the dose predicted via the ion-chamber impulse function and the ion chamber measured dose value in the center of each helical delivery. The agreement was not as good for the ion chamber impulse function prediction and that measured by film.

Conclusions: However, the differences were not outside the accuracy that can be expected from film dosimetry film was adequate for measuring the transverse dose profiles because the penumbral region only contributes once to the dose.

912 poster

EVALUATION OF IMRT PLANS FOR BREAST PATIENTS TAKING INTO CONSIDERATION INTRA FRACTIONAL MOTION OF THE TARGET

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Purpose/Objectif: Nowadays, intensity modulated radiation therapy (IMRT) is a well established method. Most clinics use multileaf collimators to generate the treatment fields which are defined as a small field technique.Small field techniques are more sensitive in view of intra fractional motion. Motion of the target can lead to under and/or over dosage compared with the planned dose. This problem can appear especially for patients with breast cancer due to breathing. An algorithm was developed in order to calculate the influence of target motion on the dose distribution and the resulting dose volume histogram.

Materials/Methods: First the used algorithm to consider the breathing was verified using measurements on a moving phantom. Film

dosimetry measurements were done depending on dose rate, number of monitor units and the starting point of the treatment.
In the next step the algorithm was used to evaluate patient treatment plans that were treated in our clinic (TPS: Eclipse, Helios / Varian, Varian Linacs, 52-Leaf MLC and 120-Leaf MLC, Sliding window mode). The resulting dose volume histograms will be presented for the target volume of two different patient groups: patients with target volumes that include the internal mammary chain lymph nodes and patients with target volumes that do not include them.
Results: Results of phantom measurements show a very good agreement between calculated and measured dose distributions and will be presented using the gamma index method. The motion of the phantom is well simulated by the algorithm. Agreement between measured and calculated dose distributions is better than 3% of the local dose and 2 mm as a distance to agreement.
The dose distribution and the dose volume histogram of real treatment plans show the sensitivity of them in view of intrafractional motion. The influence of the target motion depends e.g. on fluence complexity and number of fields.
Conclusions: In the future the presented algorithm could be very useful to determine whether a gating system has to be used for the patient.

913 poster

EVALUATION OF TWO TREATMENT TECHNIQUES FOR MESOTHELIOMA

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Purpose/Objectif: Prognosis for malignant pleural mesothelioma (MPM) is poor. Residual disease is typically left behind after radical pleuropneumectomy (PPE). Therefore, postoperative radiotherapy (RT) may improve local control. Two different RT techniques, intensity-modulated radiotherapy (IMRT) and 3D-conformal radiotherapy (3DCRT), have been evaluated.
Materials/Methods: Sixteen MPM patients, 8 right-sided cases and 8 left-sided cases, were investigated. All patients had previous radical pleuropneumectomy, consisting of resection of the parietal pleura, lung, ipsilateral pericardium and diaphragm, and followed by reconstruction of the diaphragm and pericardium. Two planning target volumes (PTV) were defined. PTV1 includes the entire preoperative pleural and pulmonary structures. PTV2 includes the area of risk of residual postoperative microscopic disease or the area of highest risk for intrathoracic relapse. The plans for 3DCRT delivered 25 x 1.8 Gy (45 Gy) to PTV1 and a boost of 7 x 1.8 Gy (12.6 Gy) to PTV2. IMRT patients were planed with 26 x 1.75 Gy (45.5 Gy) to the PTV1 including a simultaneously integrated boost of 26 x 2.15 Gy (55.9 Gy) to the PTV2. The planning system used was Eclipse version 6.5 (Varian Medical Systems) for both techniques. For IMRT, eight gantry angles were used. The 3DCRT technique is described by V. Gupta et al. (Int. J. Rad. Onc. Biol. Phys., Vol.63, 2005). The liver and kidney were shielded during the entire treatment. For left-sided tumors, the heart was shielded with a block at 19.8 Gy. After 45 Gy delivered to the PTV1, the spinal cord was shielded. The shielded liver, kidney, cardiac region and spinal cord were treated with electrons.
Results: The ipsilateral kidney was treated with doses exceeding organ function preservation due to the overlapping with PTV1. For other organs at risk (OARs), 3D-conformal and IMRT delivered similar doses to OARs except for the contralateral lung tissue and kidney were dose was lower with 3DCRT. PTV dose coverage and homogeneity were improved significantly with IMRT, were the 95% isodose line covered PTV1 and PTV2.
Conclusions: IMRT and 3DCRT both achieve acceptable plans for adjuvant RT after PPE of MPM. IMRT gives better PTV coverage and 3DCRT avoids better contralateral OARs.

914 poster

EXPERT OPTIMISATION OF BEAM ORIENTATION AND QUALITY CONTROLS FOR INTENSITY-MODULATED RADIOTHERAPY (IMRT)

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Purpose/Objectif: IMRT is mainly used for prostate and head-and-neck cancer treatments, because it can achieve an improved compromise between target coverage and organs at risk (OARs) sparing, compared with conformal radiotherapy. Nevertheless, only a small proportion of patients are currently treated with IMRT technique. The main reason is the excessive time required to perform the treatment preparation. The purpose of our study is to streamline the process thereby permitting an increase in the number of patients treated with IMRT. So, our two aims are firstly to optimise and automate beam orientation, and secondly to implement quality control optimisation, using Statistical Process Control (SPC).
Materials/Methods: Beam orientation optimisation:
We studied different optimisation algorithms, such as the simulated annealing, the genetic algorithm and the simplex algorithm, that would help to automatically find the optimal beam arrangement thereby achieving the best compromise between target coverage and OARs sparing. These algorithms require a well-defined score function which formalises the clinical goals to objectively evaluate the figures of merit for different IMRT plans. When beam orientation optimisation is concerned, plan evaluation based on dose criteria is time-consuming. Indeed, the fluence map ought to be optimised for every trial beam configuration. So a score function, based on geometrical criteria, can be introduced as a filter which reduces the search space before a more accurate score function based on dose criteria is used. The geometrical criteria aims to quantify, from a given beam angle, the proportion of irradiated target volume compared to the proportion of irradiated OARs and healthy tissues.
Statistical Process Control (SPC) for IMRT quality assurance:
SPC is a method currently used in industry for controlling and improving the quality of a process through statistical analysis. In this work, SPC is applied to quality assurance in IMRT, for the comparison between the measured dose and the calculated dose. The aims are: (1) to evaluate and if necessary improve the stability of the system when controlling all beams for one patient (100% control), (2) to determine - when the system is shown to be stable - if we can avoid this 100% control and also how to streamline the process by acting on the number and frequencies of controls, according to predefined statistical risks, instead of choosing them only by experience or intuition, and (3) to anticipate and prevent any deviations of the target values or of their dispersion, using statistical control charts.
Results: The SPC results show that both the stability and the capability of our process need to be improved. To do this, a retrospective analysis of the results is in progress. If the degree of modulation is shown to be a potential cause of the process instability, we will try to incorporate this knowledge in the beam orientation optimisation score function.

915 poster

FEASIBILITY REPORT OF IMRT AND CHEMOTHERAPY FOR ADVANCED CANCERS OF THE HEAD AND NECK: RESULTS OF THE FIRST 50

CASES TREATED AT A COMMUNITY PRACTICE IN THE USA.

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Purpose/Objectif: Our purpose is to present preliminary clinical outcomes of patients with advanced head and neck cancers treated with IMRT and chemotherapy in a community cancer center in the United States. This is light of the fact that few if any community practices have reported results despite a rapid expansion of IMRT in private practice in the USA.

Materials/Methods: From 2003 through 2005, 46 patients with advanced head and neck cancers were treated with IMRT. The majority or curative cases were stage IV. Forty pts (86%) were treated with curative intention the primary or adjuvant setting, and 6 pts (13%) were treated for palliation of either recurrent or metastaic disease. Subsites treated included oropharnx (45%), nasopharynx (15%), larynx/ hypopharynx (19%), paranasl sinus (10%) and other sites (6%). 84% of primary cases and 60% of adjuvent cases received concurrent chemotherapy. 28% of all patients also received concurrent amifostine and 70% received prophylactic fluconazole to prevent oral thrush.

Results: The median followup time was 11 months (range 1-27 months). The overall actuarial 2 year (yr) loco-regional control rate (LRC) is 82%. For pts treated with curative intent, LRC for primary disease at 2 yrs is 92% and 81% at 1 yr for adjuvent cases. Actuarial 2 yr LRC by site is 93% for oropharynx, 100 % for nasopharynx, larynx/ hypopharynx, and nasal cavity. LRC was 60% for paranasal sinus. 2 year overall survival(OS) Distant metastasis free survival (DMFS) and disease free survival rates(DFS) for curative primary cases is 86%, 84%, and 51% respectively. The 1 yr actuarial OS, DMFS, and DFS rates for adjuvent cases is 100%, 93% and 81%. The pattern of failure was primarily distant (8/12) followed by local (4/12). The 1 failure in the oropharynx was an in-field RP nodal failure. One pt experienced a grade 3 esophageal stricture. One pt died of treatment related complications 4 weeks into therapy. No other late grade 3-4 toxicities occured.

Conclusions: These preliminary results suggest that IMRT and chemotherapy delivered in this community practice are feasible, relatively safe and are encouraging for advanced head and neck cancer. Additional followup will be presented.

916 poster

FIRST COMBINED INTERNAL-EXTERNAL RADIATION THERAPY (COMBIERT) OF AN INOPERABLE NEUROENDOCRINE PANCREATIC TUMOR BY PEPTIDE RECEPTOR RADIONUCLIDE THERAPY FOLLOWED BY IMRT

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Purpose/Objectif: The radiolabeling of specific peptides which bind to somatostatin receptors on neuroendocrine tumors, with beta emitters like Yttrium-90 or Lutetium-177 enables an internal radionuclide therapy at low radiation risk for normal tissues. Especially patients where all surgical options have been used, or patients who are progressing under octreotide therapy or under combined biotherapy and those with persisting symptoms (diarrhoea, flushs) despite high dose hormonal therapy are suitable for PRRT. The total activity, however, which can be administered is limited by kidney toxicity. Our aim was to increase the effect of PRRT by IMRT without additional damage to the kidneys in a patient who had received already a significant renal dose by previous radionuclide therapies.

Materials/Methods: 59-year old patient, diagnosed with hepatic and abdominal metastases of a pancreatic glucagonoma in 1989. Over the years, the following treatments had been performed: partial recetion of the pancreas, splenectomy, resection of liver metastases and mesenteric lymphadenectomy (03/1989); resection of local recurrence and liver metastectomy (04/1995); left adrenalectomy (metastasis) in 12/1995; multiple atypical liver resections (02 and 07/1997. Treatment with interferon 1998/99, octreotide therapy since 11/1998. Chemotherapy with doxorubicine, streptocotocin in 1999, chemoembolisation and radiofrequency ablation (RFA) in 07/2000. 2002 to 2003 five courses of Y-90-DOTA-TOC therapy (total administered activity: 14.95 GBq, 404 mCi) were administered. There was a very good treatment response (partial remission) after PRRT until beginning of 2004 when the patient presented with recurrent hypoglycemia, diarrhoea, weight loss and increasing abdominal pain due to a recurrent liver metastasis and an abdominal tumor bulk. The patient was operated again in May 2004 (liver metastasis resection and lymphadenectomy (R2) and treated postoperatively with 7.4 GBq (200 mCi) Lu-177-DOTA-NOC in Oct. 2004. In Sept. 2005, the patient presented with increasing abdominal pain and diarrhoea. Receptor PET/CT with Ga-68 DOTA-NOC showed intense SMS receptor expression in a single liver metastasis in S7 and in a large abdominal tumor mass (12 x 7 cm in diameter). After interdisciplinary discussion, we decided to perform again a PRRT (using 5 GBq (135 mCi) of Y-90 DOTA-TATE) followed by external radiation therapy. Radiation treatment planning was performed using the receptor PET/CT data (molecular radiation treatment planning, MRTP). IMRT of the abdominal bulk tumor (sliding-windows technique, SD 1.8 Gy, 28 fractions, total dose 50.4 Gy) and in addition IMRT of the liver metastasis in S7 was performed (SD of 1.8 Gy, total dose 19.8 Gy). Treatment was tolerated with severe adverse effects starting at the end of external radiation therapy (probably due to tumor necrosis) and lasting for several weeks.

Results: Restaging in April 2006 (5 months after treatment) showed an impressive effect of COMBIERT: Ga-68 DOTA-NOC receptor PET/CT revealed a significant decrease of the mean standardized uptake values (SUV) in the abdominal tumor masses (partial remission) and the liver lesion. The clinical symptoms of the patient improved dramatically (weight gain of 7 kg, normal stool frequency, no significant pain).

Conclusions: This is - to our best knowledge - the first report of a combined treatment by internal (PRRT) and external (IMRT) radiation therapy (COMBIERT) of a patient with a large, inoperable primary pancreatic neuroendocrine carcinoma (glucagonoma), who has been treated before with multiple resections, chemo- and immuntherapy and 6 cycles of PRRT over 3 years and showed progressive disease with severe clinical symptoms. The combined use of beta emitting radionuclides coupled to tumor-specific peptides and external radiation therapy (IMRT, sliding-windows technique) is feasible and showed a significant better clinical and molecular tumor response (as measured by receptor PET/CT) than PRRT alone. Molecular radiation treatment planning (MRTP) using PET/CT data for determining a "biological" tumor volume (BTV) - based on the specific expression of somatostatin receptors in neuroendocrine tumors - is a novel approach which helds great promise for the future.

917 poster

FIRST EXPERIENCE WITH IMRT AT ONC. INST. ST. ELIZABETH

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Purpose/Objectif: The autors present first experience (planning and realisation) with two types of IMRT with Nomos MIMic and Milenium 120 Varian. Intensive modulated arc therapy (IMAT) was used for stereotactic radiosurgery and fractionated radiotherapy too. For valid application of IMRT and IMAT was verified on hybrid phantom.

Materials/Methods: From May 2005 to April 2006 were treated 23 patients with various type of tumors and lesion by IMRT or IMAT at linac 600C/D. Twelve (8 with meningeomas, 2 with A-V malformations, 1 with brain metatase) were treated by stereotactic IMRS delivery system, autocrane positioning of cauch and Corvus TPS. The target volume ranged 3 - 24 cm^3 (ø11,3cm^3), the dose ranged 12 - 18 Gy (ø14,8Gy). Eleven of others patients with various diagnosis were treated by fractionated IMRT (orbital lymphoma, prostate cancer, meningeomas, olfactorial neuroblastoma, retinoblastoma, astrocytoma) with Nomos MIMiC or Varian Milenium 120 MLC. The target volume ranged 12,56 - 168,10 cm^3 (ø 79,2 cm^3), the dose ranged 36 - 72 Gy (ø 56,2 Gy).

The presentation deal with a verification of aplicated geometrical parameters by connection of MIMiC to linac, verification of absolute Dose at chosen point in the own produced IMRT phantom and 2D relative dose distribution by uding of OmniPro I'mrt software of Wellhofer company.

Results: Index homogenity and factor conformity were better by IMAT with MIMiC. The differences between the calculated and measured absolute doses on phantom were within 2%, the relative doses correspond to gamma index 3-4.

Conclusions: IMRT (IMAT) is the effective treatment modality with good conformity and homogenity, sparing healthy tissue. Disadvantage this technics is the time consuming.

The first experience with verification of aplicated dose and the difference betweeen calculated and measured doses were suitable.

918 poster

IMRT FOR CSI OF PEDIATRIC MEDULLOBLASTOMA

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Purpose/Objectif: Conventional radiotherapy for medulloblastoma involves irradiation of the spine with a direct photon portal and field limits defined relative to bony landmarks. The explicit definition of a three-dimensional clinical target volume (3D CTV) is a pre-requisite for IMRT but may also be of interest for conventional treatments. A comparison of treatment plans between inverse planned IMRT, and a conventional technique planned with both classical field limits and a 3D CTV is presented for 3 patients previously treated at our clinic.

Materials/Methods: The patients had been CT scanned and treated in the supine position. Structures outlined included the oesophagus, small bowel, lungs, liver, ovaries, and kidneys. For the conventional treatment (POST_2D), the spine was treated with a single posterior field matched with the brain fields superiorly, extending inferiorly below the MRI-defined caudal extent of the thecal sac and laterally to cover the vertebral bodies with a 1 cm margin. The 3D CTV volume consisted of the spinal canal extending laterally to encompass the CSF extension to the spinal ganglia. A 5 mm margin was added for the PTV. Plans using the same conventional beam geometry as the treated plan but targeting the new PTV (POST_3D) as well as IMRT inverse plans utilizing five posterior oblique fields were generated. The planning constraints were set such that the PTV would be covered as per ICRU criteria, and the organs at risk (OARs) spared as much as possible. Assuming a prescription dose of 23.4 Gy, the doses to the OARs and body contour were averaged across the three cases and evaluated in terms of V1Gy, V2Gy, V5Gy, V10Gy, V15Gy and V20Gy. The integral doses to the liver, heart, and body contours were also evaluated.

Results: PTV coverage and dose homogeneity is superior for the IMRT plans in terms of V95% (IMRT: 100%, POST_3D: 96%, POST_2D: 98%), and V107% (IMRT: 3%, POST_3D: 38%, POST_2D: 37%). In terms of OAR sparing, the IMRT plan is better for all organs and tissue contour when comparing the V10Gy, V15Gy, and V20Gy. The POST_3D plan is superior for V5Gy and below. For the heart and liver in particular the IMRT plans provide considerable sparing in terms of V10Gy and above. In terms of the integral dose, the IMRT plans were superior for liver (IMRT: 21.9J, POST_3D: 28.6J, POST_2D: 38.6J), and heart (IMRT: 9J, POST_3D: 14.1J, POST_2D: 19.4J). The POST_3D plan was superior for the body contour integral dose (IMRT: 349J, POST_3D: 337J, POST_2D: 555J).

Conclusions: As expected, the IMRT plans provide increased OAR sparing at the higher dose levels, partially offset by an increased low dose contribution to normal tissue. Target dose homogeneity is greatly improved with the IMRT plans. In terms of integral dose, the IMRT plans were superior for the liver and heart, and the POST_3D for the body contour. The reduction in heart and liver doses may be significant enough to warrant the use of IMRT for CSI.

OAR	V_{20Gy} (%)			V_{15Gy} (%)			V_{10Gy} (%)			V_{5Gy} (%)		
	IMRT	POST 3D	POST 2D	IMRT	POST 3D	POST 2D	IMRT	POST 3D	POST 2D	IMRT	POST 3D	POST 2D
Oesophagus	30	10	24	4	8	19	3	6	15	1	3	5
Bowel	55	39	63	14	35	62	2	30	54	0	3	8
R Kidney	33	12	58	7	7	54	0	5	48	0	2	34
L Kidney	28	7	52	6	4	43	0	2	37	0	1	27
R Lung	36	19	41	11	15	36	4	11	31	0	5	16
L Lung	20	7	26	5	5	22	1	3	19	0	1	12
Heart	65	59	80	10	55	76	0	46	69	0	6	10
Liver	33	27	42	4	24	38	0	15	27	0	1	4
All Tissue	31	24	37	15	21	34	9	17	29	5	9	16

919 poster

IMRT FOR PROSTATE CANCER: IMMEDIATE BENEFIT FOR THE PATIENT?

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Purpose/Objectif: As part of the implementation of Intensity-Modulated Radiation Therapy (IMRT) in the treatment of cancer of the prostate, we performed a prospective study on the acute and subacute side-effects of both Conformal Radiation Therapy (CRT) and IMRT. We attempted to correlate these side-effects with the actual doses on the organs at risk.

Materials/Methods: Between October 2004 and June 2005, we studied 39 consecutive patients receiving radical radiotherapy for prostate cancer; IMRT: n = 13; CRT: n = 26; with total dose amounting to 72 Gy for both techniques. In CRT, a three-field technique was used. In IMRT, a five-field technique was used. For each IMRT plan, a back-up CRT plan was also created. We used the Common Terminology Criteria for Adverse Events (CTCAE) on a weekly basis during

treatment and the LENT SOMA tables for sub-acute gastro-intestinal (GI) and genitourinary (GU) side effects.
Results: Rectal D50 and D25 were respectively 47 vs. 50 (p=0.128) and 63 vs. 65 (p= 0.152) for IMRT and CRT. Rectal V70 9 vs. 15 (p= 0.003). Bladder D50 38 vs. 46 (p= 0.088). No significant differences for acute GU and GI symptoms: urgency (p=0.637), nocturia (p= 0.874), mictalgia (p=0.734), hematuria (p=0.608), frequency (p= 0.106), mucus discharge (p=0.485), red blood per anum (p=0.735), anal pain (p=0.195), diarrhea (p=0.496). No grade 3 toxicity was observed. After a follow-up of 7 months, no significant differences existed between both techniques for GU and GI symptoms. No grade 2 was seen.
Conclusions: Both IMRT and CRT are well tolerated with low (sub)-acute toxicity. Within the limits of the study, no significant differences in side effects were seen. However, a longer follow-up is mandatory, due to the existing correlation between high-dose levels and late rectal toxicity. Scoring of side-effects should be part of routine clinical management in cancer treatment.

920 poster

IMRT IN HEAD AND NECK PATIENTS: DEVELOPMENT OF A STANDARDISED KIT FOR PTV-DOSE-ADAPTED HELP VOLUMES FOR FASTER EFFICIENT PLANNING WITH OPTIMIZED PROTECTION OF THE PTV SURROUNDING NORMAL TISSUE

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Purpose/Objectif: Next to the difficulty to delineate the planning target volume (PTV) , risk organs (RO) and assassing dose constrains in Intense Modulated Radiation Therapy (IMRT) is the delineation of help volumes (HV, the PTV encompassing normal tissue like oral cavity in hypopharynx carcinoma) with applicable dose constrains, which achieve the ideal dose-conformation with steep dose gradient on the PTV with protection of the normal tissue. Even though these HV are indispensable for IMRT-planning, there are still no rules for HV. In two typic head and neck tumors we will demonstrate the development of standardised HV with dose constrains for IMRT-planning in a comparison with the in our department used Intensity Modulated Arc Therapy (IMAT).
Materials/Methods: In 15 pat., treated in 2005 in our department (Radiation Oncology, University of Regensburg), we performed beside the IMAT- an IMRT-planning with and without HV (individual thermoplastic mask for immobilisation, CT-planning, OTP/Nucletron planning system, RaySearch-IMRT-module). In 7 pat. with oropharynx carcinoma and 8 pat. with hypopharynx carcinoma we delineated PTV, RO, a ventral HV (HV-V, parts of oral cavity), a dorsal HV (HV-D, behind the PTV including vertebral bodies and muscles of dorsal neck) and a medial HV between the divided PTV in the lower neck (HV-M, to protect larynx, only in oropharynx carcinomas). Dose constrains for PTV were 56-60Gy for the first series normalized upon mean, single dose 2Gy, 28 fractions, spinal cord 45Gy at maximum and for parotids in IMRT-planning 24Gy at median. For HV the smallest dose constrains were detected and used in all IMRT plans, 7 portals every 51°, 70 segments.
Results: In both groups and all planning techniques the 95%-volumedose was with 51-55Gy marginal below the prescripted dose, but the 5%-volumedose for the spinal cord with IMAT 37Gy, IMRT 29Gy and IMRT w/o HV 30Gy shows a distinct benefit for IMRT. Comparing IMRT vs. IMRT w/o HV the use of HV managed a up to 40% better protection of the PTV encompassing normal tissue (inside HV). A reduction of dose load of the parotids from 47Gy (IMAT) to 22Gy at median could be reached.
Conclusions: Also in our collective the advantage of IMRT vs. IMAT could be shown with good protection of RO. At the same time the procedure with our standardised "help volumes-kit" allows a first step to an enhanced dose conformation on the PTV with a relevant reduction of dose in normal tissue encompassing the PTV (e.g. oral cavity) and shorter time need for IMRT-planning.

921 poster

IMRT VERIFICATION ON AN ELEKTA SLI15 WITH A STANDARD ELEKTA MLC AND A BEAM MODULATOR

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Purpose/Objectif: Purpose of this study was a dosimetric verification of our IMRT techniques using an Elekta Beam Modulator (BM) and a standard Elekta MLC (sMLC) as well as two treatment planning systems and two algorithms.
Materials/Methods:
Treatment techniques
Our radiation treatment of the prostate cancer is based on many fixed beam segments (sIMRT) that are optimised in weight. Linacs with a sMLC (2x40 leaves, leaf width 1 cm at isocenter) as well as two recently installed linacs with a BM (2x40 leaves, leaf width 4 mm at isocenter) were used. Irradiation of H&N tumors is based full fluence step-and-shoot (s&s) IMRT. Apart from the BM also the sMLC will be used for s&s IMRT treatment. All IMRT plans apply 6 MV photon beams.
Treatment Planning
Treatment plans for sIMRT were optimised on Nucletron Masterplan 1.4 (MP1.4); final dose calculation was done using Helax TMS 6.1B using the Pencil Beam algorithm (PB). Treatment plans for s&s IMRT plans were optimised, segmented and calculated using MP1.4 with PB algorithm.All treatment plans were exported for recalculation on CT scanned phantoms (hybrid verification). The final dose calculation in these phantoms was done using both PB and the Collapsed Cone (CC) algorithm in MP1.4. The CC algorithm applies a correction for the effects of off-axis spectral variation.
Treatment verificationThe absolute point dose for the complete treatment plan was measured in the isocenter or a point in a flat area of the dose distribution using a 0.04 cc ionisation chamber (IC) in the I'mRT phantom (Scanditronix-Wellhofer).Radiographic film (Kodak EDR2) was used in transversal slices (0, ±2 cm) of the I'mRT phantom. The IMRT films were analysed using the MATLAB application Doselab from N.L.Childress (http://doselab.sourceforge.net/) with some in-house extensions. Film dose, after conversion from optical density, was normalised to IC measured dose.
Results:
Absolute(isocentric) dose:

The average deviation between the IC measured and calculated dose (1SD):		
sIMRT for prostate:	11 sMLC cases:	-0.7% (1.1%) PB-calculation
	8 BM cases:	-0.7% (0.5%) id.
s&s IMRT for H&N:	14 sMLC cases:	-2.0% (1.9%) id.
	Same sMLC cases:	-0.4% (2.1%) CC-calculation

Gamma index evaluation in transversal planes: For 12 sIMRT prostate cases the correspondence between calculated and measured dose distribution in transversal slices was evaluated using the gamma index (3%;3mm) and the acceptance criteria according to Stock et al (PMB 50 (2005), 399-411).

Gamma index evaluation all 36 planes (12 central planes only)*			
Value	γmean	γ > 1	γ 1%
Acceptance criteria*	0 - 0.5*	0 - 5 %*	0 - 1.5 *
Average	0.50 (0.39) [0.45]	6.8% (2.4%) [5.8%]	1.4 (1.1) [1.5]
1SD	0.23 (0.05) [0.10]	9.4% (2.0%) [5.4%]	0.8 (0.2) [0.6]

*Acceptance criteria and values between [..] are from Stock et al 2005

Conclusions: The accuracy of the delivery of sIMRT has been verified for the sMLC and BM collimators. The gamma index evaluation for sMLC provides results comparable to those obtained by Stock et al 2005.For s&s IMRT treatments using the Elekta sMLC the calculated dose on TPS MP1.4 using the CC algorithm gives a better correspondence with measurements than the PB algorithm.

922 poster

IN VIVO MEASUREMENTS WITH MOSFET DETECTORS FOR IMRT

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Purpose/Objectif: Metal oxide semiconductor field effect transistor (MOSFET) is a fairly recent in vivo dosimeter still not widely used. The purpose of this work is to evaluate the feasibility of this type of dosimeter for nasopharynx and prostate intensity-modulated radiation therapy (IMRT).

Materials/Methods: In vivo measurements of the dose delivered to one point of the nasopharynx or the prostate by IMRT were obtained with wireless OneDose™ MOSFET dosimeters. Measurements were taken once a week for more than 10 patients.

In nasopharynx cancer patients, before setting the mask on the patient, a catheter with a MOSFET detector was introduced in the nasal cavity in order to assess the posterior wall of the pharynx (PTV).

In prostate cancer patients a catheter with a latex cover was introduced in the rectum until the anterior wall, in an attempt to reach the PTV. In this case, the MOSFET was placed in a capsule.

In both cases, the detector was marked with a gold ball (Fig.1) in order to permit us to localize its active area in a three-dimensional portal study carried out before the session. After the session the MOSFET was removed and the dose read.

The dose calculated by the treatment planning system was compared with the measured values.

Results: A total of 40 measurements were taken, 90% of which presented discrepancies between calculated and measured values within +/-5 %. Some cases were found where the measurements did not give a good result because, the MOSFET :

a) was damaged during manipulation

b) was not in optimum condition due to the batch

c) was not properly reset prior to use

d) was localized in an air density area.

Conclusions:

- Our experience demonstrates the feasibility of in vivo measurements with MOSFET dosimeters for nasopharynx and prostate IMRT.
- Our prior results do not differ from that found in the literature for other types of MOSFET.

923 poster

INTENSITY MODULATED FIELDS ? ARE THEY USEFUL FOR CONVEX SHAPED TARGETS?

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Purpose/Objectif: Intensity modulated radiotherapy (IMRT) makes high conformal dose distributions for concavely shaped targets possible. It is unclear, whether IMRT is also useful for convex shaped targets as well. The aim of this work is the usability of IMRT for these cases.

The following cases are investigated and discussed: (1) target without organ at risk (OAR), (2) integrated boost, (3) target and one or more OARs. The presented examples correspond to clinical cases in H&N, abdomen and prostate.

Materials/Methods: For inverse planning we normally use KonRad (Siemens), but for the following comparison we planned only with "Masterplan" (nucletron). Limits of the segmentation algorithm (e.g. segment numbers) are diminished. So the results are representative for different IMRT methods (sMLM, dMLM, compensators).

Results:

(1) Only one target: In the test cases, IMRT increases the volume with higher dose (60-80% of prescribed dose). For an example (prostate, target volume 113ml) the volume with 50Gy or more contains 406ml, without IMRT (same field configuration) 304ml.

(2) Integrated boost: It can be realised without IMRT as well, if few small field are added.

(3) Target and OAR: If exactly one OAR is defined, e.g. prostate and rectum , IMRT allows a specific increased gradient towards this OAR.

If more than one OAR is defined, e.g. for lymphoma in the pelvis region, IMRT allows a specific dose sparing of each OAR. A comparison of an IMRT-Plan (7 fields) with a conformal plan (3 fields) showed a better dose sparing of liver and bowel (volume with 20Gy is decreased up to factor 2, while areas without specific OAR get a higher dose.

Conclusions: Improved technique and experienced staff allow a faster IMRT, so that this technique will be attractive even for more regular targets, where IMRT is not essential but advantageous.

For targets without OAR we did not find advantages in the dose distribution. Integrated boost volumes can be planned with additional conformal fields as well.

In contrast to that, adjacent organs-at-risk can often be spared better by IMRT. If several OARs are defined, IMRT allows a more specific dose sparing of each OAR.

It can be summarized, that IM-fields can be recommended for regular target too. It is useful, specially if OARs are defined. In addition to it, the time for treatment planning can be reduced in many cases.

924 poster

INTENSITY MODULATED RADIATION THERAPY (IMRT) IN LUNG CANCER : FREE BREATHING VERSUS VOLUNTARY DEEP INSPIRATION BREATH-HOLD

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Purpose/Objectif: Deep inspiration breath-hold (DIBH) is used in order to reduce the pulmonary and heart toxicity for lung treatment cancer. This study estimates the dosimetric possibility and potential of the combination of breath-hold and IMRT by comparison with IMRT in free breathing (FB).

Materials/Methods: 8 patients treated for non-small cell lung cancer (NSCLC). For each patient, 3 CT-scanned (Computed Tomography) are done, 1 free breathing (FB) and 2 DIBH in position treatment.

Two DIBH are done for all patients in order to obtain a standard deviation of internal target volume (ITV) between 2 deep inspiration CT-scanned. For FB and DIBH, IMRT plan for a prescription dose of 66 Gy and an optimized treatment plan was done in order to cover the PTV. Konrad inverse planning program are used for dose calculation. DVHs for lung, heart, PTV and esophagus is used to evaluate the IMRT plan.

Results: For all patients lung, heart, cord, esophagus doses are acceptable and PTV coverage is optimized goodly for DIBH and FB, and the lungs and heart for DIBH IMRT plan are better sparing compared to FB IMRT plan. For DIBH IMRT, the V20 for lung (total lung volume receiving 20 Gy or more) are about 10% smaller than the V20 for the FB IMRT. The median of relative lung volume receiving 50% or more of prescription dose (66 Gy) was 30% and 20% for FB and DIBH respectively. The mean lung dose was reduce of about 5 Gy for DIBH compared to FB. The median heart volume receiving more than 50% of prescription dose was reduced for 27% (FB) to 20% (DIBH).

Conclusions: DIBH IMRT allows better organ at risk protection and keep a good PTV coverage than FB IMRT

925 poster

INTENSITY MODULATED RADIATION THERAPY (IMRT) OF NASOPHARYNGEAL CANCER: INFLUENCE OF TECHNIQUE ON PAROTID DOSE AND SALIVARY GLAND TOXICITY.

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Purpose/Objectif: Nasopharyngeal carcinoma (NPC) has always been a challenge to radiation oncologists because of its location and high radiosensitivity. IMRT, with high dose gradients, offers the opportunity for delivering high doses with optimal target coverage and concurrent sparing of organs at risk. The purpose of this study is to evaluate the difference in mean parotid dose and salivary gland toxicity between a 5 and 7 field IMRT technique maintaining the same targets coverage.

Materials/Methods: In our Department, IMRT has been used to treat NPC since March 2003. A total of 30 patients have been treated until April 2006: 13 patients with stage I-II, and 17 with stage III-IV disease. Chemotherapy with Cisplatinum was used in all but 4 patients. The median total planned dose was 70 Gy (range 70-74 Gy) in 33-35 fractions for the macroscopic disease (primary and lymph nodes), 60 Gy in 33 fractions for node echelons at high risk of microscopic spread and 54 Gy in 33 fractions for those at lower risk. For the first 8 patients a 5 fields technique was used, for the remaining 22 patients it was modified to a 7 field technique to improve organs at risk sparing, without compromising the target coverage. The mean dose to both parotid glands was calculated for the 2 groups of patients that had been treated with the 5-field (group 1) and 7-field technique (group 2). The salivary gland toxicity was evaluated using the RTOG late toxicity score criteria. Three patients are not currently evaluable for toxicity because of a follow up of less than 3 months.

Results: the mean and median follow up (FUP) is 15,6 and 14 months respectively(range 6-34). The loco-regional control is 100%, two patients died of systemic disease, one of carotid haemorrhage and one is alive with progressive systemic disease. The mean parotid dose for the 5-fields IMRT was 45.3 Gy and for the 7 fields IMRT was 33.2 Gy. Table 1 shows the variation of toxicity grade in time in the two groups.

Conclusions: The patients in group 2 show a faster and bigger reduction of the toxicity grade when compared with the patients in group 1. The decrease in mean parotids dose from 45.3 to 33.2 Gy seems to significantly improve the capacity of the salivary gland to recover in time. Those results, even with a small number of patients, confirm the hypothesis that 7-field IMRT, conforming more tightly the doses around the targets, is necessary to achieve an adequate sparing of the parotid glands, hasten their recovery and decrease their toxicity.

Tab1: salivary gland toxicity

Group 1					
Mo.	N.	G3	G2	G1	G0
3	8	8	0	0	0
6	8	8	0	0	0
12	8	4	4	0	0
18	8	4	4	0	0
24	8	4	3	1	0

Group 2					
Mo.	N.	G3	G2	G1	G0
3	19	13	3	0	0
6	13	7	4	2	0
12	7	3	1	2	1
18	3	0	0	1	2
24	/	/	/	/	/

Mo.= Months, G= RTOG Grade

926 poster

INTENSITY-MODULATED RADIOTHERAPY INCLUDING PELVIC LYMPH NODES IN LOCALLY ADVANCED PROSTATE CANCER - PLANNING PROCEDURES AND EARLY TREATMENT OUTCOME

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Purpose/Objectif: We have initiated a prospective study of intensity-modulated radiotherapy (IMRT) for locally advanced prostate cancer and present our procedures for target volume definitions, optimisation criteria, field arrangement as well as our early experiences in terms of resulting dose distributions and acute effects.

Materials/Methods: Until April 2006, 17 patients with locally advanced prostate cancer (stage T3b) have completed a course of radiotherapy (RT) where an initial seven-field IMRT plan delivers 50 Gy to the prostate, seminal vesicles and pelvic lymph nodes followed by a four-field conformal set-up delivering 20 Gy to the prostate and seminal vesicles. DVH-data for the added plans (50 Gy with IMRT, 20 Gy with CRT) were compared to the DVH-data for the summation of two CRT plans (50 Gy with CRT, 20 Gy with CRT) for the six most recent cases. In the optimisation, the highest priorities were given to target coverage and intestine sparing. Acute gastro-intestinal (GI) and genito-urinary (GU) toxicity according to the RTOG scoring system was recorded weekly throughout as well as 3 months after the treatment course. Patient-specific quality assurance included point dose verification in a dedicated phantom and fluency verification using an electronic portal imaging device.

Results: Use of IMRT reduced the normal tissue irradiation considerably compared to CRT. Volumes above 40 Gy and 50 Gy were reduced significantly for the intestine (e.g. at 50 Gy, from 95 cm^3 to 20 cm^3; $p = 0.026$), volumes above 40 Gy, 50 Gy and 60 Gy were reduced significantly for the bladder, while volumes above 30 Gy, 50 Gy and 60 Gy were reduced for the rectum and volumes above 20 Gy, 30 Gy and 40 Gy were reduced for the hip joint muscles. The minimum target dose increased for both targets when using IMRT. During the treatment course, Grade 2 GI complications were reported by two of 17 patients (12%) treated with IMRT, while Grade 2 GU complications were observed among three of these cases (18%), and this appears lower than our previous conformal RT experience for this patient group (35% of both GU and GI Grade 2 complications during treatment). Three months after RT, no Grade 2 effects have been observed among the seven cases investigated. Updated acute effect data will be presented at the meeting.

Conclusions: IMRT for irradiation of pelvic lymph nodes in prostate cancer reduces normal tissue irradiation and improves target coverage, and shows promise for also reducing toxicity. The treatment planning and verification procedures are now part of the routine workload.

927 poster

INTENSITY-MODULATED TOMOTHERAPY WITH STEREOTACTIC RADIOSURGERY FOR BRAIN TUMORS:VALIDATION OF A SUPPLEMENTARY VALUE OF C11-METHIONINE-PET IMAGES IN TREATMENT PLANNING.

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Purpose/Objectif: CT/MRI fusion technology is commonly used in radiation treatment planning of brain tumors. Recently the gross tumor volume (GTV) delineation in brain tumors, based traditionally on computed tomography (CT) and magnetic resonance imaging (MRI), was improved in using biologic imaging: 11C-methionine positron emission tomography (MET-PET). The higher specificity and sensitivity of MET-PET for brain tumors, in comparison to anatomic imaging (CT and MRI), was demonstrated in previous studies and is the rationale for the integration of biologic imaging in the radiation treatment planning. The goal of our work is to evaluate the feasibility of intracranial radiosurgery by means of helical tomotherapy system (Hi-Art from Tomotherapy Inc.) and to assess the supplementary value of C11-Methionin-PET images in treatment planning.

Materials/Methods: In eight patients (4 malignant gliomas and 4 brain metastases) with 17 brain tumors CT, gadolinium enhanced T1-weighted MRI and MET-PET were performed for stereotactic radiosurgery treatment planning. Median age was 58 years (range, 29-78 years). Median Karnofsky performance status (KPS) was 80% (range, 40-100%). These image sets (CT/MRI and CT/ MET-PET) were then fused utilizing the Pinnacle System. CT/MRI GTV (GTV1) was defined as the contrast-enhanced area on CT/T1 gadolinium-MRI image fusion images and CT/MET-PET GTV (GTV2) was defined as the area of an accumulation of CT/ MET-PET apparently higher than that of normal tissue on CT/ MET-PET fusion images. The planning target volume (PTV) encompassed the GTV plus 2-mm margin. The initial PTV was prescribed a dose of 20 Gy. This dose was prescribed to the 95% isodose line, which covered the PTV. Stereotactic radiosurgery was performed with the helical tomotherapy system and an adapted 6 MV linear accelerator. Precise and reproducible patient immobilization was achieved with a thermoplastic mask. GTV, PTV and Homogeneity Index were assessed, and compared CT/MR fusion plan to CT/MET-PET fusion plan using dose statistics, dose-volume histograms (DVH), and the Radiation Therapy Oncology Group (RTOG) stereotactic radiosurgery criteria.

Results: Mean GTV1 was 15.1 cm^3 (range, 0.2-54.9 cm^3; standard deviation, 16.1 cm^3). Mean PTV1 was 27.1 cm^3 (range, 1.1-88.0 cm^3; standard deviation, 25.1 cm^3). On CT/MET-PET fusion plan three tumors (Mean GTV1 was 0.2 cm^3: range, 0.1-0.3 cm^3) could not be detected, ten tumors (Mean GTV2 was 0.2 cm^3: range, 0.1-0.3 cm^3) were larger than CT/MR fusion plan and only one tumor (that was radiation necrosis) was smaller than CT/MR fusion plan. Mean GTV2 was 17.9 cm^3 (range, 0-62.2 cm^3; standard deviation, 19.1 cm^3). Mean PTV2 was 31.1 cm^3 (range, 0-105.0 cm^3; standard deviation, 31.6 cm^3). Our initial comparison of the CT/MRI fusion plan and the CT/MET-PET fusion plan showed the Conformity Index was 95%, respectively, and the Homogeneity Index was 106% and 107%, respectively. There was no acute toxicity all patients.

Conclusions: CT/MET-PET volumes were, in general, only slightly larger than the CT/MRI volumes. However, a few patients had a marked difference. As would be expected, the D95's were larger for the MET-PET fusion plan than they were for the CT/MRI plan except for radiation necrosis. We recommend CT/MET-PET fusion planning in irradiation to facilitate normal tissue sparing and toxicity reduction on one hand and to decrease the likelihood of geographical misses in target volume definition on the other hand. This study also show that intracranial radiosurgery by means of helical tomotherapy system is feasible with no acute toxicity.

928 poster

INVERSE PLANNING WIHT PHYSICAL CONSTRAINS IN IMRT: ANALYSIS FROM A RADIOBIOLOGICAL POINT OF VIEW

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Purpose/Objectif: At the present time it is quite frequent to use of radiobiological parameters (TCP, NTCP and UTCP) to evaluate treatment plans. The goal of this work is to use radiobiological tools to evaluate the results obtained in Inverse Planning IMRT calculations performed with physical constrains only. This work was carried out on treatment plans for prostate irradiation.

Materials/Methods: The IMRT treatment plans of 30 patients with prostate cancer were analyzed. All the plans were carried out with 7 fields. In each case three possible protection levels on the organs at risk (low, normal and high) were considered. For the 90 planned cases it was calculated the TCP for the prostatic volume (average volume: 137.04 $cm^3 \pm 44.15$ cm^3), the NTCP for rectum (average volume: 75.00 $cm^3 \pm 35.81$ cm^3), the NTCP for bladder (average volume: 201.97 $cm^3 \pm 43.69$ cm^3) and the UTCP.

Calculation of TCP, NTCP and UTCP were achieved with a special software using data obtained from the DVHs generated by a Treatment Planning.

Results: Increasing the protection level on the organs at risk (rectum and bladder) using physical constrains in Inverse Planning implies looking for the decrease of high dose in them and consequently it implies decreasing the NTCP too. Generally high protection on organs at risk is accompanied by an inadequate covering of the target volume and a decrease in the TCP as an effect of the dose decrease in some sectors of the target volume, usually near to the organs at risk.

Our analyses shows that the increase of the protection level in organs al risk based on physical constrains indeed induce to the decrease of the NTCP (this is verified in 100% of the cases for bladder and in 96.7% of the cases for rectum). Increasing the protection level induce to decreasing the TCP in 70% of the cases but in the remaining 30% increase the TCP. The behavior of the UTCP increasing the protection level on organs at risk doesn't have a defined tendency. In our study a clear tendency of increasing the UTCP was detected (100% of the cases) when we change from low level to normal level of protection, but in the contrary situation, changing from normal level to high level protection, has shown a very variable behavior (43.3% vs. 56.7%).

Conclusions: Adding radiobiological parameters to dosimetric observations or DVH analysis evidence non expected results. This implies that the use of biological parameters in the construction of objective functions used in inverse planning can improve the results obtained in IMRT treatment plans.

929 poster

OPTIMIZING THE NUMBER OF SEGMENTS IN IMRT FOR DVH, TOTAL MONITOR UNITS, AND DELIVERY TIME

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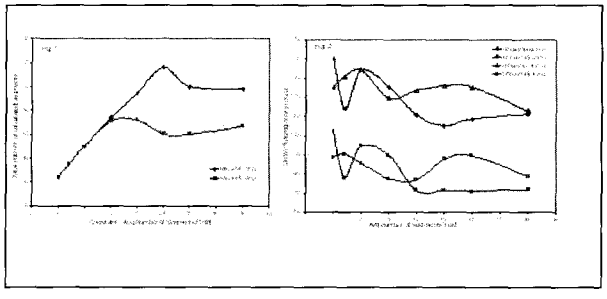
Purpose/Objectif: IMRT decreases clinical operational efficiency

due to intensive time required for planning and daily treatment delivery. To overcome this problem, we have investigated the optimum parameters for IMRT treatment. We have examined possible permutations of minimal MU per segment and average number of segments/beam on total monitor units, PTV and critical structure dose, and efficiency of beam segmentation.

Materials/Methods: Treatment planning exercises were planned using the Oncentra Treatment Planning system for a Siemens Unit with a 1 cm wide MLC. Using single sets of contours for prostate and brain, we changed the number of segments/beam (5, 7, 10, 15, 20, 25, 30, 40 per beam) for five-field, 15 MV, 500 MU/s and seven-field, 6 MV, 300 MU/s treatment plans respectively. We examined the impact of minimum MU/segment on DVH and total number of segments to execute a plan. We examined the effect of increasing the total number of segments/plan on dose homogeneity and treatment time using 2 and 4 MU minimum constraints/segment.

Results: Over the range of 1 to 15 minimum MU/segment, we found no appreciable effect on the quality of the DVH as measured qualitatively or by minimum, maximum and median values for a given number of segments. Increasing the limiting constraint of total segments/plan results in an initial linear rise followed by a plateau of the total number of segments calculated to execute a plan (fig. 1). Retrospectively, we found the total delivery time/segment in our clinic to be relatively constant with treatment time/segment for 6 MV being 11.4 s and for 15 MV being 8.4 s. The dose homogeneity is improved by increasing the total number of segments (fig 2).

Conclusions: The optimal constraint for average number of segments/field was found to be approximately 20 in order to minimize dose heterogeneity while maximizing the efficiency of beam segmentation. Increasing the minimal MU/segment from 2 MU to 4 MU resulted in fewer calculated segments/plan without compromising PTV and Critical Dose DVHs. Qualitative analysis of DVHs shows that increasing beam segmentation, results in a steeper gradient compared to less segmentation.



930 poster

PHANTOM INVESTIGATION OF THREE-DIMENSIONAL TARGET MOTION-INDUCED DOSE DISCREPANCY DURING INTENSITY MODULATED RADIATION THERAPY (IMRT) DOSE DELIVERY.

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Purpose/Objectif: To experimentally quantify the deviation of prescribed hypo/standard-fractionated IMRT doses due to 3D target motion that is synchronized/unsynchronized with treatment beam delivery.

Materials/Methods: CT-image information for two stationary targets (1 and 3.15 cm in diameter), embedded in a prototype of a commercially available dynamic anthropomorphic thorax phantom (CIRS Inc., Norfolk, VA,), were imported into a commercial TPS (Corvus Version 5.0M Rev J6, NOMOS Corporation, Cranberry Township, PA,) for inverse treatment planning. Optimized, dose fluence maps were generated for delivery with either a dynamic MLC (DMLC) (5 x 5 mm^2 pencil beam size and 7 non-opposing coplanar static gantry positions) or a MIMiC binary MLC (1-CM mode with gantry arc length of 40° and fluence modulation every 5°) platform, with beam intensity levels of 0-100% in 10% steps at machine dose rates of 300 and 400 MU/min respectively. Prescription doses of either 1.8Gy or 12Gy from a 6MV beam, covering at least 97% of the PTV, with the GTV receiving at least 95%, were specified. The optimized treatment plan for each technique was delivered to the corresponding target when; 1) stationary, 2) moving in 3D and not synchronized with linac motion (unsynchronized), and 3) moving in 3D, synchronized in phase with beam delivery. Four target motion-to-linac/MLC motion initial phase relationships were used for synchronization. The 3D, target motion cycle was 4 sec long with excursions of ±10mm S-I, ±5mm AP, and ±2mm R-L. The MOSFET 20 patient dose verification system (Thomson & Nielsen Electronics Ltd., Ottawa, ON,) was used for point dosimetry at the center of each target.

Results: For the DMLC technique with 1.8-Gy prescription dose, there was a mean 0% deviation between the static and unsynchronized dynamic doses. With a 12-Gy prescription dose, there was <2% deviation. For the MIMiC binary MLC technique with 1.8-Gy prescription dose, a 4% deviation between the static and the unsynchronized dynamic doses was recorded for the 10mm target, and a 1% deviation for the 31.5mm target. With a prescription dose of 12Gy, a 3% deviation was recorded for both targets sizes. When the initial target motion phase was synchronized with the beam, interfraction measurements were reproducible. The difference between static and motion-to-beam synchronization techniques was ≤ 4%. However, variations between mean doses of different initial phases were as much as 10%, larger variations more prominent in the small dose fraction measurements.

Conclusions: The delivered dose deviation at the center of the target between static and unsynchronized dynamic measurements is ≤ 4%. When implementing motion-to-beam synchronization techniques, errors can be as high as 10%, thus indicating the importance of correct synchronization.

Technique	Target Size (mm)	Target Motion Phase	180 cGy Mean Dose (cGy)	180 cGy % Dev	1200 cGy Mean Dose (cGy)	1200 cGy % Dev
DMLC	10	Static	180	-	1173	-
		Unsync	180	0	1195	-2
		0	175	3	1177	0
		π/2	182	-1	1205	-3
		π	174	3	1213	-3
		3π/2	173	4	1194	-2
	31.5	Static	188	-	1264	-
		Unsync	188	0	1280	-1
		0	180	4	1271	-1
		π/2	193	-3	1307	-3
		π	188	0	1267	0
		3π/2	192	-2	1251	1

Table 1: Measured mean doses (complete data will be presented). Under the "target motion phase" column, 'static' defines the reference stationary state, 'unsync' defines motion in 3D not synchronized with linac beam delivery, and the phase angles define the initial phase at which target is synchronized with the beam.

931 poster

PRE-TREATMENT VERIFICATION OF CLINICAL IMRT FIELDS

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Purpose/Objectif: After the evaluation and acceptance of treatment plans of patients that are subject to IMRT, treatment planning system (TPS) results are verified under treatment conditions and if the results are between the acceptance limits, the patients are treated. The purpose is to increase the quality of the treatment of patients treated with IMRT.

Materials/Methods: The treatment is performed with the Varian Clinac 2300CD Lineer Accelerator with 120dMLC. For head&neck 6MV, for prostate 18MV photon beams are used. The planning is performed using the pencil beam convolution algorithm in the Varian Eclipse Helios (7.5.18) TPS. Portal dosimetry is performed with aS500 Varian Electronic Portal Image Dedector (EPID). For absorbed dose measurements at reference point 0.1255cc (PTW) ion chamber, Unidose electrometer (PTW) and PTW Universal IMRT phantom are used. The network system is Varis version 6.5.

Absolute dose measurements were performed for each plan with the gantry, collimator and couch angles at zero degree and deliverable patterns for a patient plan are transferred to the phantom and doses in the phantom are computed for quality assurance. Than the plan is transferred to the treatment machine via the network system. In the treatment machine the IMRT phantom is irradiated for every field and the electrometer readings are noted. The readings are calculated based on IAEA-277 absorbed dose protocol. The basic assumption in this process is that if the dose calculated in the phantom is equivalent with the measurement in the phantom, than the dose delivered to the patient is equivalent with the dose calculated in the patient. Reference point dose difference between TPS and phantom measurements should be less than 3% following our acceptance criteria.

The verification of portal dosimetry in IMRT planning is calculated for the dMLC for all the treatment fields using TPS portal dose prediction algorithm. The plan is transferred to the treatment machine. The beaming is realized for every treatment field and the actual dMLC fluence maps are evaluated with gamma evaluation method. Typical criteria of acceptance are a dose difference of 3% and a distance to agreement of 3mm. And the gamma evaluation score should be less than 1.

We also look at fluence map and evaluate isodose overlay and profile for each IMRT field which is calculated at the TPS and acquired at EPID.

Results: We performed 226 and 197 reference point dose measurements for 33 head&neck and 38 prostate IMRT plans, respectively. Median reference point dose measured in the TPS was 252.5cGy (range 147-280) and in the phantom 248.64cGy (range 144-280). The median difference between the phantom and TPS measurements was 1.3% (range -2.6-4.1) with a standart deviation 1.6%. Only for one prostate and 3 head and neck plans the dose difference was <3%. Gamma score results were less than 1 for each IMRT field.

Conclusions: We found that the discrepancies between the TPS and phantom measurements for reference point dose was less than 3% in most of the patients. The gamma score was less than 1 for all planned fields. Portal dosimetry provide significantly faster pretreatment QA for IMRT.

932 poster

PRELIMINARY EXPERIENCE IN THE MANAGEMENT OF A PARASELLAR MENINGOTHELIAL MENIGIOMA WITH TOMOTHERAPY

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Purpose/Objectif: To evaluate the feasibility of radical radiation treatment with TT for a meningioma located around the optic chiasm, and the left optic nerve, avoiding blindness for the patient.

Materials/Methods: A 50 years old woman affected by meningothelial meningioma located around the optic chiasm and the left optic nerve was treated in our Institution.

Dose patterns were evaluated, comparing Tomotherapy (TT) with 3DCRT and IMRT.

Dose constraints were: D MAX chiasma ≤ 45 Gy, D MAX optic nerves ≤ 50 Gy, D MAX brainstem ≤ 55 Gy.

Results: If prescribing 54 Gy to GTV with 3DCRT, the optic pathways reach an unacceptable dose, due to tumor location around the optic chiasm and the left optic nerve. In comparison with TT, IMRT reaches a slightly better coverage of volumes of interests, while TT affords a better sparing of organs at risk (OAR). With TT only 43.03 Gy, dose max, are reaching the optic chiasm versus 50.0 Gy with IMRT. Due to the extension of the disease, 51.7 Gy, dose max, are delivered to the left optic nerve with TT, while 52.3 Gy is the D.MAX with IMRT. The right optic nerve reaches only 37.51 Gy with TT versus 45.4 Gy with IMRT. The median brainstem dose is 41.27 Gy, with a dose max of 52.13 Gy with TT, versus 51.7 Gy with IMRT.TT was chosen as the best treatment delivery modality. Treatment finished one year ago, and the volume of the meningioma is unchanged at MRI. No side effect appeared, except transient alopecia.

Conclusions: TT is a new modality to deliver radiotherapy which can be applied to these uncommon and aggressive neoplasm. Beyond the higher accuracy in delivering radiation treatment in comparison with 3DCRT, an additional advantage of TT is the daily megavoltage CT, that allows to check the accuracy of set-up before each fraction.

933 poster

PROSTATE DOSE ESCALATION: BLIND VERSUS GTV-ASSURED BOOST.

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Purpose/Objectif: Dose escalation is beneficial for treating prostate cancer. A blind boost of the dose to the entire prostate unfortunately results in an underdosage of the peripheral zone, where the majority of tumors is located. Modern imaging techniques may be used to direct the boost to the visible GTV. However, prostate cancer is usually a multi-focal disease. Due to limited sensitivity of the imaging techniques small, but clinically relevant tumor foci may be missed. Therefore, a boost to the visible tumor only seems inadequate. To cope with this uncertainty we propose a strategy directing the boost to the entire prostate, but steering the underdosage in the peripheral zone away from the visible tumor. This guarantees coverage of the visible GTV, while minimizing the risk of missing small foci. This approach is evaluated in a planning study.

Materials/Methods: For 5 patients with T3 prostate cancer the prostate and the peripheral zone were delineated on 3T MRI. The tumor area was determined using T2 MRI, Dynamic Contrast Enhanced MR and Diffusion Weighted Imaging MR. A 7-field IMRT technique was planned using Plato-ITP. Margin applied was 4mm. The following constraints were applied: rectum V72Gy<5%, V70Gy<25% and V50Gy<60%, bladder V72Gy<10%. Compared were 3 plans: blind prostate dose escalation (prostate corpus to 84Gy), a boost to the visible tumor only (GTV 84Gy, rest of prostate corpus 76Gy) and the GTV-assured boost (prostate corpus 84Gy, entire GTV 84Gy).

Results: When comparing the different strategies (blind escalation, a boost to the GTV only, and the GTV-assured boost) GTV V99% was 81.2Gy (75.3-83.7), 82.5Gy (81.3-83.4) and 83.1Gy (82.2-84.2) respectively. The V99% dose to the peripheral zone was 79.0Gy (76.4-82.5), 74.0Gy (72.3-75.2) and 79.3Gy (76.7-82.5) respectively. Hence, some patients do not reach the prescribed dose. Compared to blind dose escalation the GTV-assured boost yields a comparable dose to the peripheral zone, but improves the dose to the visible tumor. Margins larger than 4mm or higher doses are expected to increase this difference.

Conclusions: This planning study shows that the GTV-assured boost approach equals the results of blind dose escalation to the peripheral zone but increases the dose to the tumor.

934 poster

QUALITY PARAMETERS TO EVALUATE THE SEQUENCER OF IMRT-FIELDS IN SLIDING WINDOW MODE

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Purpose/Objectif: One of the features of quality assurance of IMRT treatment plans should be the evaluation of the MLC-sequencer output. For example, two main error causes of IMRT field generation are inter-leaf-leakage and the tongue and groove effect. Both effects depend on the fluence complexity as well as on the sequencer that calculates the leaf motion.

Materials/Methods: Four parameters are used to evaluate the sequencer results: MU efficiency, the mean segment size, the tongue and groove-coefficient and the leakage-coefficient. These parameters are calculated using the positions of leafs during the treatment.

All four quality parameters are investigated depending on the used dose rate and the fluence complexity respectively. The fluence complexity is varied by use of smoothing procedures.

Results: Results for prostate treatment plans and head and neck treatment plans will be presented. The delivery of the IMRT fields is evaluated by film dosimetry. The results of gamma analysis between measured and calculated dose distributions in a physical phantom will be correlated with these quality parameters.

Conclusions: A computer program has been developed for automatic tests of IMRT plans in clinical routine and will be presented in this study.

935 poster

SPATIAL AND DOSIMETRIC VARIABILITY OF ORGANS-AT-RISK IN HEAD AND NECK IMRT

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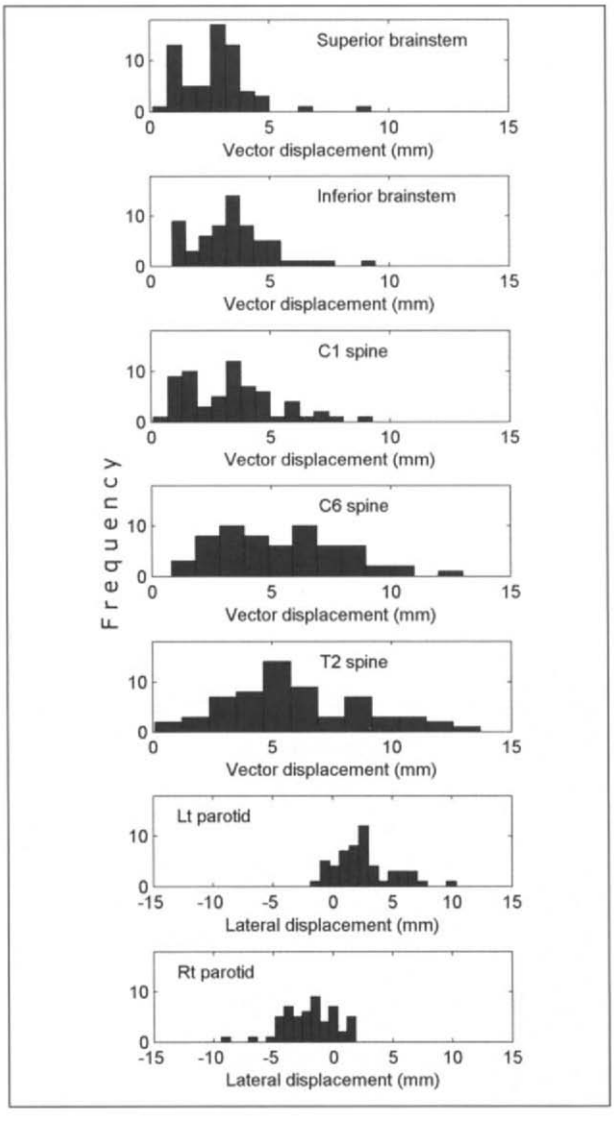
Purpose/Objectif: One of the challenges in IMRT of head and neck cancer is spatial and dosimetric variability caused by random error and systematic, anatomical change over time. The purpose of this patient study is two-fold: i) to track, using 3D imaging, the displacement of organs-at-risk (OARs) over time; and ii) to assess the dosimetric impact of these changes on OAR sparing. These two analyses, respectively, provide for improved definitions of Planning Risk Volume (PRV) margins and estimates of normal structure sparing over the course of treatment.

Materials/Methods: Fifteen IMRT H&N patients were selected randomly and were CT imaged weekly over the seven-week treatment course. Two analyses were performed: i) The original planning CT was fused to each follow-up CT by matching stable external landmarks on the immobilisation system base-plate. Landmarks were then placed at regions of interest including superior and inferior brainstem, C1, C6 and T2 spine, medial and lateral aspects of parotid glands and styloid tips. Three-dimensional translations of these landmarks were then recorded as a function of time. For the parotids glands, anatomical shift was isolated by subtracting the styloid coordinates from the parotid landmark coordinates. ii) OARs, including the brainstem, spinal cord and parotid glands, were contoured on all CT sets. The original IMRT plan was re-mapped onto each of the follow-up CT sets. This allows generation of a temporal series of dose volume histograms for each normal structure.

Results: Spatial displacement of the superior and inferior brainstem was randomly distributed over time and variability increases significantly at more inferior spinal locations. The magnitudes of the 3D displacement vector (Figure 1) among all patients and CT sets were 2.8 ± 1.5 mm (sup brainstem), 3.4 ± 1.6 mm (inf brainstem), 3.3 ± 1.9 mm (C1), 5.5 ± 2.9 mm (C6), 6.1 ± 3.2 mm (T2). In contrast, both parotid glands exhibited a systematic translation in the medial direction (Figure 1, lowest two plots), i.e. into the high-dose volume. Dose volume histograms for the brainstem and upper cord showed minimal variation over time, with maximal doses within ±10% of planned values for the majority of patients. The deviation of the maximum dose received by lower cord was close to zero when averaged over all patients and time; however, several patients showed daily deviations of 25% from planned maximum, caused by significant lateral variability. For both parotid glands, the medial shift over the course of treatment results in delivered mean dose values greater than those predicted by the initial plan.

Conclusions: Measured spatial variability along the spinal axis appears random with displacement vector magnitudes of approximately 3 mm at the level of the brainstem and upper spinal cord but increasing at more inferior locations. The parotid glands translate medially in a systematic fashion over the course of treatment, resulting in a significant increase of delivered mean dose.



936 poster

STEP & SHOOT IMAT FOR THE PROSTATE, MORE BEAMS, LESS QA

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Purpose/Objectif: Clinical introduction of IMRT is often hampered by extensive QA procedures that are required to validate that a complex linac prescription yields a desired dose distribution. A new step & shoot IMAT technique is developed for the prostate using a commercial TPS that yields high-quality dose distributions and can be directly and safely delivered without the need for extensive dosimetrical QA procedures. Aim of the treatment is to irradiate the PTV to a dose of 70 Gy while boosting the prostate itself to a dose of 76 Gy and simultaneously sparing the rectum as much as possible.

Materials/Methods: A coplanar arrangement of 13 beams is superimposed to the PTV. The gantry angles are uniformly distributed taking into account that the C-arm must be avoided at the entrance side of each beam. Each beam is split into one primary segment and one or two secondary segments depending on the geometry of the PTV and rectum. The primary segments encompass the complete PTV, whereas the secondary segments block the rectum and encompass the PTV elsewhere, resulting in approximately 28 segments in total. In the final phase, the leaf settings and segment weights are optimized using conventional dose objectives (Fig 1).

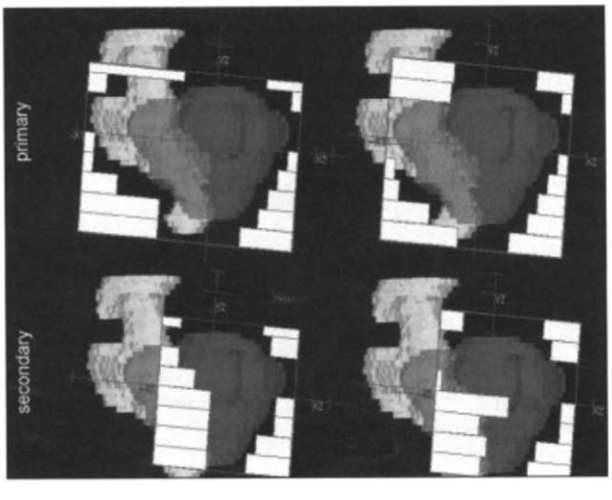
Caption Fig 1: Primary and secondary segments of an oblique beam before and after optimization.

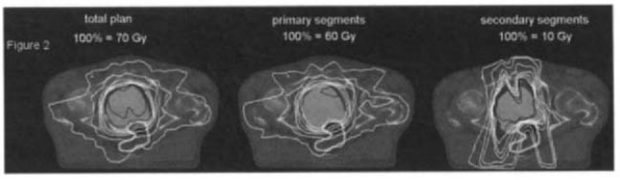
Results: The applied optimization method leads to high-quality dose distributions, that are very similar to that of a full fluence based 5-beam technique with 35 segments. Using a 'single button' delivery method, both treatments can be delivered within 4 minutes. However, the 13-beam technique has three advantages over the 5-beam technique:

1. approximately 85% of the dose to the prostate is delivered by the primary segments that are conventional in the sense that they are highly symmetrical and convexly shaped (Fig. 2)
2. due to the segmentation method no segment configurations with abutting leafs are generated, so tongue & groove effects can be neglected
3. although the shapes of the secondary segments are generally not convex or symmetrical, they are also not very unconventional, whereas full fluence based optimization techniques sometimes result in segments with exotic shapes and high intensities.

Caption Fig 2: Dose distributions of the total plan, primary segments and secondary segments. The white isodose lines indicate the 40%, 60%, 80%, 90%, 95% and 100% dose levels. The 105% and 110% isodose lines are displayed in black.

Conclusions: Due to the intrinsic characteristics of the optimization method, the step & shoot IMAT technique can be right away and safely delivered with conventional QA procedures.





937 poster

SUPERIORITY OF INTENSITY MODULATED RADIOTHERAPY OVER BEST THREE-DIMENSIONAL CONFORMAL RADIOTHERAPY COMBINED WITH BRACHYTHERAPY IN TREATMENT OF NASOPHARYNGEAL CARCINOMA: A PLANNING STUDY

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Purpose/Objectif: To investigate the benefits of Intensity-Modulated Radiotherapy using simultaneous multitarget treatment technique (SIMT-IMRT) over the best three-dimentional conformal radiotherapy combined with intracavitary brachytherapy (3DCRT + IBT) in treatment of nasopharyngeal carcinoma (NPC), a planning study was performed.

Materials/Methods: Eight NPC patients (two for each T stage) were chosen. The actual computer tomography data sets for each patient were retrieved in order to delineate Gross tumor volumes. Three sets of PTV (PTV^1, PTV^2, PTV^3) as well as at least ten different organs at risk were delineated for each case. PTV^1 and PTV^2 included GTV plus 0.5 cm and 1.5 cm margins. PTV^3 included the adjuvant volume of the neck. Both SIMT-IMRT and 3DCRT + IBT plans were prepared for each case. The mean amount of treatment fields for each modality were nine and 13, respectively. Dose prescriptions for PTV^1, PTV^2 and PTV^3 were 72.6 Gy, 66 Gy and 52.8Gy in 33 fr for SIMT-IMRT plans vs. 72 Gy (consisting of 66 Gy/33 fr for external radiotherapy and 3Gy x 2 for IBT), 66Gy/33fr and 46Gy/23fr for the combined modality plans, respectively.

Results: Generally, SIMT-IMRT plans provided more homogeneous and conformal plans than 3DCRT + IBT plans. The mean equivalent uniform dose (EUD) for PTV^1 for the two techniques were 67 Gy vs. 63.7 Gy, respectively ($p = 0.016$). The mean values for tumor control probability (TCP) adjusted and not adjusted for accelerated tumor repopulation after 28 days for the two treatment modalities were 94.3% and 98% vs. 89.9% and 95.8%, respectively ($p = 0.016$). The mean dose to middle ear and external auditory channels, parotid glands and temporomandibular joints were significantly lower in SIMT-IMRT than 3DCRT + IBT plans.

Conclusions: Our general inference from this study is that in radiotherapy treatment planning of NPC, SIMT-IMRT plans still stand superior to very complex 3DCRT plans combined with IBT in terms of tumour coverage, increase in local TCP and reduction of the dose to some organs at risk.

Dose volume statistics for organs at risk in 8 NPC patients

Parameter	SIMT-IMRT Mean	SD	XRT + IBT Mean	SD	p-Value
Spinal cord					
D_{max} (Gy)	46.4	1.8	49.5	0.5	0.016
Brain stem					
D_{max} (Gy)	56.6	1.7	60.5	1.8	0.008
Optic chiasm					
D_{max} (Gy)	31.2	20.8	23.7	17.6	0.008
Pituitary gland					
D_{max} (Gy)	62.1	12.5	56	9	0.008
D_{mean} (Gy)	52.4	16	45	15	0.008
Mandible					
D_{max} (Gy)	67.1	4.7	69.5	1.2	0.008
D_{mean} (Gy)	46	1.9	38	3.6	0.375
Temporal lobes					
D_{max} (Gy)	60.6	3.4	64.2	1.6	0.001
D_{mean} (Gy)	17	2.8	14.7	3.4	0.003
NTCP (%)	0.04	0.07	0.2	0.25	<0.001
TM joints					
D_{max} (Gy)	63.8	8.5	66.6	1.9	0.29
D_{mean} (Gy)	45.4	7.5	62.3	3.8	<0.001
NTCP (%)	2	3.6	11	6.1	<0.001
Inner ears					
D_{max} (Gy)	56.3	7.7	54.8	8.3	0.57
D_{mean} (Gy)	40.3	8	34.5	11	0.024
Middle and outer ears					
D_{max} (Gy)	52.3	9.3	63.1	6.5	<0.001
D_{mean} (Gy)	33.7	6	47.5	7.6	<0.001
NTCP-acute (%)	74.3	28.7	93.7	25	0.003
NTCP-late (%)	5.6	10.4	27.5	16	<0.001
Larynx					
D_{max} (Gy)	58.6	4.3	64.7	6.7	0.023
D_{mean} (Gy)	36.1	4.7	29	3.7	0.023
NTCP-oedema (%)	1.6	1.5	3.9	1.9	0.008
Parotid glands					
D_{mean} (Gy)	40.2	8.8	61.5	5.6	<0.001
NTCP (%)	86.5	26.6	100	0	0.001

938 poster

THE INFLUENCE OF DIFFERENT IMRT DELIVERY TECHNOLOGIES ON THE PERIPHERAL DOSE OUTSIDE THE TREATED BODY REGION ? FURTHER RESULTS

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Purpose/Objectif: Today intensity modulated radiotherapy (IMRT) is a frequently used technique for the optimization of radiotherapy, possibly with the effect of higher cure rates and/or reduced side effects. Besides the fact that radiation eradicate tumor cells it has the potential to generate stochastic effects in healthy tissue, such as induced secondary malignancies. Other authors have published data about peripheral doses in patients undergoing radiotherapy. The aim of this work is to quantify the influence of different IMRT technologies with respect to the peripheral dose outside the treated body region.

Materials/Methods: On two linacs (four energies: 6 MV, 10 MV, 15 MV, 25 MV) point dose measurements were performed at large distances (29 cm off axis inplane) from the treated region at different depths using an acrylic phantom. Field dimensions were 20 cm (crossplane) ´ 22 cm (inplane) for both an open beam and with an artificial IMRT fluence distribution. Fluence distributions consisting of stripes of high and medium intensity levels were generated by segmented multileaf-modulated (sMLM), by tin+wax compensators (TWComp) and by lead-containing MCP96-compensators (PbComp). All treatment plans were generated with Helax TMS (Theranostic). The treatments were delivered with a Mevatron Primus (Siemens OCS) and with a Precise (Elekta) linac. Point dose measurements were done with an ionisation chamber IC 04 (Scanditronix/Wellhöfer) together with an electrometer dose 1. All doses were normalised to the mean dose in 10 cm depth of the acrylic phantom in the irradiated region. Measurements with TLD 600 and 700 are started to get an idea how different IMRT-technologies influence the amount of neutrons in the peripheral region.

Results: For the open field, the peripheral relative doses (PD) increase with decreasing photon energy in depth beyond 20mm. Near the surface PD values are distinctly higher than those at larger depth, and they increase with increasing photon energy. In comparison with the open field, the PD are further increased by a factor varying from 1.2 to 1.8 when delivering the IMRT fields with sMLM, depending on photon energy and depth. When using PbComp this factor is even higher (2.0 to 2.2); using TWComp, this factor varies from 2.2 to 2.4. This increase behind compensators is similar than behind steel wedges when using older techniques with less beams. At depths beyond 20 mm and for all types of IMRT technique, the PD values slightly decrease with increasing photon energy. The PD values of the Precise linac are generally lower than of the Mevatron machine. The measurement results getting with the ionisation chamber could be approved by the TLD measurements for photons for 6MV and 15 MV.The measurements for the neutron generated peripheral dose part could not finished yet.

Conclusions: For the open field the PD and their trend with energy can be explained by Compton scattering of photons from the irradiated field towards the off-axis measuring points. The further increase of the PD in case of the sMLM method has to be attributed to MLC leakage radiation. The highest increase associated with the use of physical compensators, and especially the values for tin+wax compared to lead, can be explained by photon scattering from the compensators. The distinctly higher dose values near the surface appear to reflect secondary electron components in peripheral regions. Further experiments, focusing on neutron components in high energy IMRT beams, are going on.

939 poster

WHOLE BREAST IMRT AND RESPIRATORY MOTION: A PHANTOM STUDY

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Purpose/Objectif: To quantify the effect of respiratory motion on treatment delivery for four whole breast tangential planning techniques: 2D conventional (CP), forward-planned (FP), surface-compensated (SC) and hybrid IMRT (hIMRT).

Materials/Methods: An anthropomorphic breast phantom of beeswax (0.95 g/cc) with a cork lung insert (0.25 g/cc) was constructed. 4 half-beam blocked, tangential breast treatments were CT-planned on Eclipse 6.5. The CP technique employed dynamically-wedged fields with angles chosen for homogeneity on a single axial slice. The FP technique used 3 static MLC-defined apertures to shield volumes of dose <105% within the PTV. The SC technique used an Eclipse tool to generate dynamic MLC fields, to produce uniform dose at a beam-specific depth. The hIMRT technique employed 2 open and 2 dynamic IMRT fields, optimized for uniform dose throughout the PTV. Kodak EDR-2 film was inserted in a sagittal plane through the isocentre. Each plan was delivered to 4 films: 1 static and 3 with the phantom moving in a sinusoidal waveform (equal anterior-posterior and superior-inferior components, 15 cycles/min) with amplitudes of 1 cm (isocentre set at mid-cycle) and 2 cm (both mid- and end-cycle). The change in dose homogeneity between static and moving films were rated by a team of radiation oncologists, blinded to planning technique, as 'clinically insignificant', 'clinical relevance uncertain' or 'clinically significant'.

Results: Respiratory motion generally resulted in an increased dose gradient, with the dose decreasing near the lung interface and increasing anteriorly. Clinicians rated the change in CP dose homogeneity as insignificant in all motion films. The change in dose homogeneity for the FP treatments were rated insignificant for 1 cm motion, but 2 cm motion films demonstrated change of uncertain clinical relevance. In this step-and-shoot technique, the change in homogeneity was limited by the heavy weighting of the open field (84%).

For the SC technique, observed changes were insignificant for all motions, except for 2cm end-cycle (clinical relevance uncertain). The hIMRT treatments resulted in the greatest change in homogeneity with respiration - none were rated as insignificant. Both SC and hIMRT use dynamic sliding window deliveries. The entire dose (~400MU per field) in the SC plan is delivered through the sliding window over

an average of 20 respiratory cycles. The sliding window component of the hIMRT plan delivered ~100 MU (of 200 MU) over 5 cycles. With fewer cycles to smear the dose, respiration has a greater effect on homogeneity.
Conclusions: This phantom study indicates that respiratory motion has negligible impact on conventionally planned treatment deliveries, and little effect on surface-compensated and 3D forward-planned techniques. The change in dose homogeneity due to respiratory motion for single hybrid-IMRT fractions was judged to be clinically significant by radiation oncologists.

Posters Inverse Planning

940 poster

OPTIMIZATION AND IMPROVED EFFICIENCY OF HEAD & NECK SIB-IMRT PLANNING WITH PINNACLE-DMPO - A PLANNING STUDY WITH PHYSICAL AND BIOPHYSICAL OBJECTIVES

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Purpose/Objectif: IMRT treatment planning of H&N patients can be complex and time-consuming (trial-and-error process) due to concave, irregular target volumes which are close to or overlap with critical structures. In a clinical environment where it is essential for the patient to start treatment within a week after the CT scan, it is important that the planning procedure is straightforward and time-efficient. The goal is therefore to find a standard set of objectives with which a satisfactory clinical plan can be achieved for every patient. In version 7.6c of the TPS Pinnacle[3] (Philips), physical and biophysical (generalized equivalent uniform dose, gEUD) objectives can be employed and compared to see if gEUD objectives can improve the outcome. The optimizer DMPO integrates MLC leaf sequencing into the optimization process. Pinnacle[3] furthermore offers the possibility to create command files ('scripts').
Materials/Methods: Fifteen patients with H&N cancer (oropharynx) are planned with the inverse planning module of Pinnacle3 ('step-and-shoot' method). The treatment technique employed is a simultaneously integrated boost (SIB) technique (7 coplanar beams) with 34´1.48 Gy to the elective and 34´2 Gy to the boost target volume (accelerated schedule of 5.5 weeks with 1 fraction per day during first 4 weeks and 2 fractions per day during last 1.5 weeks). Different sets of objectives for target volumes and critical structures are tested, including dose-, dose-volume-based and gEUD objectives. Furthermore, additional contours are introduced to further sculpt.the dose distribution and subsequently simplify the planning process.
Results: Three sets of objectives are found (two consisting only of physical and one containing gEUD objectives) which all deliver clinically acceptable treatment plans in each of the 15 patients studied (no significant superiority of the gEUD objectives is seen). With a pre-defined set of objectives and 'guiding volumes', on average no more than 3 trial-and-error runs are needed, each run lasting less than half an hour (with 60 segments and 30 iterations).
Conclusions: IMRT treatment planning of head & neck patients can be customized with Pinnacle3 by finding a pre-defined set of objectives and guiding volumes and by utilizing scripts. In addition, the use of the optimizer DMPO shortens the calculation time which can result in a total planning time even shorter than for the 3D conformal radiotherapy techniques.

941 poster

USING BREATHING-MOTION KNOWLEDGE TO ALTER THE THERAPEUTIC RATIO.

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Purpose/Objectif: To study by simulation and experiment whether a priori knowledge of breathing motion can be incorporated in inverse treatment-planning and accounted for.
Materials/Methods: Respiratory motion was incorporated into an in-house inverse-planning package (Autoplan) by convolving the probability density function (PDF) of expected tumour position with the dose-deposition kernel in a 5mm spatial sampling grid. The CTV was simulated to move with an asymmetric trigonometric function, extending 20mm superiorly-inferiorly and 10mm anteriorly- posteriorly, with its planning position considered to be at the middle of its path. Two types of plan were devised; [1] a geometrically conformal (CRT) plan with the multileaf collimator's projected 1cm wide leaves conforming to the PTV (where their position does not need to be altered to compensate for the motion) and [2] an intensity-modulated (IMRT) plan with a smaller PTV but with motion-compensation. Van-Herk's method was used to grow the CTV into a PTV for the CRT case, whereas the IMRT PTV resulted from a uniform margin expansion of 5mm. These plans were subsequently delivered to a breathing anthropomorphic phantom adhering to the aforementioned motion and the delivered doses were measured with gafchromic film, placed inside sagittal planes in the CTV.
Results: Dose-volume histogram (DVH) analysis of the plans showed a sparing of the healthy lung. V20 for the CRT case was 22%, which was reduced to 19% for the IMRT with the 5mm-grown PTV. This resulted in the following minimum-maximum doses to the moving CTV respectively: (94-108)% and (91-113)%. Film measurements have verified the feasibility of reducing the PTV margin. Measured doses confirmed the DVH predictions.
Conclusions: So long as the treatment isocenter is set to the middle of the path of the tumour and the breathing motion is well known and reproducible, then motion-compensating inverse-planning can produce deliverable intensity profiles that can alter the balance of dose to the CTV and organs at risk. Potential for healthy tissue sparing by margin reduction to 5mm has been demonstrated. Finer spacing of the sampling for the PDF and the dose-deposition kernel should lead to greater gains.

Posters Legislation and Recommend. in RT

942 poster

PRESENT STATUS OF THE IMPLEMENTATION OF MED DIRECTIVE 97/43 AT THE NATIONAL LEVEL OF EU COUNTRIES

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Purpose/Objectif: European Council Directive 97/43/EURATOM on health protection of individuals against the dangers of ionizing radiation in relation to medical exposures issued in June 1997, has put on EU state member the responsibility to pass by May 13th 2000, the national acts of law establishing, among many issues: 1. the responsibilities for administering medical exposure, and 2. the quality assurance and control programs, including the conduction of clinical audits. The aim of this research was to reveal the present status of implementation of MED Directive 97/43 regulations into the national laws of European member states.
Materials/Methods: The survey was sent up to January 2006 to 67 national societies from 37 European countries. 12 responses were received by April 14th, 2006. Due to the low response the survey was sent for a second time. At the present we are waiting for further re-

plies. The questions were aimed to reveal: (1) present status of the legal environment concerning radiotherapy in European states and recommendations passed by entities other than the state , i.e. scientific societies, academic bodies; (2) progress in implementation of MED Directive 97/43/EURATOM to national laws; (3) organization and performance of clinical audits at the national level, (4) implementation and maintenance of quality assurance programs.

Results: The obtained data showed that conditions in which radiotherapy should be performed have just recently been regulated by national laws due to the implementation of the MED Directive. Although most countries have implemented the MED Directive regulations regarding the performance of clinical audit; including the steps of the audit, its comprehensiveness and the composition of the auditing team (mostly experts in medical physics, radiation oncology and engineering), in most countries it has not yet been put into practice. Most respondents confirmed that results of clinical audits do not determine eligibility of institutions to provide radiotherapy. The responsibility for regulatory control of radiotherapy departments is still with the national bodies. In some European countries (i.e. , Czech Republic and The Netherlands) lawful regulations have been also completed by recommendations elaborated by scientific societies or universities. It was reported that hospitals rarely use their own written regulations regarding radiotherapy as they base their practice mostly on national laws, and national societies guidelines. However the majority of radiotherapy departments have already implemented quality assurance programs or quality management system based on EN ISO norm 9001:2000.

Conclusions: The implementation process of MED Directive regulations into national laws is currently in progress and it is mostly coordinated by governmental bodies such as the Ministry of Health or the National Atomic Energy Agency which established working parties for this purpose. Only few of the EU countries have fulfilled the requirements of the Directive.

943 poster

RADIOTHERAPY CAPACITY AND FRACTIONATION PRACTICE IN THE UK

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Purpose/Objectif: It has been estimated in a European survey that the has only 53% of the required radiotherapy capacity (1). Correcting this deficit would require increase of 89%. Our aim was to determine if this is really required and to study the impact on patient care.

Materials/Methods: We reviewed data on all patients starting a course of radiotherapy in the week commencing 26.9.05 (2). 2592 patients were treated (excluding skin cancer). Some of these patients will have been receiving treatment for relapse and we estimate that 2099 patients received radiotherapy as part of their initial treatment for cancer.

Results: Over a year 109148 patients would have been treated, and 275,280 new cancers were diagnosed in the in 2002. Thus the access rate (proportion of patients receiving radiotherapy as part of their first cancer treatment) was 40% rather than 53% which has been recommended (3). Dose-fractionation data were collected on all patients and compared to evidence-based practice (4). Optimum fractionation remains uncertain, particularly for common sites such as breast where there is grade B evidence to support both 15 and 25 fractions - this uncertainty will not be resolved until the START trial is published. Similar discrepancies exist for other common malignancies such as lung and prostate cancer. Clinical judgement is critical in deciding treatment intent and fitness for therapy. Using minimum and maximum fractionation recommendations, the required increase in provision ranges from 0% to 35%.

Conclusions: We conclude that limited radiotherapy capacity in the decreases access: an increase of 33% would be required to provide radiotherapy as part of their first treatment to all those who are currently denied it. Those who are treated receive treatment in line with the most economical regimens supported by current evidence. However, if the highest numbers of fractions were used then an increase of 35% would be required. To account for both types of underprovision an increase in resource of 80% would be required. This is similar to the estimate that to treat its population adequately the should increase its radiotherapy capacity by 89% (1).

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944 poster

SPINAL CORD DOSES IN PALLIATIVE LUNG RADIOTHERAPY SCHEDULES

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Purpose/Objectif: We aim to check the safety of the standard palliative radiotherapy techniques by using the Linear quadratic model for a careful estimation of the doses received by the spinal cord, in all standard palliative lung radiotherapy fields and fractionation.

Materials/Methods: Patients surveyed at retrospective audit were all patients treated with palliative chest radiotherapy for lung cancer over a period from January to April 2005. Radiotherapy field arrangements, field size constraints, doses, dose points for calculation, beam quality, fractionation and treatment times were recorded. These were compared with the recommended limits of the MRC trial protocols for the dose and fractionation prescribed.

Doses delivered to structures off the field central axis were estimated using a standard CT scan of the chest. Dose estimates were made using an SLPLAN planning system. As unexpected spinal cord toxicity has been reported after hypofractionated chest radiotherapy, a sagittal view was used to calculate the isodoses along the length of the spinal cord that could lie within the RT field.

Equivalent dose estimates were made using the Linear-Quadratic Equivalent Dose formula (LQED). The relative radiation sensitivity of spinal cord for myelopathy (the a/b dose) cord has been estimated as a/b = 1Gy.

Results: Our analysis of the schedules used in current practice in a large regional cancer centre suggest that the 17Gy in 2 fraction and 39Gy in 13 fraction protocol would risk spinal cord damage if the radiotherapist was unaware of the potential spinal cord doses. Both schedules have spinal cord equivalent doses (using the linear-quadratic model) that lie within the conventional safe limits of 50Gy in 25 fractions for the 100% isodose. However when the dosimetry is modelled for a 6MV 100cm isocentric linnac in 3 dimensions, and altered separations and air space inhomogeneity are considered, the D-Max doses consistently fall above this limit on our 3 model patients.

Conclusions: For those prescribed 39 G/ 13 fractions, 36 Gy in 12 fractions may be more appropriate to be used although doses are still considered to be high. For the 17 Gy/ 2 fractions (7 days apart), doses are also high along the spinal cord. Alterative doses are suggested below 15.5 Gy/ 2 fractions (7 days apart) would the most acceptable.

Posters Lung Cancer

945 poster

3D CONFORMAL SINGLE HIGH-DOSE BOOST RADIOSURGERY(SRS) FOR PERIPHERAL STAGE I NON-SMALL CELL LUNG CANCER(NSCLC) USING C-ARM LINEAR ACCELERATOR AND A SPIRO-ANALYZER.

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Purpose/Objecti: To reduce the normal tissue damage, we have developed a respiratory gating system using spiro-analyzer to control respiratory organ mortion. This study was performed to evaluate the clinical outcomes of three-dimensional (3D) conformal single high-dose boost radiosurgery (SRS) for peripheral T1 non-small cell lung cancer (NSCLC) using this system.

Materials/Method: From November 2000 to July 2004, 25 patients with peripheral stage T1 NSCLC were itreated in our institue and were followed for < one year. The majority of patients were accompanied by medical problems. Only three patients refused surgery. Nineteen patients had T1 tumors and six had T2 tumors. The size of T1 tumors ranged from 15 mm to 30 mm in diameter and T2 tumors were less than 45 mm in diameter. All patients were treated with a standard fractionation of 30Gy/10 fractions or 40Gy/20 fractions and a single high-dose boost of 20Gy using 3D non-coplanar SRS with 18 ports. 3D treatment plannning was performed to maintain the target dose homogeneity within 10-15%. C-arm linear accelerator (Mitsubishi Co. Ltd) was used for SRS and a spiro-analyzer was adopted to gating respiratory tumor mortion.

Results: Of the 25 tumors, 12 tumors (48%) almost disappeared, and nine tumors (36%) decreased in size by 50% or more after the treatment. Therefore, 21 tumors (84%) showed a local response. The cumulative in-field progression rates at 2 years were 6% in T1 and 60% in T2, respectively. No patient developed an isolated regional failure. Five patients died from intercurrent disease, and the two-year overall and cause-specific survival rates were 70% and 85%, respectively. During the potential follow-up of 12-55 months (median 24 months), no radiation pneumonitis greater than grade 1 of National Cancer Institute-Common Toxicity Criteria was noted except for one patient had grade 2 pneumonitis.

Conclusions: 3D conformal single high-dose boost SRS using our spiro-analyzer respiratory gating system was useful for radiation therapy of peripheral T1-stage NSCLC.

946 poster

A RETROSPECTIVE ANALYSIS OF SURVIVAL, LOCAL CONTROL AND PROGNOSTIC FACTORS IN NODE POSITIVE PATIENTS TREATED WITH 3D-CONFORMAL ADJUVANT RADIOTHERAPY

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Purpose/Objectif: Adjuvant radiotherapy (RT) in patients (pts) with resected non small cell lung cancer (NSCLC) has been discussed controversial in the last years. Different trials have stated that adjuvant RT increases the rate of intercurrent death and has no benefit on overall survival (OS). Still, there exist evidence, that better local control rates can be achieved by 3D-conformal RT with minimal toxicity. The aim of this retrospective study was to evaluate OS, time to progression (TTP), local control, side effects and to define risk factors influencing the treatment outcome. Further changes in the lung function test in correlation with the dosimetric findings will be presented.

Materials/Methods: 102 eligible pts with node positive, resected NSCLC (stage IIA: 6, IIB: 20, IIIA: 62, IIIB: 10, IV: 2) treated from 1997-2005 with 3D-conformal RT to a total dose of 50-60Gy in conventional fractionation have been evaluated. All pts underwent surgery and 20 pts received chemotherapy before RT. Data were analysed until February 2006. Factors included in the multivariate analysis were age, sex, stage, T-stage, histology, nodal status, positive resection margins, surgery (pneumectomy vs. lobectomy) and family history.

Results: The mean OS was 29 months (range 2-113m), with a 3y survival of 36,3% and 5y survival of 30,14%. The mean TTP was 24m (2-68m) and time to local recurrence was mean 28m (4-68), with a local control rate of 76% after 3y and 72% after 5y. The rate of intercurrent death (ID) was 20%. OS was reduced in pts with a FEV1 $\leq$ 1,4l before RT ($p \leq 0{,}021$). In the multivariate analysis positive resection margins had a significant influence on OS ($p \leq 0{,}028$), TTP ($p \leq 0{,}014$) and local control ($p \leq 0{,}038$). For TTP, histology ($p \leq 0{,}026$) and sex ($p \leq 0{,}013$) also were significant. Grade 3 pneumonitis was seen in 5% and grade 3 oesophagitis in 2% of pts. No grade 4 toxicity was observed.

Conclusions: Postoperative 3D-conformal RT results in good local control and OS in node positive NSCLC patients without severe toxicity. Potential risk factors influencing the treatment outcome are low FEV1 before RT, positive resection margins, sex and histology

947 poster

COMPARISON OF PATIENT-SPECIFIC AND GENERIC INTERNAL TARGET VOLUME (ITV) MARGINS FOR PLANNING RADICAL RADIOTHERAPY IN LYMPH-NODE POSITIVE NON-SMALL CELL LUNG CANCER (NSCLC)

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Purpose/Objectif: Radical radiotherapy for stage II and III NSCLC includes both the primary tumour and any positive lymph nodes in the Clinical Target Volume (CTV). These have been shown to move independently of each other in magnitude and direction during respiration. To prevent this motion resulting in a geographical miss, a generic margin is usually added to the CTV to create an ITV. Previous studies have investigated the use of additional breath hold (BH) CTs to generate patient-specific ITVs for primary tumours alone. We have employed a similar technique to investigate the generation of patient-specific and generic ITVs for CTVs that include mediastinal/hilar lymph nodes.

Materials/Methods: 13 patients with node positive NSCLC had 2 BH CT scans performed when they attended for their free-breathing radiotherapy planning CT scan. These additional 2 scans were performed at the limits of tidal respiration and were restricted to the region of interest. The CTV was segmented on each CT scan and a rigid registration performed on the vertebral columns to align all 3 CT volumes. Different methods for generating an ITV were then compared, as listed below. ITV_{Ref} was used as the reference volume as it contained the most data about tumour motion. The margins for ITV_2 were generated by assessing the displacement of the BH CTVs

from the planning CTV in selected coronal and sagittal planes to produce specific expansion margins in six directions.
ITV_{Ref} (Combination of the CTVs from all 3 CT scans)
ITV_1 (Combination of the CTVs from the BH CT scans only)
ITV_2 (Planning scan CTV with a specific margin generated from the BH scans)
ITV_3 (Planning scan CTV with a 0.5cm margin)
ITV_4 (Planning scan CTV with a 0.8cm margin)
ITV_5 (Planning scan CTV with a 1.0cm margin)
ITV_6 (Planning scan CTV with the following margins: 1.0cm superior-inferior axis, 0.5cm axially)
Results: The mean results are displayed below (with the range in brackets)

ITV	Volume (cm3)	Coverage of ITVRef		Volume Outside ITVRef (cm3)	% of ITV Outside ITVRef
-	-	Volume (cm3)	% of ITVRef	-	-
Ref	96.8	-	-	-	-
1	85.7	85.7	89.1 (75.9-95.3)	0	0(0-0)
2	180.7	94.5	97.0 (90.2-99.9)	86.2	48.9 (35.1-62.1)
3	159.5	92.6	95.9 (89.2-100)	66.9	45.4 (36.1-60.1)
4	222.5	95.4	98.8 (94.7-100)	127.0	60.2 (51.0-75.7)
5	273.3	96.3	99.6 (97.5-100)	177.0	67.9 (56.6-82.3)
6	193.8	94.6	98.1 (91.3-100)	99.3	54.5 (44.9-69.9)

Conclusions: The use of simple expansion margins to create an ITV from a CTV that includes malignant lymph nodes is not optimal. In general these margins may have provided good coverage of the reference ITV (mean >95%); however, with the exception of ITV_5, there were cases for each ITV where coverage was inadequate. As the ITV margins were increased, there was a small improvement in reference ITV coverage, but at the expense of a large increase in the volume of normal tissue (lung and mediastinum) included within the ITV. From our results the optimum method for producing an ITV is to co-register additional CT scans, representing the target's position at the limits of a normal respiratory cycle, to the planning CT scan. Further work needs to be done to determine whether end-tidal breath-hold scans are truly representative of tumour position at the limits of tidal respiration, or whether 4D-CT and its derivatives offer more reliable information.

948 poster

CONCOMITTANT BOOST TECHNIQUE VERSUS CONVENTIONAL RADIOTHERAPY IN LOCALLY ADVANCED NON-SMALL CELL LUNG CANCER

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Purpose/Objectif: Chemoradiotherapy with conventional fractionation still remains the main treatment modality in unresectable locally advanced non-small cell lung cancer (NSCLC). Shortening of the overall duration of radiotherapy (RT) might reduce the possibility of tumor cell repopulation and improve the treatment results. The data confirms that very accelerated shemes (CHART) are superior to conventional RT in achieving local tumor control and survival in locally advanced NSCLC. A prospective randomised trial was conducted to compare the results of a mild accelerated RT sheme of concomittant boost technique (CBRT) with the conventional RT.
Materials/Methods: Thirty-five patients with unresectable stage IIIA/IIIB were randomised to two treatment arms. The large volume including the mediastinum, ipsilateral hilar nodes and primary tumor was irradiated up to a total dose of 46 Gy with 2 Gy per daily fractions in CRT group, And 14 Gy of additional dose was given to the small volume of primary tumor in 7 daily fractions (BED^{10}=72Gy, BED^3=100Gy). In CBRT group, while the large volume was taking 45 Gy with 1.8 Gy/fraction, a boost dose of 0.7 Gy was added to the small volume at the same sessions up to 17.5 Gy total dose (BED^{10}=71.8Gy, BED^3=93.5Gy). Age, KPS status and stage distribution were similar in two arms. Neoadjuvant (neoadj.) and concomitant chemotherapy (CT) were given 12/18 and 17/18 in CRT group, 6/17 and 12/17 in CBRT group, respectively. The median reduction in overall treatment time was 7 days in CBRT arm.
Results: Median follow-up time was 18 months. Performance status, neoadj. CT and weight loss were found to be the significant prognostic factors in univarian analysis while neoadj. CT and CBRT were significant in multivarian analysis. Local control and survival rates are shown in the table. Acute skin reactions were significantly higher in CRT arm while there was no difference in esophagial, hematologic and pulmonary toxicities between two groups.
Conclusions: As a result, CBRT was found to be a feasable and well tolerated schedule, but beter local control and survival rates than CRT could not achieved. However, well-designed randomised trials with larger patient numbers are necessary to try the efficacy of moderately accelerated RT shemes in locally advanced NSCLC.

Table. Results of the analysis of primary endpoints for all patients

	CRT	CBRT	
Tumor response after RT±CT	6 (%34)	4 (%24)	
Complete or parsiel response	10 (%55)	10 (%58)	
Stable disease	12(%11)	3 (%18)	
Progression			
Median survival	23 months	19 months	(p=0.3)
1-year Overall survival	%81	%73	(p=0.4)
2-year Overall survival	%45	%38	(p=0.3)
1-year Progression-free survival	%81	%69	(p=0.4)
2-year Progression-free survival	%30	%28	(p=0.3)
1-year Disease-free survival	%81	%69	(p=0.4)
1-year Metastasis-free survival	%86	%91	(p=0.7)

949 poster

CORRECTING 4TH DIMENSION IN 3-D CONFORMAL RADIATION THERAPY FOR LUNG CANCER

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Purpose/Objectif: Gross tumor volume (GTV) of lung cancer defined by CT scan represents an image of moving tumor captured at a point in active respiratory movement. However, the method for defining internal margins beyond clinical target volume (CTV to account for its expected physiologic movement and deformation during the administration of radiation has not been established. The goal of this study was to determine the internal margins with expansion margins beyond individual CTVs defined with (1) fast scan at shallow free breathing, (2) breath-hold scans at the end of tidal volume inspiration and (3) breath hold scan at the end of the tidal volume expiration.
Materials/Methods: 23 patients of histologically confirmed medically inoperable stage I, II lung cancer with good performance status & ability to perform voluntary breath holds at end tidal volume expiration and inspiration are selected for study. Patients were positioned supine with arms above the head and immobilized on vacuum cushions with a standard wingboard, A series of Spiral CTscans were acquired with (1) a fast helical scan at shallow free breath-

ing and (2) breath-hold scans at the end of tidal volume expiration and inspiration. Images of 3 datasets acquired are transferred to a commercial virtual simulation workstation - Coherence Dosimetrist. Individual GTV, CTV are contoured in all the sequences. Images of 3 datasets are fused (breath-hold scans & shallow free breathing scans) to generate the composite CTV(ITV). 8mm margin is grown beyond the ITV to give PTV and the patients are treated on Linac. The centroid of the CTV defined by the shallow free breathing fast helical scan was set as the reference, and the amount of displacement in all three orthogonal directions: right-left (x axis), SI (y axis), and AP (z axis) was measured according to the distance between the centroids of the reference and breath hold scan CTVs. The internal margin is the expansion margin beyond each CTV to approximate the s ITV. To determine the internal margin for the individual CTV of each scan defined by (a) fast helical scan at shallow free breathing, (b) breath-hold scans at the end of tidal volume inspiration and expiration, a bounding box was calculated and used to estimate the necessary margins to approximate the composite CTV (ITV) along the three orthogonal axes (x, y, and z).

Results: Substantial tumor movement was noted by either the extent of internal margins beyond each CTV or the movement of the centroid. Even for tumors in the same lobe of the lung, a wide range of internal margins and significant variation in the centroid movement in all directions (x, y, and z) was observed. The CTV of a single fast helical scan at free breathing required the largest internal margin (mean: 6 mm; maximum: 22 mm; SD: 4.2 mm) to match the composite ITV, compared with fused combined breath-hold and fast helical scans (mean 1.1 mm, maximum 26 mm, SD 3.9 mm). Internal margins required to approximate the composite CTV in 95% of cases were 23 mm and 18 mm for the CTVs of a single fast scan and breath-hold scans at the end of tidal volume inspiration and expiration, respectively

Conclusions: The internal margins required to account for the internal tumor motion in three-dimensional conformal radiotherapy are substantial. CTV defined with breath-hold scans at the end of tidal volume inspiration and expiration have a narrower range of internal margins in all directions than that of a single fast scan.

950 poster

DOSE ESCALATION BY PTV VOLUME REDUCTION IN RT OF NON-SMALL CELL LUNG CANCER PATIENTS

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Purpose/Objectif: Radical radiation treatment of lung tumours often includes large radiation fields due to the risk of internal tumour movement. This leads to restrictions on the treatment dose in order to avoid unacceptable risks of radiation induced normal tissue complications. As an alternative strategy treatment fields can be reduced in size. As a consequence, part of the tumour may be outside the treated volume some fraction of the radiation time (miss fraction, MF). However, the decrease in treatment field area allows an increase in MU per treatment for a given level of NTCP. If this increase in MU more than compensates for the MF the tumour may receive a larger dose during each fraction.

Materials/Methods: This retrospective planning/NTCP study includes 20 non-small cell lung cancer patients who have received radical RT. For each patient a reduced PTV is constructed and the actual treatment plan is modified in order to irradiate a correspondingly smaller volume. Lung DVHs for the original and the new volume-reduced plan is used to assess the risk of radiation pneumonitis. The dose in the volume-reduced plans are escalated until the estimated NTCP in the dose escalated, volume-reduced treatment plan equates the risk in the original plan. Finally, it is estimated whether the increase in dose compensates for the MF, such that an improved tumour control probability is expected.

Results: Preliminary results suggest that by reducing margins by 5 mm the dose can be increased by 15-20 % without an increase in V_{20} or MLD. Thus, if the clinical target occupies the extreme 5 mm of the PTV in less than 15 % of the time the entire tumour will receive a higher dose with this new volume-reduced planning scheme.

Conclusions

As this is work currently in progress solid conclusions cannot be made at this time. However, preliminary results indicate that improved tumour control will be possible due to three factors:

A reduction in the margins from GTV to PTV will lead to a significant reduction in treated normal lung tissue (the volume of a sphere increases with the cube of the radius).

- The tumour will only be in the extreme positions for a very short time, and thus the MF will be fairly small.
- Most of the tumour (the central part) will receive the total dose.

951 poster

EARLY RESULTS OF CONTINUOUS ACCELERATED RADIOTHERAPY (CAIR) FOR LA-NSCLC PATIENTS.

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Purpose/Objectif: To evaluate the tolerance and early results of continuous accelerated radiotherapy for LA-NSCLC patients.

Materials/Methods: Between June 2001 and January 2006, 58 patients were enrolled into the randomized clinical trial. Thirty patients were irradiated 7 days a week with 1,8Gy per fraction to the total dose of 72Gy within 40 days (CAIR arm). Twenty eight pts were conventionally treated with 1,8Gy per fraction to the total dose of 72Gy within 57 days (Control arm). Clinical and pathological prognostic factors were evaluated in both groups. Acute esophageal, lung and skin reactions according EORTC/RTOG classifications were assessed. Two years local relapse free survival (RFS), metastases free survival (MFS), disease-free (DFS) and overall survival (OS) were compared in both groups.

Results: The mean age at diagnosis was comparable in both groups - 62 y. for CAIR arm and 61 y. for control arm (p=0,7). Clinical stage, histopathological types and histological grade were not significantly different in analyzed groups.

There was no grade 3 acute reactions for critical organs. The majority of esophageal reactions graded 1 and 2 was observed in CAIR arm: 88% vs. 72% in Control arm, however the difference was not significant (p=0,2).

Eighteen percent of patients in both groups gained complete regression evaluated in CT one month after completion of radiotherapy. Only one patient (4%) irradiated continuously and five irradiated conventionally (18%) progressed. The rate of tumor regression was comparable in both groups (p=0,2). The mean time of follow-up in CAIR group was 13 months and 14 months in control arm. There was no statistical difference in analyzed survival parameters. The actuarial 12-months RFS was 47% in CAIR arm and 32% in control arm (p=0,067). Nobody in control group survived two years without local failure. Twenty four-months MFS in CAIR group and control group was 54% and 33%, respectively (p=0,96). The actuarial 24-months DFS was 19% for CAIR arm 6% for control arm (p=0,74). The actuarial 24-months OS was 14% for CAIR arm 20% for control arm (p=0,3).

Conclusions

1. Continuous accelerated radiotherapy for LA-NSCLC patients is well tolerated with low risk of acute reactions.
2. There was no difference in all survival parameters assessed.

3. The trend in better local control in patients irradiated continuously was observed, however with no improvement in the overall survival.

952 poster

EARLY TOXICITY DATA FOR DEFINITIVE DOSE-ESCALATED CHEMO-RADIOTHERAPY OF LOCALLY ADVANCED NON-SMALL CELL LUNG CANCER (LAD-NSCLC) WITHIN A PROSPECTIVE RANDOMIZED MULTICENTER TRIAL - ESPATÜ

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Purpose/Objectif: In patients (pts) with LAD-NSCLC (stages IIIA/IIIB) the curative combined chemo-radiotherapy is being optimized by risk-adapted dose-escalation within the prospective randomized ESPATü-trial.

Materials/Methods: Pts are planned for 3 cycles induction chemotherapy (CTx) (cisplatin (P) 50 mg/m^2, d1+8, and paclitaxel 175 mg/m^2 d1, qd 21) followed by concurrent (cc) chemoradiotherapy (CTx/RT) (accelerated-hyperfractionated, 45 Gy, 2x1.5 Gy/d, plus P 50 mg/m^2, d2+9 of RT, and vinorelbine (NAV) 20 mg/m^2, d 2+9). Staging mediastinoscopy is mandatory in all patients. Evaluation of operability is performed by an interdisciplinary panel after 45 Gy. Operable patients will be randomized to surgery or definitive chemo-radiotherapy boost (20-26 Gy, 2 Gy qd, cc CTx: P 40 mg/m^2, d2 of boost-RT, NAV 15 mg/m^2, d 2 + 9). Pts with persistent inoperability will also receive definitive boost irradiation as outlined. A modest dose escalation up to 71 Gy is planned according to dose volume histogram (DVH(total lung)) constraints.

Results: Between 01/2004 and 01/2006 102 pts have been enrolled, 52 pts received definitive chemo-radiotherapy (m 37, w 15, median age 59 (40-75) y, stage IIIA 8, IIIB 44 pts). 21 pts received a cumulative dose of 65 (63-67) Gy, 31 pts 71 Gy, in 2 pts treatment was terminated early due to metastatic disease. The incidence of severe leucopenia (<=grade 3) during the concurrent treatment phase was 60%, anemia 13%, thrombopenia 13%, esophagitis 25%. Clinical relevant pneumonitis (grade 2) was observed in 10 pts, 2 pts experienced a grade 3 pneumonitis. All grade 2 pts have recovered completely.

Conclusions:

This intensive treatment regime is safely feasable within the multicenter setting. The pulmonary toxicity remains within the expected range.

953 poster

EFFICACY OF INDUCTION CHEMOTHERAPY WITH DOCETAXEL PLUS CARBOPLATIN FOLLOWED BY CONCOMITANT CHEMORADIOTHERAPY IN LOCALLY-ADVANCED NON SMALL CELL LUNG CANCER

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Purpose/Objectif: Surgical resection is the optimal treatment for non-small-cell lung cancer (NSCLC) but frequently patients are ineligible because of advanced disease. We conducted a pilot trial to determine the efficacy of induction chemotherapy with docetaxel and carboplatin followed by concomitant chemotherapy (CT) and radiotherapy (RT) in increasing the number of operable patients.

Materials/Methods: A total of 23 patients (19 males and 4 females; mean age: 62 years; range: 49-74) with NSCLC, histologically confirmed, Stage IIIA (8 patients) and Stage IIIB (15 patients) were enrolled in the study. Patients received docetaxel 100 mg/sqm on day 1 plus carboplatin AUC 6 on day 2 every 21 days for 2 cycles. After induction therapy, patients received RT, with a total dose of 45 Gy, 1.8 Gy/fr., combined with a lower dose of CT with carboplatin AUC 2 and docetaxel 15 mg/sqm on the first day of each week of RT. Patients also received amifostine 500 mg s.c.

Patients underwent a CT scan of the chest and bronchoscopy before treatment and 28 days after completion of the therapy, in order to determine tumour downstaging and resectability (primary efficacy variable); RT and CT toxicity, time to progression and survival were considered secondary efficacy variables. Patients who were considered inoperable, received an additional dose of RT, limited to the residual tumour volume, to a total dose of 60-64.8 Gy and then further 4 cycles of CT (carboplatin AUC 5, docetaxel 75 mg/sqm).

Results: Of the 23 patients with initial Stage IIIA or IIIB, 13 (57%) were considered operable at the end of the treatment: 5/23 (22%) underwent a lobectomy, 2/23 (9%) a pneumonectomy and 6/23 (26%) only a thoracotomy. The remaining 10/23 (43%) patients were considered inoperable. Overall no severe haematological toxicity was recorded. Three patients had severe mucositis (Grade 3). Eight patients (35%) had a radiological complete response (CR) and among these a pathological CR was confirmed in 2 (9%); 8 (35%) had a partial response; 3 disease stabilization (DS) (13%) and 4 disease progression (17%), with an overall response (CR, PR and DS) in 83% of cases. Median survival (Kaplan Meier) was 26 months.

Conclusions: The results of this preliminary prospective study suggest that this regimen of treatment increases the number of patients who can undergo surgical resection and the median survival with an accettable toxicity.

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EXPERIMENTAL STEREOTACTIC IRRADIATION OF NORMAL RABBIT LUNGS WITH A NEW COMPUTED TOMOGRAPHY-TYPE KILOVOLTAGE X-RAY RADIOTHERAPY MACHINE

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Purpose/Objectif: We developed an experimental stereotactic radiotherapy unit that uses kilovoltage X-ray energy. The unit was pro-

duced by modification of a diagnostic computed tomography (CT) system in order to realize simultaneous irradiation and confirmation of the isocenter position with CT imaging. To evaluate the biological effect of stereotactic irradiation using this unit we irradiated lungs of normal rabbits and compared the subsequent acute and subacute radiation sequelae seen on CT images to those from a control study previously performed using megavoltage stereotactic irradiation.
Materials/Methods: Six Japanese white rabbits were anesthetized and the target isocenter was set as the center of the middle portion of the left lung for each rabbit. The rabbits were stereotactically irradiated with a modified CT machine (Aquilion, Toshiba) using three non-coplanar arcs (gantry tilt angle: 0 deg ± 25 deg). A mechanical filter was attached to the X-ray tube to modify the beam-shape. A collimated fan-shaped X-ray beam was employed. The beam energy was 120 kV. For each irradiation event, the X-ray tube was continuously rotated in one direction. The irradiation doses were <60 Gy (single fractional dose), which were calculated as approximate doses following the dose rate of previous experiments using this machine. During irradiation, doses were regulated by changing the beam-on duration and were subsequently estimated using the Monte Carlo simulation code, EGS4. In the procedure, the isodose distribution was calculated around the target of irradiation by CT data from the irradiated rabbits. All the rabbits were scanned with the same CT machine biweekly for 24 weeks after being irradiated. Image data were collected as DICOM standard files and were analyzed visually on a viewer. The CT radiographical changes observed were compared to those of control rabbit experiments previously performed using a 4 MV X-ray linear accelerator.
Results: In three rabbits irradiated with 60 Gy (approximate dose), localized attenuating changes were first observed in the irradiated area of the left lung from 10 to 16 weeks after irradiation. Changes continued to persist following the initial observation. This finding was similar to the changes seen from a single fractional dose of 60 Gy using a megavoltage X-ray linear accelerator.
Conclusions: This new kilo-voltage X-ray stereotactic irradiation unit provided a radiation effect of nearly equal intensity as the current megavoltage energy X-ray linear accelerator in normal rabbit lungs.

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FACTORS AFFECTING BRAIN METASTASES DEVELOPMENT IN STAGE III NON SMALL CELL LUNG CANCER PATIENTS TREATED WITH DEFINITIVE TREATMENT

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Purpose/Objectif: The incidence of brain metastasis (BM) and prognostic factors that are related, in definitively treated non small cell lung cancer (NSCLC) patients were investigated.
Materials/Methods: The records of 124 definitively treated NSCLC patients were reviewed. The incidence of BM and time to BM were calculated. Age (≤ 60 vs < 61), sex, disease stage (III A vs III B), histology (adeno vs non adeno) and surgery were analyzed as prognostic factors influencing BM.
Results: Median age was 60. Eighty one percent were male, 19% were female, 43% were stage IIIA, 57% were stage IIIB. Twenty five percent patients had adenocarcinoma. Sixty nine patients (55%) received primary chemoradiotherapy (concomitant or sequential), 22 (18%) patients received primary RT, 33 (27%) received surgical resection. Nineteen percent of patients developed BM and in 91% of these patients brain was the first site of distant failure. Thirty percent of patients had 1-3, 70% had < 3 BM. With a median follow up of 12 months, the median survival time was 15 months; 2 year overall survival rate was 30% for all patients. The 2 year actuarial BM development rate was 29%. In univariate analysis adeno histology (p=0.001), age ≤ 60 years old (p=0.03), non - surgical treatment (p=0.05) were found to be significant variables for the development of BM (54%, 41%, 37% for 2 years respectively). No impact of stage and sex were observed on BM development. In multivariate analysis histology (p=0.006), surgery (p=0.01) and age (p=0.05) were found to be of prognostic value for BM development.
Conclusions: Adenocarcinoma histology, ≤60 age, non surgical treatments are prognostic factors for the risk of BM development. The impact of prophylactic brain irradiation in this subgroup of patients needs to be investigated in the future prospective studies.

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FROM CONVENTIONALLY FRACTIONATED RADIATION THERAPY TO HYPERFRACTIONATED RADIATION THERAPY ALONE AND WITH CONCURRENT LOW-DOSE DAILY CARBOPLATIN/PACLITAXEL IN PATIENTS WITH EARLY STAGE (I/II) NON-SMALL CELL LUNG CANCER (NSCLC). SINGLE INSTITUTION EXPERIENC

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Purpose/Objectif: Single-institution experience in 250 patients with early stage (I/II) non-small-cell lung cancer (NSCLC) treated with either conventionally fractionated (CF) radiation therapy (RT), or hyperfractionated (Hfx) RT or the same Hfx RT with concurrent low-dose, daily paclitaxel/carboplatin (T/C) was evaluated.
Materials/Methods: 78 patients were treated with 60 Gy in 30 daily fractions (CF), 116 patients were treated with 69.6 Gy, using 1.2 Gy b.i.d. fractionation (Hfx RT) while 56 patients underwent Hfx RT (67.6 Gy using 1.3 Gy b.i.d. fractionation) with concurrent low-dose daily C, 25 mg/sqm and T, 10 mg/sqm, both given Mondays to Fridays during the RT course, preceded by 30 mg/sqm of T on day 1. In all patients, RT was administered with 6-10 MV photons using linear accelerators. The typical target volume included the primary tumor and ipsilateral hilum with a 2-cm margin (Stage I), while in cases of Stage II patients, it also included ipsilateral mediastnum from the suprasternal notch to a level 6 cm below the carina (upper and middle lobe lesions), or to the diaphragm (lower lobe lesions).
Results: The median survival time (MST) for all 250 patients was 27 months and 5 year survival rate was 27%, respectively. When cause specific survival (CSS) was used as an endpoint, the median time was 27 months, while 5-year CSS rate was 32%. The median time to local progression was 32 months while 5-year local progression-free survival rate was 45%. The median time to distant metastasis was not achieved while 5-year distant metastasis-free survival rate was 68%. Survival in patients treated with CF alone were significantly inferior to that obtained with either Hfx RT alone or with Hfx RT/TC (p=0.0332 and p=0.0013), with no difference between the two HFX RT regimens (p=0.1934) (overall, p=0.0064) MST for the three treatment groups was 20 vs 29 vs 35 months, respectively with 5-year survival being 17% vs 29% vs 36%, respectively. The same was observed using cause-specific survival and local progression free survival as endpoints, but the distant metastasis-free survival was not different between the three groups. Only acute hematological high-grade (<3) toxicity was more frequent with Hfx RT/TC than with RT alone, other toxicities being similar between the three treatment groups.
Conclusions: CF was significantly inferior to either Hfx alone or Hfx/TC, but the latter one carried higher incidence of acute high-grade hematological toxicity.

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HOW DOES THE MULTIDISCIPLINARY TEAM MEETING (MDM) AFFECT DECISION-MAKING IN LUNG CANCER?

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Purpose/Objectif: To study how an established weekly lung cancer MDM affects decisions about oncological therapy.
Materials/Methods: All non-surgical patients presented at the lung cancer MDM over 4 months were studied at 3 time points. The presenting physician recommended treatment prior to the MDM (T1). An observer recorded the MDM discussion and recommended outcome (T2). These were compared with the actual decision later taken by the patient in consultation with the doctor (T3).
Results: 55 patients were presented. The MDM discussion lasted a median of 282 seconds (range 100 - 462 seconds). A mean of 5 professionals contributed to each discussion (range 3-8). At T1, 21% of recommendations were for curative treatment and 79% palliative. The MDM discussion changed the treatment intent in 13%. The final treatment intent differed from the MDM recommendation in 8%. The exact treatment given (eg chemotherapy, radiotherapy, combination etc.) was predicted by only 34% of presenting physicians and by 57% of MDT discussions. The commonest reasons for differences between T2 and T3 were that the patient's general condition had deteriorated so they were not well enough for treatment or that the symptoms that needed palliating at T3 were different from those at T2.
Conclusions: The treatment accepted by the patient is often different from that recommended by the MDM or referring physician. While the MDM may have educational, team-building and organisational benefits, its role in influencing and improving decision-making merits further research.

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HYPOFRACTIONATION RADIATION THERAPY OF INOPERABLE STAGE I/II NON-SMALL CELL LUNG CANCER: A DIFFERENT APPROACH.

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Purpose/Objectif: An RTOG protocol is running to investigate the benefits of hypofractionation irradiation for lung cancer. In this protocol, no IMRT approaches are allowed and no tissue heterogeneity is taken into account. This protocol has been compared to an approach with heterogeneity corrections using IMRT.
Materials/Methods: Following the RTOG-0236 protocol, ten non-opposing and non-coplanar beams were used with approximately equal weighting. No additional margin for dose build up at the edges of the MLC beyond the PTV were used and also no corrections were made for tissue heterogeneity. The plan was normalized such that 60 Gy (100%) corresponds with the iso-centre (centre of the PTV). 95% of the PTV should get at least 100% of the prescribed dose and 99% of the PTV should receive a minimum of 90% of the prescribed dose. Besides other limitations, the ratio of the volume of the 50% iso-dose to the volume of the PTV was restricted. To evaluate the effect of tissue heterogeneity, the dose has been recalculated taking tissue heterogeneity into account. In this recalculation, the beam set-up and monitor units were taken from the calculation without heterogeneity corrections.
The treatment plans were compared with the results from a technique developed at the NKI-AvL. This technique used 10-19 static beam directions also non-opposing and non-coplaner. The DMPO algorithm of the Pinnacle system version 7.4f was used to create optimal segments and beam weights. In the optimization, the number of segments was equal to the number of beams, which resulted in one segment per beam direction. All calculations were performed including heterogeneity corrections.
Results: The volume of the PTV receiving a dose of 60 Gy calculated according the RTOG protocol was 96%. Using the RTOG protocol with tissue inhomogeneity this percentage dropped to approx. 80%. Using inhomogeneity corrections with IMRT, this percentage returned to 95%. Looking at 54 Gy, the volumes were 100%, approx. 92% and 100%, respectively. For the RTOG approach with heterogeneity corrections, 95% of the PTV was covered by 51-54 Gy instead of the prescribed 60 Gy. The volume of the 50% isodose is restricted to a maximum percentage of the PTV, which itself is dependent on the size of the PTV. For a typical case, the maximum ratio was 3.7. However, the ratios obtained were 4.4, 4.7 and 5.2, for the RTOG protocol without inhomogeneity corrections, the RTOG protocol with inhomogeneity corrections and the IMRT approach, respectively.
Conclusions: By recalculating the RTOG dose based on the inhomogeneous tissue, this approach was found to result in an under dose of parts of the PTV. The IMRT approach for hypofractionation of the treatment is able to correct this under dose. Neither one of the three approaches was able to comply with the maximum ratio of the 50% isodose volume. The IMRT technique has been introduced at the AvL/NKI. Based on this work, the prescribed dose had to be reduced to 54 Gy.

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IMPACT OF INDUCTION CHEMOTHERAPY PRIOR TO CHEMORADIOTHERAPY ON SURVIVAL IN PATIENTS WITH LOCALLY ADVANCED NON-SMALL CELL LUNG CANCER (NSCLC)

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Purpose/Objectif
The aim of this study is to investigate influence of induction chemotherapy with docetaxel-cisplatin administered three-weekly on the outcomes of patients treated with concomitant chemoradiotherapy with weekly docetaxel-cisplatin.
Materials/Methods
Totally 90 patients who administered to Radiation Oncology Clinic of Dr. Lutfi Kirdar Kartal Education and Research Hospital with the diagnosis of stage IIIA or IIIB medically or surgically inoperable NSCLC between dates February 2003 and December 2005 were enrolled into the study. Patients with supraclavicular lympadenopathy or pleural effusion were excluded in the study. Of the 90 patients, 50 received 3 cycles of chemotherapy consisting of docetaxel (75 mg/m^2/3 weeks) and cisplatin (75 mg/m^2/3 weeks) before chemoradiotherapy (Group 1) while 40 were treated with chemoradiotherapy alone (Group 2). Total 6600 cGy radiotherapy was administered to both groups in 33 fractions with concomitant docetaxel (30 mg/m^2/7 days). and cisplatin (20 mg/m^2/7 days). Primary endpoint was overall survival (OS). Other endpoints were time to progression (TTP), response rates and toxicity.
Results
Median age in the study was 60 years (37-80 years). Eighty eight patients (97%) were male and 2 Patients were female. Performance status of 82 patients was ECOG 0-1, 8 patients ECOG 2. Eighty four percent of patients had history of tobacco use (smokers and ex-smokers). Forty one patients (45,56%) complained of hemoptysis, 44 (48,89%) dyspnea, 66 (73,33%) cough, 16 (17,78%) disphony, 35 (38,89%) loss of appetite, and 39 (43,33%) weight loss. Histological type was squamous cell carcinoma in 62 patients (68,88%), adenocarcinoma in 8 patients (8,89%) and undifferentiated histologies in 20 patients (22,22%). TNM stages were stage IIIA in 10 cases (11,1%) and IIIB in 80 cases (88,9%). In general, there were no significant differences between two groups in terms of age, sex, performance status, presenting symptom, stage, or histopathologic subtype. Patient characteristics are summarised in Table 1. Median follow-up time was 13,6 months (1-40 months). Median survival was 26,56 months in

the group that received induction chemotherapy, and 21,30 months in the group treated with concomitant chemoradiotherapy alone. In the analysis, there was no statistically significant overall survival benefit of adding induction chemotherapy (p=0.1351) (figure 1). One-year and 2 year survivals were better in the group 1 (79%, 55%) than group 2 (65%, 40%). There was also no significant difference between groups in terms of TTP (p=0.818). Response evaluation done after chemoradiotherapy revealed an overall response rate of 71,3% (CR 13,5% and PR 57,8%); and 19 patients (21,1%) showed stationary disease, and only 1 patient (1,1%)progression. Overall toxicity was generally acceptable, and there was no statistically significant difference between groups. Toxicities most frequently encountered in the study are listed in Table 2.

Conclusions

Addition of induction chemotherapy with docetaxel plus cisplatin to concurrent chemoradiotherapy did not show any advantage over concurrent chemoradiotherapy alone in locally advanced NSCLC.

Table 1. Patient Characteristics

Characteristics	Group 1 (n)	Group 2 (n)	Total n (%)
Sex			
Female	1	1	2 (2.2)
Male	49	39	88 (97.8)
Age	60 (42 - 80)	60 (38 -75)	60 (37 - 80)
Stage			
IIIA	5	5	10
IIIB	45	35	80
Performance status			
ECOG 0-1	48	34	82
ECOG 2	2	6	8
Histological type			
Squamous cell carcinoma	33	29	62
Adenocarcinoma	5	3	8
Undifferentiated	12	8	20
Smoking habit	47	37	84
Presenting symptoms			
Dysphony	8	8	16
Hemoptysis	20	21	41
Dyspnea	24	20	44
Cough	35	31	66
Loss of appetite	22	13	35
Weight loss	21	18	39

Figure 1. Overall survival

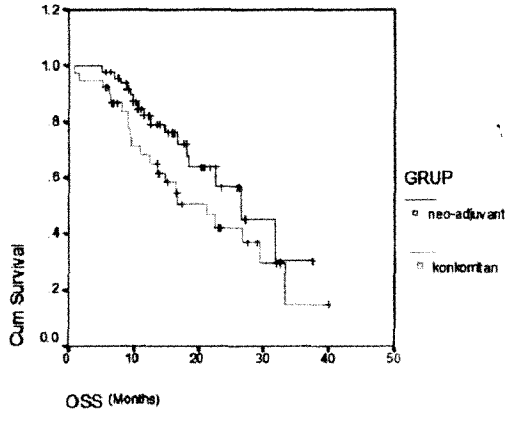

Table 2. Toxicities

Type of Toxicity	Group 1 (%)	Group 2 (%)
Esophagitis		
No	16	10
Grade 1	12	15
Grade 2	34	30
Grade 3	32	45
Grade 4	6	0
Nausea/vomiting		
No	56	62
Grade 1	30	20
Grade 2	12	18
Grade 3	2	0
Grade 4	0	0
Radiation pneumonia		
No	62	65
Radiologic	20	12.5
Symptomatic without treatment	0	2.5
Symptomatic with treatment	18	20
Leucopenia		
No	66	72.5
4000-3000	16	18.5
3000-2000	14	5
2000-1000	4	5
Dyspnea	8	10
Ototoxicity	6	0
Allergy	0	2

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INCORPORATION OF TUMOUR MOBILITY WITH SLOW CT SCAN IN THE 3-D CONFORMAL RADIOTHERAPY TREATMENT (3-D CRT) PLANNING FOR INOPERABLE STAGE I NON-SMALL CELL LUNG CANCER - A RETROSPECTIVE ANALYSIS OF THE CLINICAL OUTCOME.

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Purpose/Objectif: The low local tumour control (40-70%) and poor 5-year overall survival rate (5-30%) observed after 3-D CRT for stage I non-small cell lung cancer (NSCLC) can be partially attributed to the geographical mismatch due to lung tumour motion. The most accessible method to incorporate tumor mobility into the treatment planning is the definition of a mobile gross tumor volume (GTV_{mobile}) with a slow CT scan (4 s per slice). We investigated the clinical results (local control, overall survival and disease-free survival) of this technique.

Materials/Methods: The case records of 41 consecutive patients who were treated for stage I NSCLC between 2000 and 2005 with 3-D CRT using a GTV_{mobile} in the treatment planning were analysed. Fourteen patients were treated with 70 Gy (2.5 Gy/fraction), 27 patients with 60 Gy (3 Gy/fraction).

The GTV_{mobile} was defined by expanding the GTV_{slow} (GTV defined on the slow CT) with 5 mm to take the extra motion into account that might not have been captured on the slow CT. The planning target volume equalled the GTV_{mobile} after addition of 5 mm for the microscopic extension and 5 mm setup margin with the application of an offline setup protocol. No elective irradiation was performed.

Twelve patients had a histologically confirmed NSCLC. From the patients without histological confirmation, 24 patients and 5 patients were accepted for radiotherapy based on a positive FDG-PET scan and a new or growing lesion on CT scan, respectively.

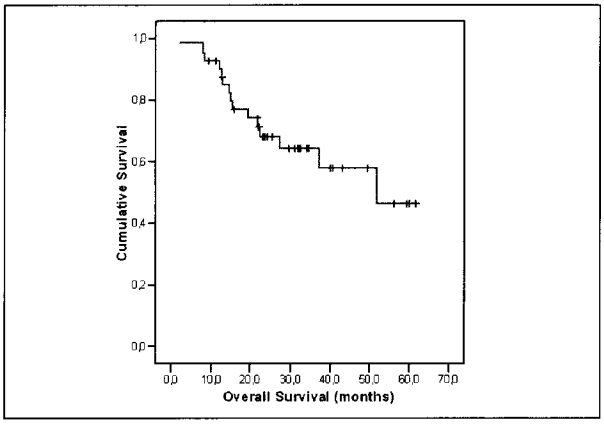
The reason for not proceeding to surgery was the existing comorbidity for all patients, excepting one patient who refused surgery. The Charlson comorbidty score of the patients was: 0=2 patients, 1-2=21 patients, 3-4=15 patients, >4=3 patients. Median age of the treated population was 75 years (range 55.9-87.2 years).

Thirty patients had a T1N0M0 tumour and 11 patients had a T2N0M0 tumour. Response evaluation was usually performed by means of chest X-rays and classified according to criteria proposed by Green et al.

Results: With a median follow-up period of 23.6 months (range 2.1-61.6 months), the estimated 5-year overall survival, 5-year disease

free surival and 5-year local control was 46%, 68% and 84%, respectively. Grade 1 and 2 acute radiation pneumonitis (SWOG) was observed in 8 and 2 patients, respectively.

Conclusions: The incorporation of tumor motion with slow CT in the 3-D CRT treatment planning leads to better 5-year overall survival rate and local control compared to conventional 3-D CRT.



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INDUCTION CHEMOTHERAPY WITH VINORELBINE AND A PLATINUM COMPOUND FOLLOWED BY CONCURRENT CHEMORADIOTHERAPY AND CONSOLIDATION CHEMOTHERAPY WITH THE SAME DRUGS FOR STAGE III NON-SMALL-CELL LUNG CANCER (NSCLC) - A PHASE II STUDY

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Purpose/Objectif: A prospective phase II study was conducted to determine the response rate (RR), toxicity, time to progression (TTP) and survival (S) of induction Chemotherapy (ChT) with Vinorelbine (Vrb) and Cisplatin(Cis) or Carboplatin (Carbo) followed by concurrent chemoradiotherapy (ChRT) and consolidation ChT with the same drugs, for stage III NSCLC.

Materials/Methods: 32 eligible patients (pts) were included from 05.02.2004 to10.02.2006. Pts characteristics were: median age 57(39-73), M/F=31/1, PS 1/2=20/12, stage IIIA/IIIB=2/30, squamous cell cc 26, large cell cc 3, adenocc 3. Treatment consisted of 2 cycles of induction ChT with Vrb (25 mg/sqm, d1, 8, q21) and Cis (100 mg/sqm, d1, q21), or Carbo (AUC 5, d1, q21), followed by 2 more cycles given concurrently with radiotherapy (RT) and 2 cycles of consolidation ChT with the same drugs. When given concurrently with RT the doses have been reduced: Vrb 15 mg/sqm, d1, 8, q21, Cis 80 mg/sqm, d1, q21 or Carbo AUC 2.5, d1, q21. RT has been administrated at the liniar accelerator (15MV) with 2Gy/fraction to a total dose of 60-68 Gy, the last 8 patients benefited of conformal-3D technique. At least 4 cycles of ChT have been completed by 81% of pts , 68% completed 5 or 6 cycles of ChT. The optimal doses of RT have been received by 75% of pts.

Results

32 pts were evaluable for toxicity. Severe grade 3 or 4 neutropenia occured in 4 pts (12%), anemia in 3 (9%). There was a grade 3 trombocitopenia in 1 patient. (3%) and grade 3 neuropatia occured also in 1 patient (3%). After induction ChT were obtained 3(9%) complete responses (CR), 17(53%) partial responses (PR), 10(31%) pts had stable disease (SD) and 2(6%) progressive disease (PD). Of the 30 pts evaluable for response after ChRT, 9 (30%) achieved a CR,10 (33%) achieved a PR for an overall RR of 63% (CI:46-81), 7 pts (23%) had SD, and 4pts (13%) had PD of 13%. TTP at 1 year was 35% (CI:18-56%) with a median value of 9 months (CI:6.9-17.9). The disease specific S at 1 year was 49% (CI:28%-70%) and the median S was 10 months (CI:8.1-19.9). For the 20 patients still alive the median follow-up was 6 months. All evaluations were done considering α=0.05.

Conclusions

Preliminary analyses indicate that induction ChT followed by concurrent ChRT with Vrb and Cis or Carbo, followed by consolidation ChT with the same drugs given for advanced stage III NSCLC is feasible, well tolerated and has a positive effect on the RR and S.

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IS THERE A SELECTION BIAS IN RADIATION DOSE ESCALATION PROTOCOLS?

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Purpose/Objectif: Eligibility criteria in dose escalation trials regularly include dose limitations to normal tissue. In general for EORTC and RTOG dose escalation trials, normal tissue constraints remain constant while the tumor dose increases for each dose step. As tumor dose and normal tissue constraints are competing demands, a point will be reached where tumor dose cannot be increased without exceeding normal tissue constraints. This might lead to a selection bias, which results in an inadequate determination of maximum tolerated doses (MTD) and the generalization of treatment results that are applicable only to a subgroup of the patient population.

Materials/Methods: In nine patients with NSCLC and a wide variation in tumor volumes, respiratory gated IMRT planning was performed during expiration. The tumor dose was escalated from 66 Gy to 78 Gy in 4 Gy-dose steps while the limiting normal tissue doses remained the same for all dose steps. We differentiated between patients whose IMRT plans met the given eligibility criteria for all dose steps and those patients eligible only for lower doses. For both groups dosimetric values, radiobiological (TCP and NTCP) values, and other planning parameters were compared.

Results: Seven of nine patients were eligible for all dose steps (group A). Two of nine patients (group B) qualified only for lower total doses (95% binomial CI 0.075, 0.6, sign.). In group A mean planning tumor volumes were smaller (132 versus 404 cc, n.s.), mean monitor units per fraction significantly lower (448 versus 802, p=0.0008), and the average composite score for plan quality better than in group B (0.012 versus 0.068, n.s.). Average TCP values were higher for group A (0.33 versus 0.23, n.s.). NTCP values for normal tissue were lower for group A than B (lungs p=0.028, esophagus p=0.68).

Conclusions: In this study, patients eligible for higher dose steps had significantly superior estimated outcome parameters and smaller tumor volumes. To eliminate the selection bias, either (1) dose limitations for normal tissue should be adjusted to the increasing dose levels, or (2) to be eligible normal tissue tolerances should be met at the highest dose level planned for the trial irrespective of the dose level planned for each patient.

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MODELS COMBINING CLINICAL DATA WITH MEDICAL KNOWLEDGE ARE MORE ACCURATE THAN DOCTORS IN PREDICTING NSCLC AFTER (CHEMO-)RADIOTHERAPY

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Purpose/Objectif: The steady increase in the types of treatment for lung cancer requires advanced treatment decision-making, accounting for patient and treatment characteristics. However, physicians often fail to consistently and accurately predict outcomes, which can subsequently lead to suboptimal treatment choices. The purpose of this study was to investigate whether new methods to build multivariate models would improve prediction of survival of NSCLC patients at the time-point of 2 years (S2y) and compare them with predictions from radiation-oncologists.
Materials/Methods: First, all the relevant variables with consistent results and hazard ratios for survival were identified in a literature review. Based on these, a knowledge-based (KB) model was constructed. Second, a set of 195 NSCLC patients, stage I to IIIB, was split into a training set (n=134) and a validation set (n=61). Two different data-driven (DD) models, based on linear discriminant analysis (LDA) and the relevance vector machine (RVM), respectively, were learned from the training data. Third, the KB and DD models were combined by a learned ensemble method to further improve prediction accuracy. The fourth methodology used multivariate logistic regression to predict S2y. The performance of the models was assessed on the validation set. To study robustness of these models, 65 patients from a second insitution were also evaluated. Next, predictions from 4 physicians and 4 residents, using only variables available to the computer models, were collected on 30 randomly chosen patients. Prediction accuracy was expressed in terms of Area Under the receiver operating characteristic Curve (AUC). Its maximum value is 1.0, indicating perfect predictions; a value of 0.5 indicates that patients are correctly classified in 50% of the cases, i.e. as good as chance.
Results: The KB model for S2y consisted of stage, gender, WHO-ps, histology and overall treatment time. The cross-validated AUCs of the KB model and the two DD models were 0.61, 0.69 and 0.65 on the training data, respectively; the predictions in the validation set resulted in AUCs of 0.66, 0.66 and 0.64, respectively. Combining the KB model (with weight 0.7, learned from training data) with the two DD models (with weights 0.2 and 0.1, respectively), yielded an improved AUC of 0.71 on the training data, and 0.69 on the validation set. For comparison, logistic regression resulted in an AUC of 0.63 on the validation set. When applied to the second institution, similar results were observed. Physicians and residents achieved an average AUC of 0.57 (range: 0.49 to 0.67), with a standard deviation of 0.06, indicating quite a low consistency.
Conclusions: All four models were able to predict S2y more accurately than the radiation-oncologists. Prediction accuracy was consistent across patients from two different institutions. Finally, the combination of the knowledge-based model with the data-driven approaches led to the best performing model.

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PATTERNS OF CARE FOR LUNG CANCER IN RADIATION ONCOLOGY DEPARTMENTS OF TURKEY

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Purpose/Objectif: To determine patterns of care for lung cancer in radiation oncology centers of Turkey.
Materials/Methods: A questionnaire with 10 questions was prepared for evaluating approach of centers in diagnosis and treatment of lung cancer (LC) according to different disease stages. It was mailed to 24 radiotherapy (RT) centers (university, state hospital, private center) that could be reached. The forms of 21/24 (87,5%) centers which sent back their answers were evaluated.
Results: The distribution of the institutions was 15 universities (71,5%), 4 state hospitals (19%), and 2 private centers (9,5%). The most frequent histology was NSCLC. The stage distribution with respect to the number of patients treated last year was I-II 10%, III 48%, IV 42%. Limited and extensive stages were balanced in SCLC (49%; 51%). Complete blood count, routine biochemistry, chest X-ray, bronchoscopy, and thorax CT were the minimum routine staging procedures. For diagnosis and staging, while sputum cytology (SC) (48%), transthoracic fine needle aspiration biopsy (TTFNABx) (62%), and mediastinoscopy (29%) were routine tests in NSCLC, SC (52%), TTFNABx (62%), and mediastinoscopy (19%) were routine in SCLC. Further routinely used diagnostic tests for NSCLC and SCLC were respectively: upper abdominal CT 86%/90%; upper abdominal ultrasonography 33%/43%; thoracic MRI 4%/4%; bone scintigraphy 44%/76%; brain CT 38%/71%; brain MRI 14%/43%; PET 4%/4%. The most common postop RT indications were close or positive surgical margins (95%) and presence of pN2 disease (%91). While 24% of centers did not explain their indications for postop chemotherapy (CHT), the first 2 indications of postop CHT were < stage IB disease (19%) and presence of pN2 disease (19%) among the answering centers. In stage IIIA potentially resectable disease NSCLC, the most frequent treatment approach was found as neoadjuvant concomi-

tant chemoradiotherapy (CCHRT) (57%). In stage IIIA unresectable and stage IIIB disease, the most frequent approach was definitive CCHRT (91%). In limited SCLC, the most common treatment approach was as follows: CCHRT with cisplatin+etoposide (EP) in the 1st-3rd cycles (71%), completion of CHT to 4-6 cycles after CCHRT, and finally prophylactic cranial irradiation in patients with complete response. Six cycles of EP CHT and palliative thoracic RT was the most commonly (81%) used treatment in extensive SCLC. Sixty-two percent of centers did not have the facility of endobronchial brachytherapy (EBB). It was observed that high dose rate EBB (Ir192 HDR) was preferred and 2/3 of centers used EBB alone.
Conclusions: For LC, there is an extensive variation with regard to diagnostic tests, treatment strategies, indications of postop RT and CHT, RT features, and facility of EBB in . In order to establish standards, national RT guidelines should be prepared using a multidisciplinary approach.

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PET-CT SCAN INTEGRATION AND CO-REGISTRATION FOR USE IN RADIATION TREATMENT PLANNING OF NON-SMALL CELL LUNG CANCER

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Purpose/Objectif: To prospectively integrate, co-register and utilize PET-CT scan images in radiation therapy treatment planning for patients with Non-Small Cell Lung Cancer.
Materials/Methods: Integrating PET-CT scanning, using PET-CT scan images, in the process of clinical radiation planning was undertaken to design a treatment planning process that incorporates PET-CT as an integral part of complete radiation therapy.
A procedure for patients to undergo a PET-CT scan and a CT simulation scan (CTSim) in the same treatment position was developed. To allow accurate image co-registration, 6 fiducial markers were positioned and secured with tape to ensure they do not move between the two scans. After the PET/CT scan, the patient immediately undergoes the CTSim.
Mutual co-registration of the scans using fiducial marker mapping was accomplished. Fiducials were first transferred from the CT volume from PET/CT to the PET volume, where the two image sets are naturally co-registered, being reconstructed in the same frame of reference. Then, the PET volume was co-registered with the CTSim volume using the same fiducials.
Results: Tumor volumes are contoured on both scan image sets and two radiation treatment plans are designed. Volumes were defined on the CTSim scans in the usual way. We have developed a procedure for the PET based gross tumor volumes (GTV_PET) outlining. Overlaid PET images have been used as the guide-for-the-eye, while the actual GTV_PET contours have been assigned to the CTSim volume. Despite relatively poor inherent spatial resolution of the PET images, software in use (Soma Vision) produces a Gaussian-smoothed PET intensity maps that allow for easier and more accurate target delineation. In this way, the GTV_PET volume is outlined on a more precise spatial map (<1 millimeter) corresponding to the spatial resolution of the 3D CT volume.
Information from the two image sets is compared to determine dose-volume histogram (DVH) parameters and Monte Carlo dosimetry: radiation dose to the tumor, dose to normal tissues (healthy lung, spinal cord, heart and esophagus), and high/low dose regions.
Conclusions: Integrating PET CT scans into radiation treatment planning and using Monte Carlo dosimetry may allow improved lung cancer treatment with improved target definitions, reduced treatment related toxicity, and determination of high and low dose radiation regions.

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POST-OPERATIVE RADIOTHERAPY (PORT) IN NON SMALL CELL LUNG CANCER (NSCLC); TREATMENT OUTCOME AND PROGNOSTIC FACTORS IN 70 PATIENTS (PTS)

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Background: Results of PORT were analyzed 70 pts with NSCLC treated in our department from 1990-1999.
Materials/Methods: Included are 70 pts with early stage NSCLC treated with resection and PORT. Patient characteristics: Sex distribution: male: 60 pts (86%), female 10 pts (14%), mean age: 62 years (range 33-80), ECOG Performance Score (before RT): 0: 3 pts, 1: 9 pts, 2: 43 pts; 3: 11 pts; unknown 10 pts.Pathology: adenocarcinoma: 29 pts, squamous cell carcinoma: 27 pts, large cell undifferentiated carcinoma (LCU): 14 pts. pTNM stage I: 3 pts, IIA: 4 pts, IIB: 23 pts; IIIA: 24 pts, IIIB: 16 pts, pN0: 21 pts, pN1: 33 pts, pN2: 16 pts.Treatment characteristics: surgical resection consisted of a wedge rsection or segmentectomy in 4 pts, a lobectomy in 26 pts, a bilobectomy in 2 pts and of a pneumonectomy in 38 pts; R0, R1 or R2 resection were performed in 40, 21 and 9 pts respectively.The Planning Target Volume 1 (PTV 1) encompassed the bronchial stump, homolateral hilum, the mediastinum and homolateral supraclavicular area. The PTV 2 encompassed the bronchial stump and, if applicable, the localisation of positive nodes. The dose to the PTV1 was 50 Gy in 2 pts, 40-49 Gy in 61 pts and <40 Gy in 6 pts. In 8 pts no PTV2 was irradiated. The total dose to PTV 1 and 2 was <42 Gy in 6 pts, 50-59 Gy in 39 pts and 60-66 Gy in 25 pts.
Results: The 5 yr actuarial overall survival (OS), disease-free survival (DFS), local disease-free survival (LDFS) and distant disease-free survival (DDFS) was 27%, 40%, 80% and 40% respectively.Poor prognostic features for OS were: age < 60 yrs (p=0.03), pathology of LCU (p=0.03), total dose < 42 Gy (p=0.01); for DFS age < 60 yrs (p=0.02), total dose <42 Gy (p=0.003); for LDFS R2 resection (p=0.05).The 5 yr actuarial risk for dying of complications from RT was 9%, for dying of intercurrent disease 5%. Pts with an interval < 10 weeks between surgery and RT had a significantly higher 5-yr actuarial risk for dying of complications or intercurrent disease of 48% vs 94% if RT was started within 10 wks post-operatively (p=0.02). The 5 yr actuarial complication-free survival was 76%. No complications were seen in 50 pts, grade 1 or 2 in 6 pts, grade 3 or 4 in 5 pts (lung 3x, oes 1x, heart 1x). In 5 pts complications of RT might have contributed to death. In 9 pts no sufficient data were present to assess complications.
Conclusions: For patients with R0-1 resections no dose-effect relation of PORT < 50 Gy could be shown. As in 9% of the patients radiotherapy might have contributed to death, doses higher than 50 Gy are not justified. PORT should only be considered for patients fit enough to start PORT within 10 wks post-operatively.

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PRE AND POST-TREATMENT PET/CT TO EVALUATE THE RESPONSE OF NON-SMALL CELL LUNG CANCER (NSCLC) TREATED WITH CURATIVE RADIOTHERAPY ALONE (RT).

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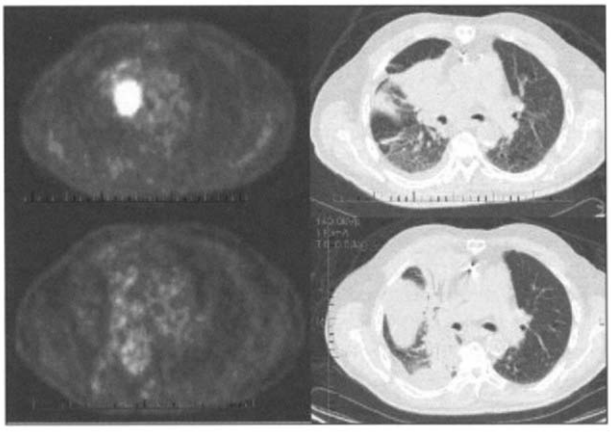
Purpose/Objectif: Radiation pneumonitis, atelectasis or inactive tumors all can mimic local recurrence making it difficult to assess the efficacy of the radiation treatment in the local control of NSCLC patients. FDG-PET/CT is a functional imaging method that seems to be an attractive alternative for early assessment in this group of patients. We report our preliminary experience with this modality.

Materials/Methods: PET/CT is now part of the routine work-up of NSCLC patients at our institution. Early stage, medically inoperable NSCLC patients are treated with 3-D planning hypofractionated RT, dose of 52.5Gy/15 fractions, without chemotherapy. Fifteen patients had a PET/CT performed before and after the treatment and are the subject of this analysis. All these 15 patients had no increased lung symptoms when the 2nd PET-scan was requested. Follow-up was every 3 - 4 months and always included a chest x-ray (CXR). CXR and the chest-CT at the time of the 2nd PET/CT were scored as "normal" when they showed expected lung fibrosis unchanged when compared to the previous imaging studies, or "abnormal" when there was an increase in the radiographic abnormalities. Post-treatment PET metabolic responses were scored as "negative" when there was a complete or almost complete response, or "positive" if there was partial, increased, and/or new hypermetabolic disease when compared to the pre-treatment PET/CT.

Results: Median age=76 years. Stages: T1=5, T2=8, T3=1 and T4=1 patient. Median PTV = 142 cc. Median follow-up was 12 months. Median time between RT and the 2nd PET was 7.8 months. All patients were alive when this analysis was performed. CXR was considered "abnormal" in 3 and "normal" in 12 out of the 15 cases. The 3 cases with "abnormal" CXR also had "abnormal" chest-CT but all 3 had "negative" PET (Figure). From the 12 cases with "normal" CXR, 7 had "negative" PET and 5 had "positive" PET. Biopsies were not done to confirm progressive disease.

Conclusions: All 3/15 cases with "abnormal" CXR and CT scan had "negative" PET. Five out the 12 cases with "normal" CXR had positive PET. The significance of these findings is unclear. If positive PET does reflect active cancer, there may be a role for PET/CT in the early assessment of local control in NSCLC patients treated with RT, but longer follow up and further evaluation is necessary to confirm the PET findings.

Figure: T3N0 right lung tumor. Pre (above) and post (below) treatment PET and CT (6 months after RT)



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RADIATION THERAPY FOR NON SMALL CELL LUNG CANCER (NSCLC) IN BELGIUM : A SIXTEEN CENTRES OVERVIEW.

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Purpose/Objectif: Lung cancer is a frequent disease, 5000 new cases being diagnosed each year in Belgium. It is the first cause of mortality due to cancer in men, and the third in women. Large variations remain regarding its treatment. The present study evaluates the management of a specific NSCLC case by radiation oncologists (RO).

Materials/Methods: A clinical case was sent to 16 radiotherapy centres nationwide. It consisted of a PET-positive 4-centimetre upper lobe squamous-cell carcinoma, namely a stage Ib (T2N0M0). RO were asked for a treatment schedule, the patient being deemed medically inoperable.

Results: Radiation therapy is prescribed by all RO with curative intent. Only 25% of them add chemotherapy, with variable schedules. Neo-adjuvant, concomitant and adjuvant chemotherapy are prescribed by 2,3 and 1 physician respectively. All use a 3D conformal radiotherapy technique, the average number of beams being 3.4 (range 2 to 5). None uses gating or assisted breathing control techniques for this apex tumor. The target volume consists of the tumor alone for 15 RO, whereas elective node irradiation is performed by 1 RO only. Tumor volume delineation is based on CT-scan alone in 31.3% of centres and on CT and PET images co-registration in 68.7%. Mean GTV is 25.7 cc (range 20.0 to 47.1 cc). Mean expansion margins applied to the GTV to obtain a CTV are 5.6 mm in the anterior-posterior (AP) and medial-lateral (ML) axis and 5.9 mm in the cranial-caudal (CC) axis (range 0 to 15 mm). The resulting mean CTV is 57.1 cc (range 43.6 to 96.5 cc). Mean expansion margins applied to the CTV to obtain a PTV are 8.8 mm in the AP axis, 8.5 mm in the ML axis, and 10.3 mm in the CC axis (range 5 to 15 mm). The resulting mean PTV is 167.0 cc (range 98.4 to 324.3 cc). Regarding the prescription dose, 81.3% of RO prescribe 1.8 to 2.5 Gy fractions up to an EQD_{2Gy} of 60 to 70 Gy. One RO performs dose escalation (80.1 Gy in 2.67 Gy fractions) and two perform hypo-fractionation (60 Gy in 7.5 Gy fractions).

Regarding organs-at-risk, the maximal tolerated dose to the spinal cord ranges 42 to 50 Gy. The spinal volume-at-risk ranges 12 to 298 cc, 25% of RO applying a 3 to 5 millimetre PRV (planning risk volume). Lung toxicity is most often parametered by the V_{20}. When applied to both lungs together (by 56.3% of RO), V_{20} ranges 25 to 37%. When applied to the lungs separately (by 43.7% of RO), V_{20} ranges 22 to 50% for the treated lung and 0 to 37% for the contralateral lung. Mean lung dose is used in 18.8% of the centres (3/16) only.

Conclusions: Large inter-observer variations exist in delineated volumes. No consensus exists regarding the margins to be applied for CTV and PTV expansions. Elective node irradiation is out of fashion in stage Ib lung cancer.

Even in the absence of nearby critical structure, most RO prescribe conventional radiotherapy fractionation up to less than 70 Gy doses.

There are large variations in dose constraints to organs-at-risk, especially regarding lung V_{20}.

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RADIOTHERAPY TREATMENT MARGINS FOR NON-SMALL CELL LUNG CANCER (NSCLC): CONTROLLING TUMOUR MOTION WITH ACTIVE BREATHING CONTROL (ABC) CANNOT BE CONSIDERED IN ISOLATION

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Purpose/Objectif: Conventional assessment of ABC has been on its ability to control tumour motion and the effect this has on the internal margin (IM) within the planning target volume (PTV). During radical fractionated radiotherapy (RT) patient movement with ABC needs to be taken into account. We determined the IM and set-up error with ABC and the combined effect on the PTV and physical lung parameters compared to standard margins used with free-breathing.

Materials/Methods: 10 patients with NSCLC undergoing radical RT had 3 CT scans in the treatment position with an ABC device in deep inspiration breath-hold (William Beaumont Hospital, USA) prior to and in the middle and final week of treatment. The gross tumour volume (GTV) was localised and interfraction tumour motion was defined as the displacement of the centre of the GTV on the second and third scans relative to the first. A generic PTV with ABC was created by combining the systematic and random tumour motion with the systematic and random set-up error as proposed by the "van Herk" formula, where GTV was equivalent to clinical target volume. Two identical treatment plans were produced per patient using our standard GTV-PTV margin of 1 cm radially and 1.5 cm in the superior-inferior (y) direction and for the generic PTV with ABC. The effect of PTV size on mean lung dose (MLD), percentage volume of lung irradiated to 20 Gy and 13 Gy (V_{20} and V_{13}) was compared using the Wilcoxon matched paired t-test.

Results: The systematic and random motion of the tumour was 0.15 and 0.17 cm in the right-left (x), 0.28 and 0.3 cm in the y, 0.2 and 0.23 cm in the anterior-posterior (z) directions. The systematic and random set-up error was 0.15 and 0.24 cm in the x, 0.19 and 0.29 cm in the y, 0.19 and 0.22 cm in the z directions. The GTV-PTV margin with ABC was 0.74 cm in the x, 1.14 cm in the y and 0.91 cm in the z directions. With the standard PTV the mean (± 1 SD) MLD was 10.24 Gy (± 3.39), V_{20} 16.43% (± 5.67) and V_{13} 24.18% (± 7.96) compared to the ABC PTV MLD of 9.37 Gy (± 3.26), V_{20} 14.85% (± 5.25) and V_{13} 22.19% (± 7.4), p = 0.002.

Conclusions: The reduction in PTV size with ABC compared to our standard PTV resulted in an 8-10% relative reduction in physical lung parameters. The apparently limited benefit of breathing control on the PTV and lung parameters is due to patient set-up error. This confirms that attention to patient immobilisation is as important as attempts to control tumour motion.

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RELATION OF GTV TO TNM CATEGORIES AND THEIR PROGNOSTIC SIGNIFICANCE FOR PATIENTS WITH NSCLC MANAGED WITH 3D-CONFORMAL RADIOTHERAPY (3D-CRT).

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Purpose/Objectif: The purpose of the study was to evaluate the impact of GTV (Gross Tumor Volume) on overall survival (OS), local progression free interval (LPFI), and distant metastases free interval (DMFI) in relation to TNM stage and its categories in NSCLC patients treated with definitive 3D-CRT.

Materials/Methods: Between 1998 and 2004, 220 patients with stages I-IIIB NSCLC, were treated with definitive 3D-CRT in consecutive clinical trials carried out in the institution. Forty-five percent of patients received platinum-based chemotherapy before RT. TNM stages distribution was: I - 15%, II - 13%, III - 72%. Radiation doses were 66-74 Gy in 2 Gy/fraction, 60 Gy in 40 fractions - 3 times a day 1,5 Gy; 56,7-58,8 Gy in 21 fractions (simultaneous boost); 57 Gy b.i.d. 1,8 Gy/fraction and boost of 1,2 Gy/fraction; 48-52 Gy in 4 Gy/fraction for peripheral tumors. GTV were extracted from initial treatment plans for all patients. GTV was defined as pre-chemotherapy macroscopic tumor extension visible in CT and complemented by bronchoscopic description. Lymph nodes were included in GTV if exceeded 1 cm in short axis in CT (no PET available). OS, LPFI, and DMFI rates were evaluated by univariate and multivariate analysis with regard to GTV and other known NSCLC prognostic factors. GTV prognostic value was checked for each TNM stage separately.

Results: Median follow up time was 30 months (range: 15-86). Median GTV was 92 cm^3 (range: 7-412 cm^3). Estimated 3-year OS, LPFI, and DMFI rates were 22%, 31% and 52%, respectively. Estimated 3-year OS rates for stages I, II and III were 42, 25, and 19%, respectively. Estimated 3-year OS rates for particular quartiles of GTV (in increasing sequence) were 38, 20, 18, and 12% (p<0,001). The median GTV for stages I, II and III were 33, 73, and 109 cm^3, respectively (p<0,001), but ranges overlapped between stages. There was a strong correlation of GTV with N categories (R=0,6 and p<0.001), week with TNM stage (R=0,4 and p<0.04) and no with T categories. When analyzed in subgroups for particular stages there was no statistically significant impact of GTV on studied outcomes. Cox model demonstrated negative influence on OS of larger GTV analysed by quartiles and in log10 transformation (HR=1.21, p=0,01) as well as poor performance status, bulky nodal disease, weight loss and male gender. GTV was the strongest independently related to LPFI factor (HR=1.37, p=0,002) followed by gender, performance status. GTV was not statistically related to DMFI. Only presence of bulky mediastinal disease influenced significantly DMFI. TNM stage and its categories lost their prognostic significance in Cox model for analysed outcomes.

Conclusions: Despite a correlation of GTV with N categories and increasing median values of GTV for particular stages, Cox model demonstrated a high prognostic value of GTV but not TNM categories for local control and survival for NSCLC patients managed with radiotherapy.

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RISK OF ELECTIVE NODAL FAILURE IN 3D-CONFORMAL RADIOTHERAPY (CRT) FOR NSCLC PATIENTS: DOES IT DEPEND ON DOSE RECEIVED BY PARTICULAR LYMPH NODE STATION OR IS DISEASE-RELATED?

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Purpose/Objectif: To estimate elective nodal failures (ENF) in NSCLC patients treated with 3D-CRT in relation to the dose received by particular lymph nodes station (LNS) and prognostic factors.

Materials/Methods: This is an analysis on 220 patients with I-IIIB stage treated in 1998-2004 with 3D-CRT in consecutive clinical trials differing in an extent of ENI. According to the extent of ENI, 3 groups were distinguished: 1/ complete ENI - 124 patients; total doses: 57 Gy b.i.d in 4 weeks, 66-74 Gy in 2 Gy/fr., 60 Gy in 40 fr. - 3 times a day 1,5 Gy; doses prescribed to elective region-PTV_{elect} - 39-54 Gy, me-

dian - 50 Gy, 2/ partial ENI (ipsilateral hilum, 4R, 4L, gr.7, and gr.5 for left side) - 61 patients; 56,7-58,8 Gy in 4 weeks (simultaneous boost); dose to PTVelect - 39,9 Gy, 3/ without ENI - 35 patients; 66-74 Gy in 2 Gy/fr., or 12-13 x 4 Gy for peripheral tumors. In the initial treatment plans the LNS were delineated for all patients according to the Atlas from University of Michigan recommendations (Chapet; IJROBP 2005,63;170). DVH for each LNS were created. Minimum dose and % of volume receiving ≥ 40 Gy (V_{40}) for particular LNS were analyzed according to the extent of the ENI. ENF was defined as regional nodal failure occurring without local progression, regardless of distant metastases status. ENF free interval (ENFFI) was estimated by Kaplan-Meier method and evaluated by univariate and multivariate analysis with regard to known NSCLC prognostic factors.

Results: With a median follow up of 30 months and the estimated 3-year overall survival of 22%, the estimated 3-year ENFFI was 88%. Ten out of 17 ENF occurred in LNS not included in $CTV_{elect.}$ Min. doses received by these LNS were 0-42 Gy. Only in 1 out of 10 cases the min. dose was >40 Gy. In 8 out of 17 patients, distant metastases occurred before, simultaneously or up to 3 months after ENF. In univariate analysis higher nodal status, bulky mediastinal disease (BMD), larger GTV, and partial response to RT were related to higher risk of ENF. BMD was the only independent predictor of shorter ENFFI (RR:5,8, CI:2,01-16,17), it was the same as for distant metastases control. The doses received by LNS in patients with omission of ENI were insignificant: min. doses ≥40 Gy: 3% - hilar region and 17% - gr.7. For patients treated with partial ENI mean min. doses in untreated LNS differed significantly from mean min. doses in respective treated LNS in patients with complete ENI (even when adjusted for different doses prescribed to PTV_{elect}) (p=0,01), however V_{40} for particular LNS did not differ significantly for two groups.

Conclusions: ENF is more likely to occur in case of more advanced nodal status. Use of more extended ENI in theses cases may be considered, however its impact on survival remains uncertain, as the same factor is related to the risk of distant metastases. Incidental irradiation to untreated LNS seems play a role in a partial ENI, but not in cases with omission of ENI.

972 poster

SEQUENTIAL (GEMCITABINE/VINORELBINE) AND CONCURRENT (GEMCITABINE) RADIO-/CHEMOTHERAPY, WITH FDG PET BASED TARGET VOLUME DEFINITION, IN LOCALLY ADVANCED NON-SMALL CELL LUNG CANCER: FIRST RESULTS OF A PHASE I/II STUDY

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Purpose/Objectif: The aim of the study was to determine the maximal tolerated dose of gemcitabine every two weeks and concurrent radiotherapy, administered during an aggressive program of sequential and simultaneous radio-/chemotherapy for locally advanced, unresectable non-small-cell lung cancer (NSCLC) and to evaluate effectiveness of this regime in a phase II study.

Materials/Methods: 30 patients with histologically confirmed NSCLC were treated with a combined radio-/chemotherapy protocol. This included two cycles of induction chemotherapy with gemcitabine (1200 mg/m²) and vinorelbine (30 mg/m²) at day 1, 8 and 22, 29 followed by concurrent radiotherapy (2.0 Gy/d; total dose 66.0 Gy) and chemotherapy with gemcitabine every two weeks at day 43, 57 and 71. Radiotherapy planning included [^{18}F] fluorodeoxyglucose positron emission tomography (FDG PET) based target volume definition. 10 patients were included in the phase I study with initial gemcitabine dose of 300 mg/m². The dose of gemcitabine was increased in steps of 100 mg/m² until the maximum tolerated dose (MTD) was realized.

Results: MTD was defined for the patient group receiving gemcitabine 500 mg/m², due to grade 2 (next to grade 3) esophagitis in all patients resulting in a mean body weight lost of 5kg, representing 8% of the initial weight. Six weeks after the completion of radio-/chemotherapy most patients still presented treatment induced esophagitis. In accordance with expected complications as esophagitis, dysphagia and odynophagia, we defined the MTD at this dose level, although no dose limiting toxicity (DLT) grade 3 was reached. In phase I/II local tumour response six to twelve weeks after finishing radio-/chemotherapy was as follows: 9 complete remissions, 14 partial remissions, 1 stable disease, 3 progressive diseases, 3 patients died during treatment because of lung embolism, myocardial infarction or histologically proven atypical pneumonia caused by cytomegalovirus. 8 of 18 patients without local complete remission had metastases at the first follow up. Haematological toxicity was moderate. 7 patients developed grade III esophagitis and 5 patients showed grade III pneumonitis in the phase II. No grade IV toxicity was observed.

Conclusions: After induction chemotherapy, the maximum tolerated dose and frequency of gemcitabine was 500 mg/m² every two weeks for three times during a maximum of 7 weeks of thoracic radiotherapy. It represents an effective and tolerable therapy regime in the treatment of NSCLC.

973 poster

STEREOTACTIC RADIOTHERAPY FOR PRIMARY LUNG CANCER AND PULMONARY METASTASES: A NONINVASIVE TREATMENT APPROACH IN MEDICALLY INOPERABLE PATIENTS

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Purpose/Objectif: Stereotactic irradiation of extracranial targets (ESRT) offers a non-invasive treatment modality for patients with localized tumors, which are not amenable for surgery or other invasive approaches because of age or medical conditions. The clinical results using stereotactic radiotherapy for treatment of inoperably lung metastases and small lung tumor irradiation at the Medical University Vienna will be presented.

Materials/Methods: Irradiation was performed as hypofractionation with three fractions of 12.5 Gy or five fractions of 7 Gy, prescribed to the 65% isodose. The goal of conformal planning was that this isodose fully encompasses the planning target volume (PTV). Patients were immobilized with a stereotactic body frame and the isocenter was localized by stereotactic coordinates. In total 14 pts. with stage I-II non-small-cell-lung cancer, 4 pts with bronchial relapse tumours and 66 pts. with pulmonary metastases (N=34 multiple; N=32 single metastasis) were treated. Treatment were performed within one to two weeks. The median PTV for targets in the lung was 23.4 ccm³. Median follow-up was 7.9 months for primary lung tumors and 12 months for metastases. Local control was defined as complete or partial remission and stable disease, measured after 4 weeks and in 3 months intervals. Treatment toxicity was evaluated according to WHO score.

Results: Local control was 100 % for lung cancer patients and 80 % for patients with lung metastases after a median observation time of 7.9 months (range 0.3-54 months). Time to local tumor progression was median 5,2 (range 2.6-20.3 months). Time to systemic local progression was 4.14 months (0-20.3 months). No severe acute or late toxicity was observed, and only one patient developed symptomatic Grade 2 pneumonitis, which was successfully treated with oral

steroids. Lung function (FEVT1, VC, and FEV1/VC%) recovered after three to six months.

Conclusions: ESRT for lung tumors and lung metastasis offers a very effective treatment option in medically impaired patients who are not amenable to surgery. Side effects are predictible, the method accepted by all patients. Patient selection is important, because those with low risk of systemic progression are more likely to benefit from the approach.

974 poster

THE DELINEATION OF GROSS TUMOR VOLUME (GTV) IN THE RADIATION TREATMENT OF NON-SMALL CELL LUNG CANCER (NSCLC) WITH FUSED FDG-PET/CT: ARE WE READY FOR THE ALTERATIONS?

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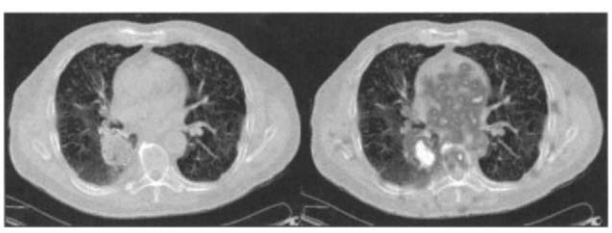
Purpose/Objectif: According to the literature PET may alter in about half of the cases the GTV delineation in comparison with CT targeting alone in patients with NSCLC. However, PET may give false negative or positive results. We performed a study to confirm the impact of PET/CT fusion on the GTV delineation, and also to correlate the alterations with pathology.

Materials/Methods: 32 patients, seen between May/2004 and May/2005, with histologically proven NSCLC on examination of tissues coming from the mediastinum and/or the primary lung tumor, with pre-treatment chest-CT and PET/CT available for review were identified. For each patient two data sets with theoretical GTVs were contoured as if they were to receive curative radiotherapy. The 1st was set of contours was made based on the clinical information and the chest-CT only. The 2nd set of contours was done separately and also included the co-registered PET/CT data (Figure). Two major differences in the GTV contours were defined: 1) when the difference between the GTVs > 30%, and 2) there was tumor or nodal regions included as GTV within one plan but not in the other. Results were compared between the two sets of contours and also with the available pathological information.

Results: PET altered the contour of the GTV in 18/32 (56%) cases compared to CT: 16 had differences in the GTV volume >30% and 2 had only changes in the nodal status. In these 18 cases, 12 had a decrease (range: 20% - 100%) and 6 an increase (4% - 237%) of the initial planned volume. PET altered the TNM stage in 14/32 patients (44%) compared to CT, but only 6 of them were confirmed by pathology. Pathological findings changed 69% and 53% of the CT and PET-TNM stages respectively.

Conclusions: Fused PET/CT altered the contour of GTV in over 50% of patients in comparison with CT targeting, similar to what is reported in the literature. Pathology showed that both CT and PET TNM-stage were inaccurate in 69% and 53% of the cases respectively. Defining the exact size of the tumor with PET was almost impossible. Whether FDG-PET/CT-based radiation planning will improve outcome or quality of life for NSCLC patients is unknown and needs to be established.

Figure: Example of one case. Left image: shows both the CT and the PET contours. Right image: shoes the fused PET/CT showing the "PET target".



975 poster

THE IMPLICATIONS OF LUNG VOLUME CHANGES DURING UNCOACHED QUIET RESPIRATION FOR LUNG CANCER TREATMENT PLANNING

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Purpose/Objectif: To determine the influence of variation in lung volume on DVH parameters used for predicting radiation pneumonitis in lung cancer patients.

Materials/Methods: Multiple repeat computed tomography (CT) images were obtained for 8 patients with stage I non-small cell lung cancer. The variation in lung volume was studied in four scans per patient acquired during uncoached quiet respiration.

For each patient and each set of CT images, two separate clinical tumour volumes (CTV) were defined, one for the primary tumor alone, one for the primary tumor and the ipsilateral mediastinum.

Corresponding planning target volumes (PTV) were generated, and separate treatment plans were then produced.

The following dosimetric parameters were generated from the dose-volume histogram (DVH) for total lung: lung volume, mean lung dose (MLD), volume of lung receiving at least 20 Gy (V20).

These parameters are used for assessing the risk for radiation pneumonitis.

Results: The mean variation in pulmonary volume within a patient was 6.6% (range 1.8-17.2). Variation in lung volume results in variation in DVH-parameters. This applies to the tumor-CTV as well as to the combined tumor and mediastinal CTV.

The larger the lung volume, the lower the MLD as well as the V20. The mean variation of the MLD was 0.6Gy (range 0.3-1.0Gy) and the mean variation of V20 was 1.0% (range 0.4-2.2%). The relative change in MLD was 4.4% and the relative change in V20 was 5.7%.

The small differences in DVH parameters did not lead to changes in the estimated pneumonitis-risk.

Conclusions: The results of this treatment planning study have provided evidence that the pulmonary volume varies during CT acquisition during quiet respiration. This results in a small, but clinically irrelevant variation in DVH parameters.

976 poster

THE QUALITY OF LIFE (QOL) OF PATIENTS WITH LUNG CANCER TREATED WITH HIGH DOSE RADIOTHERAPY OR CONCURRENT CHEMO-RADIATION ONLY SHOWS A TEMPORARY, REVERSIBLE DECLINE: A LONGITUDINAL DATA ANALYSIS OF SYMPTOMS, FUNCTIONING AND ESOPHAGEAL TOXICITY TO GLOBAL

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Purpose/Objectif: There are numerous treatment regimens for lung cancer with nearly similar clinical efficacy. As a consequence, an increasing interest in determining quality of life (QoL) per treatment option has arisen. The purpose of this study was to investigate the evolution of QoL in patients with lung cancer, selected for curative radiotherapy (RT) or chemo-radiation. Since we hypothesized that espohagus toxicity may have a considerable impact on the QoL of the selected study population, we besides studied the relationship between QoL and esophagus toxicity.

Materials/Methods

73 lung cancer patients completed a longitudinal QoL measurement (from baseline till 18 months after RT), using the EORTC QLQ-C30 with the lung cancer module, EORTC QLQ-LC13. Esophageal toxicity was scored according the CTC 3.0 guidelines. The analyses

were performed with SAS software: continuous data were analysed with a general linear model and ordinal data with a cumulative logit model.
Results: QoL decreased short after the end of RT (p=0.019) but increased back to baseline within 3 months. Overall, esophageal toxicity had no effect on global QoL. In the sub-analysis, esophageal toxicity had only significant effects on pain and swallowing (p=0.036 and p=0.037, respectively).
Conclusions: The majority of the symptoms and functioning scores did not seem to change much over time, and if they did, it was only shortly after finishing radiotherapy and reversible. The esophageal toxicity had no impact on QoL. High dose radiotherapy or concurrent chemo-radiation in the treatment of lung cancer seems to be a well tolerated treatment option with preservation of QoL.

977 poster

THE USE OF HIGH DOSE RATE ENDOBRONCHIAL BRACHYTHERAPY (HDR-BT) TO PALLIATE SYMPTOMATIC RECURRENCE OF PREVIOUSLY IRRADIATED LUNG CANCER.

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Purpose/Objectif: Lung cancer continues to remain a challenge. At the time of presentation over 70 % of patients have disease in advanced stage excluding radical treatment. Unfortunately, even in patients treated radically recurrence within the bronchus occurs in up to 40 % of patients. Successful treatment of these recurrences is difficult, as chemotherapy is of limited value and often surgery or external beam radiotherapy can not be safely given. Patients who develops endobronchial recurrences often become very symptomatic with cough, dyspnoea, hemoptysis. In order to palliate symptoms and improve the quality of life brachytherapy appears to be a treatment of choice. This paper reports our results of repeated palliative treatment with HDR-BT in patients with recurrent endobronchial lung cancer.
Materials/Methods: Between July 2000 and December 2005, 270 patients with endobronchial tumors that had recurred after first given brachytherapy were treated with high dose rate intraluminal irradiation. Criteria for inclusion in this study were: 1. recurrent disease as documented by bronchoscopy with significant endobronchial tumor, 2. acceptable remission after first treatment. It made 270 of 1036 patients (26 %) treated on lung cancer with HDR-BT in this period. 32 of patients were irradiated then third time and 6 - fourth time. There were 206 men and 64 women, age ranged from 29 to 85 years (median age - 62 years). First brachytherapy treatment consisted of total dose 22,5 Gy given in 3 fractions every week - 223 patients and one single fraction of 10 Gy - 47 patients. For single 10 Gy fraction patients were qualified when Karnofsky scare was smaller than 60 points. Repeated brachytherapy treatment was given 10 Gy as one single fraction or 8 Gy depending on size of the recurrent tumor and tolerance of mucosa - taking into account of previous treatment. It was undertaken clinical and endobronchial observation with estimating of local remission and symptomatic relief in first, third, sixth and twelve months of observations.
Results: After 4 weeks of the end of repeated treatment in 216 (80 %) patients has been ascertained subjective improvement (symptomatic relief). In 25 cases was found out complete remission (CR), in 198 partial regression (PR), in 47 - progression of disease. Tolerance of repeated treatment was good in most of cases but in 166 of patients (61,5 %) we observed superficial mucosal necrosis, in 6 cases broncho-esophageal fistula.
Conclusions: Repeated HDR-BT for recurrent intraluminal tumors: 1. provided in most of cases good symptomatic relief. 2. was easy to utilize as an outpatient procedure and have well tolerated complication rate. 3. influenced the extant of superficial mucosal necrosis caused by previous treatment (external beam radiotherapy and first given brachytherapy).

978 poster

THE USE OF PET-CT FOR TREATMENT PLANNING AFTER INDUCTION CHEMOTHERAPY IN NON-SMALL CELL LUNG CANCER MAY LEAD TO GEOGRAPHIC AND MARGINAL MISS.

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Purpose/Objectif: The use of PET-CT in radiation treatment planning target volume delineation has been shown to alter treatment volumes. PET has been shown to improve GTV delineation, improve diagnosis of involved lymph nodes and improve delineation of malignant tissue from atelectasis. The purpose of this study was to identify changes to the PET-CT delineated GTV in patients who underwent a course of induction chemotherapy.
Materials/Methods: Between March 2005 and April 2006, 19 patients with pathologically confirmed NSCLC were enrolled into an ethically approved PET-CT treatment planning study. All patients had a staging PET-CT scan and were referred for radical radiotherapy prior to study entry. 7 of the patients who had good performance status received induction chemotherapy of 3-4 cycles of Gemcitabine/Carboplatin. All patients had their PET-CT planning scan in the treatment position using a hybrid PET-CT scanner. The planning PET-CT scan was carried out on completion of chemotherapy. Patients were planned and treated using the CT images alone following current practice. As part of a planning study, Gross Tumour Volumes (primary tumour mass and involved nodes on PET) were outlined by a clinical oncologist using (1) CT scan alone, (2) PET scan alone , and (3) fused PET-CT images. Planning target volumes were compared for each of the three imaging modalities.
Results: All 7 patients who had induction chemotherapy had a reduction in their GTVPET. One patient had a complete response on PET but not CT in the primary tumour mass making GTV delineation more difficult particularly as the primary was also associated with atelectasis. Another patient who had extensive mediastinal nodes on staging PET-CT had a complete response on PET after chemotherapy in the mediastinum, changing nodal gross tumour volume significantly.
Conclusions: Caution is required when using PET-CT for target volume delineation in patients who have had treatment with chemotherapy as there is an increased chance of geographic or marginal miss. Planning target volumes can be reduced following induction chemotherapy and although this could be used to allow dose escalation such changes in standard practice should only be undertaken as part of research studies.

979 poster

TIME AND VOLUME ADAPTED RADIOTHERAPY OF SMALL-CELL LUNG CANCER IN A COMBINED RADIO-CHEMOTHERAPY

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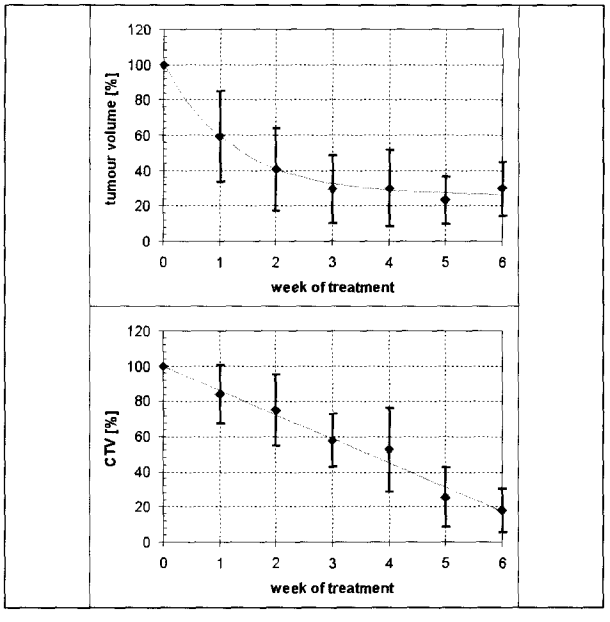
Purpose/Objectif: The primary combined radio-chemotherapy is the standard treatment procedure of small-cell lung cancer in limited disease state. Due to the initially large and fast responding tumour volumes, a time and volume adapted radiotherapy should decrease the risk of normal lung tissue damage without reducing local tumour control.
Materials/Methods: 21 patients with SCLC limited disease received a combined radio-chemotherapy using cis-platinum and CPT11. Treatment planning was repeated using weekly performed CTs after doses of 9, 18, 27, 36 and 45 Gy. The clinical target volume was adapted to the actual tumour volume depending on the tumour response. For each treatment plan the dose volume histograms for the lung were evaluated and risk parameters for expected lung damage were determined. Additionally, the lung function parameters FEV1, vital capacity and diffusion capacity were aquired before, during and up to 2 years after treatment.
Results: According to a significant reduction of tumour volumes within the first 20 Gy of treatment, it was possible to reduce the clinical target volume about 30 to 60% for 16 patients during therapy. This resulted in a continuous decrease of all lung risk parameters. The lung function parameters FEV1 and vital capacity remained constant. The diffusion capacity decreased slightly.1 patient showed a radiation pneumonitis. 3 patients showed local recurrences, whereas these have been found in 2 patients after the occurence of distant metastases.
Conclusions: The reduction of irradiated lung volume during the treatment using a time and volume adapted radiotherapy can preserve lung function and reduce pulmonary toxicity in patients with limited stage small-cell lung cancer.



980 poster

WORK-UP AND TREATMENT STRATEGY FOR NON SMALL CELL LUNG CANCER (NSCLC) IN BELGIUM : A SIXTEEN CENTRES OVERVIEW.

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Purpose/Objectif: Five thousand new cases of lung cancer are diagnosed each year in Belgium. Though being a common pathology, large variations remain regarding its work-up and treatment. The purpose of the study is to evaluate oncology practice amongst radiation oncologists (RO) in Belgium.
Materials/Methods: A questionnaire was sent to 16 radiotherapy centres nationwide. (1) RO were asked about the routine work-up procedure to perform in NSCLC. (2) Then, they were presented a PET-positive 4-centimetre upper lobe squamous-cell carcinoma, with PET-negative enlarged mediastinal node. They were asked to stage this patient. (3) Finally, whatever their personal opinion regarding staging, they were instructed to consider it a stage Ib (T2N0M0) and to propose a treatment strategy, the patient being deemed medically inoperable.
Results: (1) Regarding the work-up procedure, thorax magnetic resonance (MR) is not systematically performed. Only 25% of RO perform it, i.e. in case of thoracic wall invasion. All RO routinely perform a PET-scan. In the presence of a dubious lesion on CT (such as an enlarged node), 87.5% of RO say they would trust a negative PET and would ask for histological sampling of the lesion only when PET is positive. The remaining 12.5% would ask for histology whatever PET results. Despite also performing PET, 37.5% and 75% of RO respectively perform bone scan and liver CT. After completing work-up, physicians of all centres discuss lung cancer cases within a weekly multidisciplinary meeting.
(2) Regarding the clinical case, all RO consider it to be a T2. Only 56.2% of them (9/16) consider it to be N0, whereas others stage it Nx (6/16) or N2 (1/16) due to the enlarged node.
(3) Despite the theoretical inoperability of the patient due to cardiologic history, 43.8% of RO would ask for surgeon and anesthaesiologist's opinion about surgery. If ruled out, they would all prescribe radiation therapy (RT) with curative intent. Only 25% of them (4/16) would add chemotherapy (ChT). Concomitant ChT is prescribed by 3 RO and consists of weekly cisplatinum. Neo-adjuvant and adjuvant ChT are prescribed by 2 and 1 RO respectively and consist of cisplatinum plus either vinorelbine, gemcitabine or etoposide.
Conclusions: PET-scan is in theory widely accepted as part of the work-up procedure of NSCLC. Only 12.5% of RO say they would ask for complimentary analysis of PET-negative CT abnormalities. Despite that, when confronted with a practical case, only 56.2% of RO dare to stage as N0 a patient presenting with PET-negative enlarged mediastinal node. Multidisciplinary approach of NSCLC is standard. A significant proportion of RD (43.8%) would question theoretical inoperability of a patient with stage Ib disease, emphasising the importance of surgery in the treatment of early localized NSCLC.The use of combined modalities (associated RT and ChT) is not a standard in inoperable stage Ib NSCLC. There is no consensus regarding ChT schedule.

Posters Lymphoma/Leukemia

981 poster

DO PATIENTS AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANT (HSCT) FOR HEMATOLOGICAL DISEASES EXPERIENCE A NORMAL QUALITY OF LIFE?

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Purpose/Objectif: To assess retrospectively the health-related quality of life (HRQL) in adult survivors of allogeneic HSCT for hematological diseases with special emphasis on rehabilitation in social and

professional life.
Materials/Methods: One hundred and twenty four patients (pts) who underwent allogeneic HSCT between May 1984 and May 2004 accepted to participate in this HRQL study. The European Organization of Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ)-C30 and the Functional Assessment of Chronic Illness Therapy Questionnaire, with specific modules for bone marrow transplant (FACT-BMT) and fatigue (FACIT-F), were sent by mail between 9 months and 21.4 years (median 7.3 years) after HSCT. Return to work issues were assessed as well.
Results: The median age of the pts at HSCT was 34 years. Hundred and nineteen pts had an occupation or were in school or training before HSCT. After HSCT 60 % of these pts took up their activities again, 30% went back to their employment full time, 22% part time, and 8% pursued training or school. Forty % of the pts never went back to work and were taken in charge by the disability insurance. The general quality of life (QOL) was significantly worse when compared to that of the general population data from EORTC. Employment status post HSCT had a significant impact on all the functional scales of the EORTC QLQ-C30, with a worse perception for their QOL in pts without occupation.
Conclusions: Our retrotrospective data showed that the perception of QOL of the pts is good, but nevertheless below the one of the general population. Getting patients back to work may become a priority, as active patients tend to have a better QOL. Issues to increase work-related capabilities and improve social support need to be addressed to the medical community.

982 poster

EFFICACY OF RADIOTHERAPY IN PRIMARY CUTANEOUS B-CELL LYMPHOMA. PROGNOSTIC FACTORS

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Purpose/Objectif: Primary cutaneous lymphomas (PCL) are those non-Hodgkin lymphomas originating in the skin without evidence of extracutaneous disease at presentation. The skin is the second most common site of extranodal involvement after the gastrointestinal tract. The aim of this study is to analyze the results of the treatment with radiotherapy in primary cutaneous B-cell lymphomas (PCBCL) and identify prognostic factors.
Materials/Methods: Between September 1990 and March 2005, 53 patients with PCBCL (31male and 22 female) were treated with radiotherapy in a single centre. Median age was 50 years (Range, 24-79). According to the WHO-EORTC classification, 30 (57%) patients with primary cutaneous marginal zone B-cell lymphoma (PCMZL), 15 patients (28%) with primary cutaneous diffuse large B-cell lymphoma (PCLBCL), 7 (13%) with primary cutaneous follicle center lymphoma (PCFCL) and one patient with primary cutaneous diffuse large B-cell lymphoma leg type. Lesions were located in head and neck in 22 patients, trunk 12, upper limbs 7, legs 6 and several body regions 6. Single lesion in 28 and multiple lesions in 25. Median total dose administrated was 40 Gy in 5 fractions of 2 Gy per week, using electron beam fields. Nine patients received chemotherapy. Median follow up was 65 months (6-177). Survival rates were calculated by the Kaplan-Meier method, survival curves were compared by the long rank test and the multivariate analysis by the Cox method.
Results: 98% patients underwent complete clinical remission. There was no acute toxicity in 70% of the patients, and no late toxicity in 85%. At the analysis time 74% remained without disease relapse, 23% have been developed cutaneous relapse, and only one patient systemic relapse. Disease free survival at 5 years was 79%: 64% and 87% for indolent and intermediate PCBCL, respectively. Multivariate analysis revealed age ≥ 60 years, disseminated primary lesions, and IPI ≥1 as unfavourable prognostic factors
Conclusions: Radiotherapy is an effective treatment option for PCBCL with low morbidity and excellent results. In our serie)8% of the patients achive a complete clinical remission.

983 poster

FOLLICULAR LYMPHOMA, IMMUNOCYTOMA, AND MANTLE CELL LYMPHOMA: RANDOMIZED EVALUATION OF CURATIVE RADIOTHERAPY IN LIMITED STAGE NODAL DISEASE

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Purpose/Objectif: Indolent lymphomas in early stage nodal disease can potentially be cured by radiotherapy alone. In Follicular lymphoma grade I or II (FL) the extent of target volumes required has long been a source of international controversy. Results of involved field irradiation are flawed by a high rate of out-field relapses, while large field techniques bear the risks of higher toxicity. In Immunocytoma (IC) and Mantle Cell lymphoma (MCL), the experience is limited to anecdotal cases. Therefore, this study aims to determine adequate age-adapted irradiation volumes in FL patients (pts) (randomised (RD) trial) and to evaluate standardised radiotherapy in IC and MCL pts (prospective observation (OBS) trial).
Materials/Methods: In FL stage I-II and limited (£ 4 involved regions, £ 10 cm æ) stage III disease, pts aged 18-65 years (ys) are randomised to Extended field (EF) or Total lymphatic irradiation (TLI), dosis 30 Gy, plus boost of 10 Gy to macroscopic lymphoma < 3 cm æ, and of 14 Gy to manifestations of 3-10 cm æ (abdominal bath 25,5 Gy, 5x1,5 Gy/week, boost doses 16 and 20 Gy, resp.). Pts aged 66-75 ys are treated exclusively by EF. In IC or MCL, stage I-II pts aged 18-75 ys receive a modified EF limited to one side of the diaphragm (doses as in the RD trial). In pts < 75 ys with FL, IC, and MCL, only involved field (IF) radiotherapy is applied with 40-44 Gy.
Results: From Feb. 2000 to April 2006, a total of 265 pts was recruited, 202 pts with FL were randomised to EF or TNI. In the RD trial, median age was 54 (23-65) ys, stage I, II, and III were 56%, 34%, and 10% in the pts, resp. In the OBS trial 63 pts, median age 70 (30-85) ys,

were included, 51 with FL, 2 with IC, and 10 with MCL. Generally, EF / TLI were well tolerated, WHO IV toxicity occurring only as leuko- (0% / 16%) and thrombocytopenia (3% / 12%, resp.). In the combined analysis of both (RD + OBS) trials, 162 pts are evaluable for response and survival after median observation period of 24 months. Complete remissions were obtained by 149/162 pts (92%), relapses occurred in 34/149 pts (23%, including 4/5 pts with MCL).
Conclusions: In FL, this ongoing randomised trial contributes to the crucial question of the optimal irradiation volumes necessary for potential cure in early stage disease. Additionally, the analysis of the relapse patterns will provide the basis for further treatment improvements. In MCL, local therapy does not seem to be able to control the disease.

984 poster

INFLUENCE OF CONDITIONING REGIMENS WITH AND WITHOUT TOTAL BODY IRRADIATION ON THE INCIDENCE OF ACUTE GVHD AFTER STEM CELL TRANSPLANTATION

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Purpose/Objectif: Conditioning regimen for hematopoietic stem cell transplantation frequently includes total body irradiation (TBI). Acute Graft-versus-Host Disease (aGvHD) is a serious side effect. Aim of this analysis was to examine the influence of conditioning regimens on the incidence of aGvHD retrospectively.
Materials/Methods: Two hundred and sixteen patients were treated by allogeneic stem cell transplantation between 2002 and 2005 at a single institution. All patients received chemotherapy in combination with other conditioning modalities: high-dose chemotherapy without TBI (HD-CTX, n = 113), fractionated full-dose TBI (FD-TBI: 6 x 2 Gy, n = 67), single-fraction TBI with reduced total dose (RD-TBI: 1 x 4 Gy, n = 20), radioimmunotherapy (RIT; n = 15) as well as RIT plus FD-TBI (n = 6). 216 patients underwent single transplantation, 5 patients multiple transplantations. Median age of patients at the time-point of stem cell transplantation was 45 years (17-65 years). Diagnoses were AML, n= 83; ALL, n= 38; MDS, n= 29; CML, n= 28; Multiple Myeloma, n= 17; NHL, n= 9; others, n= 12. Indications for RD-TBI were restricted to patients with AML and MDS with an increased transplantation risk within a current treatment protocol (FLAMSA). GvHD-prophylaxis with Ciclosporin A (CSA) was given to 197 patients, either alone (n= 4) or in combination with other immunosuppressive medication (n= 193). In 17 patients donor stem cells were T-cell-depleted, 2 patients did not receive GvHD-prophylaxis at all (syngeneic transplantations). 194 patients were transplanted with HLA-matched (78 of them received material of HLA-identical siblings) and 22 with mismatched grafts. 106 patients (49%) received Anti-Thymocyte-Globuline (ATG) during conditioning. 22 patients received donor-lymphocyte-infusions.
Results: Median follow-up time was 9 months. 122 patients (55%) developed signs of aGvHD and 14 patients were suspicious of aGvHD. Conditioning with HD-CTX showed highest incidence of aGvHD (n= 42; 19 %), followed by FD-TBI (n = 24; 11%). Conditioning with RD-TBI showed lowest incidence (n= 10; 5%). RIT led to aGvHD in 6 patients (3%), RIT plus FD-TBI did not result in aGvHD, but patient numbers were limited. Incidence of aGvHD was independent of diagnosis. Univariate analysis showed a significantly lower rate of aGvHD for FD-TBI vs. HD-CTX. Multivariate analysis showed only a significant influence of Anti-Thymocyte-Globuline on the incidence of aGvHD. However, the small number of patients treated so far with RD-TBI has to be considered.
Conclusions: The inclusion of TBI within the conditioning regimen may influence the rate of aGvHD, suggesting a correlation between the intensity of conditioning and incidence of aGvHD. Conditioning regimens with TBI showed lower rates of aGvHD.

985 poster

LOW DOSE RADIATION IN FOLLICULAR LYMPHOMA INDUCES A HIGHLY EFFECTIVE P53 RESPONSE AND RAPID TUMOR REGRESSION.

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Purpose/Objectif: Involved field radiation therapy with 20 to 30 Gy is a valuable palliative local treatment for follicular lymphoma (FL). We previously showed that very low dose radiation (2x2 Gy, days 1 and 3) may be as effective for this purpose with rapid and often long lasting remissions in up to 90% of FL patients (Haas et al, JCO, 2003). Purpose of this study was to investigate the biological mechanism underlying this extremely effective response in vivo.
Materials/Methods: Gene-expression profiling using 35K spotted 60-mer oligo-arrays was performed on lymph node biopsy samples from 15 patients taken before treatment and 24 hours after the second fraction of 2 Gy. The clinical response was excellent in all patients (10 CR, 4 PR, 1 unknown, early unrelated death).
Results: In all patients, a major and consistent induction of p53 and p53 target genes (NOXA, PUMA, BAX, TRAILR2 and FASLR) was seen, reflecting both proliferation arrest and apoptosis induction. P53 upregulation, proliferation arrest and apoptosis were substantiated using immunohistochemistry with dramatic increase of p53 protein levels in B-cells, T-cells and accessory cells and significantly increased numbers of caspase 8 and 9 positive cells and morphological features of apoptosis, suggesting a relatively early stage in the apoptotic process. The third set of induced genes revealed an 'immune signature', with biologically meaningful genes related to inflammation, TH1 type immune response and the clearance of apoptotic cells. Immunohistochemical analysis did not show an increase in T-cell subsets and macrophages density, rather suggesting an activation of resident macrophages by radiation and/or apoptotic cells than recruitment of novel cell populations.
Conclusions: Biopsies after low dose radiotherapy in vivo show a p53 related apoptosis induction in vivo in human lymphoma. Moreover, the 'inflammatory' signature suggests that radiation-induced apoptosis in FL is an immunologically active process and further identifies FL as a disease of immunological functional cells in interaction with its microenvironment.

986 poster

PRIMARY NON-HODGKIN'S LYMPHOMA OF THE NASOPHARYNX: PROGNOSTIC FACTORS AND OUTCOME OF 113 INDIAN PATIENTS.

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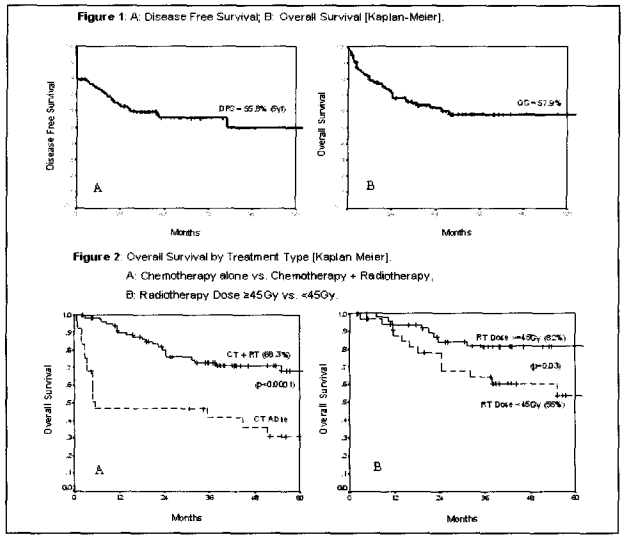
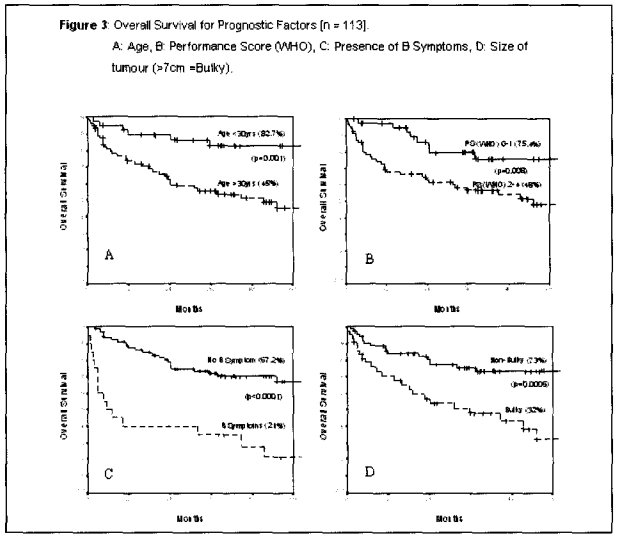
Purpose/Objectif: To evaluate the prognostic factors and treatment outcome of Indian patients with primary Nasopharyngeal Non-Hodgkin's Lymphoma (NPx-NHL) treated at a single institution.
Materials/Methods: 113 patients with NPx-NHL treated at Tata Memorial Hospital , Mumbai, from January 1990 to December 2002 were included. The median age was 40 yrs (range: 17 to 75yrs) and majority of the patients (69%) were males. Systemic 'B' symptoms

were present in only 18% of patients. Majority had Diffuse Large B-Cell Lymphoma (83%); 28% patients presented with stage I disease and 62% had stage II disease. Treatment comprised of a combination of chemotherapy (CTh) and radiotherapy (RT) in majority of the patients (76%). Among these patients, 59% received an RT dose of ≥4500cGy.

Results: The complete response rate was 61%. After a median follow-up of 56 months, the 5 year DFS & OS for the whole group were 55.8% and 57.9% respectively. Multivariate analysis showed that; age <30 years (HR=6.59, 95%CI=2.59-16.7, p<0.0001), WHO performance score ≥2 (HR=2.34, 95%CI=1.01-5.46, p=0.050), T-cell lymphomas (HR=2.81, 95%CI=1.14-6.96, p<0.001), and the presence of B symptoms (HR=3.65, 95%CI=1.77-7.53, p=0.025), had a negative influence on survival. Patients treated with a combination of CTh & RT had a significantly better outcome than those treated with CTh alone (OS: 69% vs. 31%, p<0.00001). The hazard ratio for death (HR) in the chemotherapy alone group was 3.73 (95% CI=1.95-7.13). The CR (p=0.01), DFS (p=0.01) and OS (p=0.03) rates were significantly better for patients receiving a RT dose of ≥4500cGy. The HR in the subgroup that received a RT dose of < 4500cGy was 2.51 (95% CI= 1.04-6.06).

Conclusions: Age at diagnosis, WHO performance score, T-cell histological type and presence of B symptoms significantly influence outcome in patients with primary NPx-NHL. Combined modality treatment, comprising of CTh & RT (with an RT dose of ≥4500cGy), results in satisfactory outcome in patients with this rare neoplasm.





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PROLONGED FOLLOW-UP CONFIRMS THE EFFICACY OF 4 GY INVOLVED NODAL RADIOTHERAPY IN 215 INDOLENT AND AGGRESSIVE B-CELL LYMPHOMA PATIENTS.

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Purpose/Objectif: Previous series have shown the efficacy of 4 Gy involved nodal radiotherapy (IN-RT) in lymphoma patients. This study investigates the duration of response of this regime in a large population of lymphoma patients with indolent and aggressive subtypes after prolonged follow-up.

Materials/Methods: IN-RT to a dose of 4 Gy (either 1 fraction of 4 Gy or 2 fractions of 2 Gy, interval 48 hours) was given in 215 patients with B-cell lymphomas (131 follicular lymphomas, 29 CLL/SLL, 18 marginal zone lymphomas, 17 mantle cell lymphomas, 13 diffuse large B-cell lymphomas and 7 lymphocyte predominance Hodgkin lymphomas). This group included 111 males and 104 females with a median age of 63 years (range 31-93 years). Median time since primary diagnosis was 49 months (range 3-358 months). Patients were pretreated by a median of 2 chemotherapy and/or radiotherapy regimens (range 1-11). Bulky disease (≥5cm) was present in 133 patients. Endpoint of the study was in-field lymphoma control. Median follow-up for patients still in remission was 19 months (range 3-91 months).

Results: IN-RT resulted in 57% CR (n=123), 33% PR (n=71), giving an overall response rate (RR) of 90%. RR was independent of sex, age, intensity of prior treatment, time since diagnosis, histology or tumour size. Median time to progression (MTP) was 13 months and the median time to local progression (MTLP) was 24 months. As expected, toxicity was very mild to absent.

Conclusions: Prolonged follow-up (up to 7.5 years) confirms the efficacy of 4 Gy IN-RT in recurrent and/or chemotherapy refractory indolent and aggressive B-cell lymphoma patients.

Pathology	#	%CR	%PR	%non-resp	RR	MTP	MTLP
FL	131	63	30	7	93	14	25
SLL/CLL	29	48	41	11	89	14	23
MZL	18	67	28	5	95		
MCL	17	35	47	18	82	9	20
DLCL	13	38	38	24	76		
LPHL	7	57	29	14	86	Not reached	
Total	**200**	**57**	**33**	**10**	**90**	**13**	**24**

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RADIATION THERAPY FOR EXTRAMEDULLARY PLASMOCYTOMA: A RETROSPECTIVE EVALUATION

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Purpose/Objectif: Extramedullary plasmocytoma (EMP) is a rare malignancy with the incidence 0,04 cases per 100,000 individuals. EMP is histopathologically characterized by both infiltrates of plasma cells of diverse maturity and their monoclonal immunoglobulin (Ig) products. Due to the proven radiosensivitiy of the disease, radiation therapy (RT) plays a major role in the treatment of EMP, although the optimal dose is still debatefull. Head and neck (H&N) is the more prominent region in 85% of cases. EMPs usually remain

localized and progression to multiple myeloma (MM) is uncommon with local growth pattern. This study was aimed towards evaluating the characteristics and treatment results of EMP cases irradiated with curative intent in our department.

Materials/Methods: We evaluated 10 patients with EMP treated at our department, from 1995 to 2005. All patients had biopsy proven EMP. Complete blood count, blood chemistry, skeletal survey were all within normal range in all patients and they all had a bone marrow biopsy with less 10% of plasma cell. Serum and urine protein electrophoresis were examined for all of them. EMPs consisted of nine patients located in the H&N (90%); one retrobulbar region, one nasopharynx, two nasal cavity, one soft palate, one submental, two maxilla, one orbita and consisted of one patient located retroperitoneal. Except the retrobulbar localization none of them have bone erosion. Excisional biopsy was performed only in two patients. All 10 patients received curative RT. Cases were compared according to RT dose, age and Ig secretion status; survival curves were estimated by Kaplan-Meier method and compared with log-rank test.

Results: Median age was 56 (range 30- 87) years, male/female=1. Median follow-up was 45 months. The symptoms were nonspecific and reflected the mass effect of the tumor. Ig secretion was present in five of 10 patients (50%) and Bence-Jones proteinurea was not present in any patient. All patients were treated with local RT. Median RT dose was 48, 7 (range 40- 56) Gy delivered conventionally. Local control was achieved in nine patients (90%). Two patients (20%) developed MM during follow-up and both had abnormal Ig secretion at diagnosis. The median survival of patients with and without abnormal Ig secretion were 43 months and 18 months; respectively (p=NS). The 5-year rate of disease free survival was 55%. At the time of data analysis, 90% patients were alive and only one patient (10%) died from non cancer-related reasons.

Conclusions: Radiation therapy is an effective modality of treatment for EMP with high local control rates. Progression to MM is the commonest pattern of failure and no definitive predictors of disease progression have been identified. The patients then receive RT in a dose of 40- 50Gy, may have better locoregional control as a result of cure.

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RADIOTHERAPY IN PRIMARY ORBITAL LYMPHOMA: REPORT ON 48 CASES OF A SINGLE ISTUTUTION EXPERIENCE

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Purpose/Objectif: Background and purpose: Primary orbital lymphoma is a rare disease that accounts for 10% of all orbital tumors. Radiotherapy on the orbital cavity is the treatment of choice for this infrequent presentation of localised non-Hodgkin's lymphoma. We evaluated the effectiveness and the toxicity of radiation treatment in patients with primary orbital lymphoma.

Materials/Methods: Fortyeight consecutive patients with primary orbital lymphoma were treated in our department between march 1981 and may 2005. Median age at diagnosis was 61 year (range 41 - 83). Fortyone (85%) had a low grade and 7 (15%) a high grade lymphoma. Four patients had a stage of disease greater than I.Either ^{60}Co g rays (17 patients) or 6 MV x rays (31 patients) were used to deliver daily fractions of 1.8 or 2.0 Gy, , 5 days week, by a one field technique with lens shielding on the orbital cavity with total doses ranging from 36 to 50 Gy. Eight patients that had disease greater than stage I and/or high grade lymphoma were treated with systemic chemotherapy also. Local control and disease free survival, and late side effects, such as cataract, xerophthalmia and keratitis , were evaluated in all patients.

Results: At a median follow up of 50 months (range 7 - 120) local control was achieved in 100% of the patients. Distant relapse occurred in 12 (25%) patients, that were treated with chemotherapy or radiotherapy. Late toxicity such as cataract, xerophthalmia and keratitis occurred respectively in 6 (13%), 11 (23%) and 17 (35%) of the patients.

Conclusions: Radiotherapy is an effective treatment for primary orbital lymphoma. A dose of 36 Gy provides excellent local control and an acceptable risk of long term complications.

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THE DOSES IN THE LUNGS FROM ELECTRON THORAX WALL IRRADIATION DURING TOTAL BODY IRRADIATION

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Purpose/Objectif: The purpose of electron irradiation of chest area during total body irradiation (TBI) was to increase dose in thorax walls - too low due to previous shielding of the lungs during antero-posterior (A-P) photon beams. The aim of this study was to check the agreement between doses measured with thermoluminescent detectors (TL) during electron beam irradiation of the chest area with doses calculated with treatment planning system (TPS).

Materials/Methods: The doses in chosen points of Alderson-Rando phantom's lung area were calculated for electron beams generated by Mevatron KD2 (Siemens) linear accelerator, beam size of 25 ´ 25 cm^2, A-P field and energy of 12 MeV using CadPlan 3.1.2 (Varian) TPS. The dose measurements were performed in the TBI conditions, which included distances, field sizes and patient set-up. The phantom was irradiated at a source-skin distance (SSD) of 110 cm. The doses were measured using TL detectors placed in the phantom at chosen 30 points inside the lung region. The paraffin block used during measurements was shaped to fit the phantom lung area and to shield area outside the lung. Measurements were repeated six times.

Results: Comparisons of calculated and measured doses were made using a two-tailed Sign test and the Wilcoxson's test. The results for 6 out of 30 dosimetrical points showed agreement ($p>0.05$) between measured and calculated doses. The analysis of differences between doses in 30 points lying in the lung volume in the phantom showed that in 15 points measured doses were lower than those calculated, in 11 more than by 10%. For 14 points measured doses were higher than those calculated by from 0.4% to 21.0%. The points where large differences were revealed lay in the places where doses were very low and therefore their excessive values had no clinic impact.

Conclusions: The agreement between measured and calculated doses was revealed in all points of clinical importance.

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THE EFFECT OF TOTAL BODY IRRADIATION ON BLOOD HOMEOSTASIS.

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Purpose/Objectif: We hypothesized that TBI causes an increase in fibrinogen level after radiation and that leads to a hypercoagulative status which may be a factor in the reduction of the radiation tolerance doses of the paranchymal organs. We aim to test the changes of coagulation parameters after the TBI by thromboelastography.

Materials/Methods: Eleven patients who underwent TBI during

2005 in our department were included in this study. The diagnosis of the patients were 6 with leukemia, 4 with lymphoma and 1 with multiple myeloma. A total of 1200 cGy was given to 6 patients with leukemia and 600 cGy to the remaining patients, in 200 cGy fraction doses bid. Lung shielding with 1 HVL cerrobend was applied to all patients receiving 1200 cGy TBI.Blood samples were taken from all patients immediately before the delivery of TBI and 12 hours after the completion of TBI. Complete blood counts, partial thromboplastin time (aPTT), prothrombin time (PT), and the fibrinogen levels were measured. FIB-EXTEM, extrinsic (TEG-EXTEM), intrinsic (TEG-INTEM) clotting pathways, and trombocyte functions were measured by rotational thromboelastogram (ROTEM). ROTEM is a system that meaures globally the clotting time, clot formation time, alpha angle and maximum clot firmness. The clotting parameteres and blood counts were measured before and after TBI and compared by using wilcoxon-paired test.

Results: There was no difference in the PT, aPTT, thrombin and thrombocyte counts before and after TBI. However, maximum clot firmness was decreased after TBI in FIBTEM measurement (18.6 vs 15.5, $p<0.05$). The clot formation time was also significantly prolonged (115.8 vs 121.7 seconds, $p<0.05$) and maximum clot firmness was decreased in EXTEM measurements. The fibrinogen levels were significantly decreased after TBI.

Conclusions: Our results demonstrated that the clot formation was significatly decreased in the early period after TBI. There was no hypercoagulative status as we hypothesized. Prolongation of clot formation time and decrease in maximum clot firmness in extrinsic pathway after TBI indicates disturbance in thrombocyte funtions. The hematological effects and their biological outcomes of TBI should be studied further in larger patient populations.

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THE EVALUATION OF DOSES IN THE LUNGS UNDER SHIELDS DURING TOTAL BODY IRRADIATION

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Purpose/Objectif: The aim of this study was to evaluate the reproducibility of the lung shielding during fractionated total body irradiation (TBI).

Materials/Methods: Measurements were performed with the use of the whole body female Alderson's radiation therapy phantom (ART). The lungs were protected by the individually shaped blocks made from Wood's alloy. 53 thermoluminescent detectors (TLD) were used to measure doses. The irradiation of phantom was performed at Siemens Mevatron KD2. Two trays were used during the measurements.Thermoluminescent detectors (TLD) were calibrated before measurements and sorted. Required reproducibility of TLD calibration of 3% coefficient was not exceeded. These TLD which were accepted, were distributed to wholes in the whole lungs volume. The whole lungs were shielded during AP/PA fields, when the ART was situated on the floor, at similar to patient position in TBI. The blocks were positioned on tray under ART phantom. Size and shape of the shields were revealed using CT scans. The photon beam of 15 MV was used, field size of 40 cm by 40 cm. The irradiation conditions: distance between source and ART surface (SSD), dose rate, irradiation time, field size and patient set-up were repeated in each set of irradiations. Additionally, the dose was measured in ART in a reference point (depth 10 cm in the central axis) using ionization chamber.Doses from whole lungs area were analysed statistically to evaluate accuracy and reproducibility of shielding. The dose limit in the shielded volume was set to 10% of the dose in a reference point and outside the shielding.

Results: The decrease in dose in shielded area was 11.5% of the dose in the reference point, the top of the lung accumulated 16.2%, the central body edge of the lung (point close to field's center) absorbed 18.6%, respectively. The reproducibility of measurements did not exceed 3%.

Conclusions: The protected area acumulated doses larger by 1.5% than the limit, due to probably large penumbra. The doses at the edges of the lungs were significantly higher.

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THE TREATMENT RESULTS OF STAGE IA DLBCL OF HEAD AND NECK

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Purpose/Objectif: Recently, chemotherapy, especially (R-)CHOP regimen in non-Hodgkin's lymphomas (NHL), showed good clinical prognosis in young patients. But in the elderly patients, full dose chemotherapy sometimes causes risky side effects. The usual standard treatments of early stage head and neck lymphoma in elderly patients are not proposed yet. We present the results of radiotherapy with or without chemotherapy for high-aged (over 75 years) patients with head and neck stage IA DLBCL. Mild chemotherapy, radiotherapy alone, and combined chemoradiotherapy have been performed, but it is uncertain which is the best therapy. The aim of this study is to determine whether single-modality radiotherapy is better management for patients in stage IA head and neck non-Hodgkin's lymphoma (DLBCL) of early (over 75 years) patients.

Materials/Methods: From January 1999 through December 2004, 116 high-aged patients with stage IA DLBCL (of the head and neck) were treated in 47 cooperative institutions. 58 patients were treated with radiotheray alone (RT) and the other 58 patients with chemoradiotherapy(CRT). RT was done mainly for the patients with various complications (liver, renal, or cardiac dysfunction) and/or no agreement with chemotherapy. The median radiation dose were 40Gy for RT and were 39.6Gy for CRT.

We compared the patients background and the survival curves between combined modality therapy and radiotherapy alone among elderly (over 75 years old) 116 patients. The treatment modalities were distributed as follows: CRT, 58 patients; and RT, 58 patients.

Results: The patients backgrounds which were sex, tumor bulk, LDH elevation, performance status, and IPI were not specific in statistical analysis.

The CR rates were 90% for RT and 86% for CRT. Only 28% were treated by full dose chemotherapy. 16% patients could not carry out the planned-cycle chemotherapy.

The 3-year overall survival(OS) rates of RT and CRT were 82% and 77%, respectively (n.s. : P=0.73, log rank). The 3-year cause specific survival (CSS) rates were 88& and 91% (n.s. : P=0.39). Those of relapse-free survival (RFS) rates were 77% and 82% (n.s. : P=0.98).

Conclusions: This retrospective study supports that radiation alone is not inferior to combined therapy in the elderly patients with early stage head and neck lymphoma.

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TOTAL BODY IRRADIATION: QUALITY ASSESSMENT USING CLINICAL PARAMETERS

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Purpose/Objectif: To assess the quality of the performed Total Body Irradiations (TBI), using follow-up clinical parameters, according to the TBI Working Group coordinated by the Italian National Institute of Health (ISS).
Materials/Methods: Between June 1996 and June 2005, in our institution, 125 adult patients underwent TBI before bone marrow transplantation (BMT). 95 patients received high-dose TBI. The patients were 65 male and 30 female. Median age was 35.4 years (range 15-66). Initial diagnoses were acute lymphoid leukemias (40 patients), acute myeloid leukemias (23 patients), chronic myeloid leukemias (12 patients), chronic lymphoid leukemias (2 patients), lymphoma (9 patients), multiple mielomas (7 patients); sarcoma (1 patient). All patients received chemical conditioning regimen after radiotherapy.
Treatment consisted in fractionated TBI delivering 12 Gy to whole body (including lungs and skin) in 6 fractions. TBI was performed in semiembrional position with 6 MV anterior-posterior opposed fields (dose-rate). A home-made lead beam-modulator ensured the prescribed dose rate (5 cGy/min), so that the entrance dose along the overall patient body varied within ± 1%. During each irradiation, dose delivering to the patient was verified by in vivo dosimetry. Commercial MOSFETs were used to control the midline dose; a new type of sensors ("skin MOSFETs") were developed and applied for patient skin dosimetry.
We considered 4 follow-up clinical parameters for efficacy and toxicity: bone marrow engraftment, treatment related mortality (TRM), cataract, interstitial pneumonitis.
Results: Median follow-up from BMT was 22 months (range 0 -113). We obtained bone marrow engraftment in 98% of patients and only 10 patients showed TRM (10.5%). Interstitial pneumonitis occurred in 3 patients (3.1%). Cataract was evaluated in 55 patients in which follow-up is more of 12 months; it occurred in 11 patients (20%).
Conclusions: In a TBI Institution, follow-up is an important tool to verify the overall quality of the procedure. Our results, when compared with the best published data, prove that our TBI procedure is characterized by good efficiency and low collateral effects. We think that this treatment quality is mainly due to precision and reliability of the patient dosimetry.

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TOTAL SKIN ELECTRON IRRADIATION WITH ROTARY - DUAL TECHNIQUE IN THE TREATMENT OF MYCOSIS FUNGOIDES

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Purpose/Objectif: Mycosis fungoides (MF) is a low - grade non - Hodgkin lymphoma of skin homing T lymphocytes. It is the common seen disease entity among primary cutaneous lymphomas. Total skin electron irradiation (TSEI) therapy has been in use for the therapy of MF for several decades, and a number of technical modifications have been made with the goals of optimizing dose and distribution and improving clinical outcome. Our purpose was to evaluate the efficacy and toxicity of TSEI with the rotary - dual technique (RD) in patients with MF at various stages of development.
Materials/Methods: The study group consisted of 21 patients (17males and 4 females), treated between January 2001 and March 2006. The median aged was 57 years (ranging from 40 to 82 years). The follow - up period lasted from one to 52 moths. After the staging evaluation the patients were classified as having IB (12 patients), IIA (3 patients), IIB (3 patients), III (3 patients) stage of MF. The patients were irradiated with 1,5 Gy per day for the whole skin, four times weekly to the total dosage of 21 - 40 Gy. All but one had been treated with topical regiments, photochemotherapy, local X-radiotherapy, and polychemotherapy without improvement prior to presentation.
Results: The average aged was 57 years (ranging from 40 to 82 years). There were 17 males and 4 females. The median dose for entire group was 35 Gy. The overall complete response rate was 86% and 19 patients were alive at last evaluation. Two partial remissions were achieved and one case presented an exacerbation of his lymphoma with death in two months after completing TSEI. One patient died due to non - treatment - related condition. From all the study group 11 patients are still free of the disease with the remission lasted from one to 39 months, whereas another 8 presented relapses occurring from 2 to 8 months after the completion of radiation. The most common acute side effects from TSEI regimen include: generalized erythema, skin dryness and desquamation, pruritus, onycholysis and alopecia, which healed in 7 months after the end of the therapy.
Conclusions: The study suggests that TSEI with rotary - dual technique gives good results for relapsed mycosis fungoides and might improve complete response for advanced stages of the disease.

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TOTAL SKIN RADIATION WITH ELECTRON IN PATIENTS DIAGNOSED WITH CUTANEOUS LYMPHOMA

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Purpose/Objectif: The technique of total skin irradiation with electron (TSEI) is indicated in the treatment of cutaneous T and B lymphoma with curative intention in early stages (T1-T2) and with palliative intention in most advanced stages.With Stanford technique, we get a homogeneous radiation in the whole skin surface avoiding radiation in other organs. The aim was to assess the clinical response and tolerance to treatment in 29 patients radiated with cutaneous lymphoma since July 1999 until April 2006 in our Department.
Materials/Methods: The 29 patients were treated with TSEI Stanford technique, 21 of them with radical and 8 with palliative intention; 17 males and 12 females; mean age 56 years (range 17-86 years). The patients with mycosis fungoide disease belonged to the stages: Ia (3 patients), Ib (9), IIa (1), IIb (6), III (5) and IV (1). There was 4 patients with cutaneous B lymphoma.The majority of them received previous treatment with PUVA (12) topic chemotherapy (2), superficial radiotherapy in restricted volumes (3), chemotherapy (8), interferon (8) and topic corticoids (13); all cases with partial responses and limited duration.The fraction schedule was 1Gy/per day and 5 sessions per week, reaching a total dose of 36 Gy in curative patients and 30 Gy in palliative ones.Boost of the areas with bulky lesions and underdosed areas such as, the palms of the hands, footplants, axillas, perineum and scalp and in some cases the body folds depending on the anatomy of each patient, was carried out. During the treatment sessions we have used eye protectors to safeguard the cornea and the lens.
Results: The mean follow up was 37 months (range 4-80). The acute toxicity was (RTOG score): Cutaneous: G0 7%, G1:58%, G2:32%, G3:3%; Pruritus: G0 45%, G1:38%, G2:17%; Ocular discomfort: G0 73%, G1:17%, G2:10%. At the end of RT have been detected reversible alopecia in all patients. No case with severe dermatitis.When evaluating late toxicity, we have only detected light skin dryness in 10 patients and no other sign has been valued.Early local response was 96.5%. Four years local control was in T1-T2: 71,3% and in T3-T4: 50.7%; 4 years overall survival: 77%. With the 8 patients treated with palliative intention, 4 relapsed between 0 and 9 months after finishing the RT. All these patients were without symptoms during the period of clinical response. Patients treated with curative intention (21), six of them relapsed between 3 and 17 months after finishing the RT.

Conclusions: The TSEI is a good therapeutic option for patients diagnosed with cutaneous lymphoma, and they achieved good local control with minimal toxicity in patients with radical intention. The TSEI has favourable results in the control of symptoms for the palliative patients and don't need additional treatment during the period of clinical response. ☒

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TREATMENT OUTCOME OF PRIMARY ORBITAL MALT LYMPHOMA : RADIOTHERAPY VERSUS CHEMOTHERAPY

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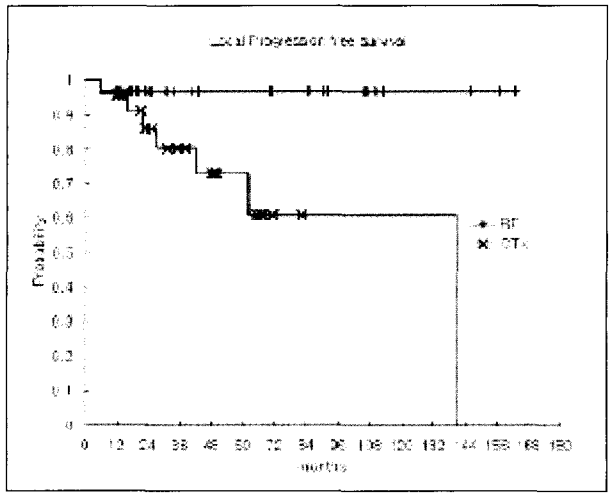
Purpose/Objectif: The role of chemotherapy (CTx) in treatment of orbital lymphoma has not been studied systematically. A retrospective study was carried out to assess the outcome and complications in patients with primary orbital marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue (MALT) treated with radiotherapy (RT) or CTx.

Materials/Methods: Fifty-seven patients treated for localized primary orbital MALT lymphoma between January 1990 and August 2004 were reviewed. There were 33 males and 24 females, with a median age of 48 years (range 20-76). Thirty-two patients had tumors in the conjunctiva, 14 in the orbital soft tissue, 8 in the eyelid and 3 in the lacrimal gland. All patients had Ann Arbor stage IAE disease, but bilateral involvement of the orbit was observed in 9 patients (15.8%). As an initial treatment, 32 patients underwent RT with a median dose of 39.6 Gy (range 27-54). A lens-sparing approach was used in 25 (78%) of 32 patients. Twenty-five patients received a median 6 cycles (range 3-6) of CVP or CHOP CTx as an initial treatment. There were no significant differences in age, bilateral orbital involvement, LDH elevation, and international prognostic index between the RT group and the CTx group.

Results: The median follow-up was 42 months (range 12-163). Complete remission was achieved in 31 of 32 patients (97%) after RT, and 15 of 25 patients (60%) after CTx (p=0.0009). In radiation group, one patient developed local recurrence, and four patients experienced recurrences in contralateral eye. After salvage RT, all patients achieved complete remission. In CTx group, 6 of 10 patients with partial remission developed local progression. Three patients were treated by salvage RT and achieved complete remission. Other three patients who received salvage CTx showed partial remission. One patient experienced local and distant recurrence. The 5-year local control rate of the RT group and the CTx group was 94% and 60%, respectively (p=0.0006). The 5-year local progression free survival rate of the RT group and the CTx group was 97% and 73%, respectively (p=0.0053). Cataracts developed in 4 patients (12.5%) and dry eyes were experienced in 2 patients (6.3%) after RT.

Conclusions: RT showed better local control and local progression free survival than CTx as an initial treatment for localized primary orbital MALT lymphoma.



Posters Miscellaneous

998 poster

A 25-YEAR SINGLE INSTITUTION EXPERIENCE IN THE TREATMENT OF EWING SARCOMA FAMILY OF TUMORS (EFT): HAVE TREATMENT OUTCOMES IMPROVED IN THIS PERIOD?

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Purpose/Objectif: To describe a 25-year single institution experience in treatment of EFT, to evaluate if treatment outcomes have improved in this period and to evaluate the effect of late relapses on treatment outcomes.

Materials/Methods: Retrospective analysis of 100 consecutive patients treated between 1977 and 2002, median follow up ~12 yrs. From 1987 onward 28 patients were treated in Intergroup protocols and 35 were treated according to these protocols.

Results: Median age at diagnosis was 19.5 years. Of the 100 patients, 63 were male, 73 presented with localized disease; tumor location was axially in 46 patients (22 pelvic). Local treatment in patients with localized disease was surgery (S: n=22), surgery with or without radiotherapy (S±RT: n=34) and definitive radiotherapy (RT: n=15). The 5-yr overall survival (OS) rates for localized disease at diagnosis was 50% and for metastatic disease 15% (p<0.001). In localized disease factors predictive (univariate) for improved OS were: non pelvic location, age <15 yrs and S±RT. Although OS increased with subsequent treatment protocols, results were not significant, when analyzed in 5-yr time blocks. Survival did not differ significantly between patients treated in or according to Intergroup protocols (43% vs. 53% ns.). Local recurrence after RT was significantly higher than after S and S±RT: 26% vs. 8% and 9%, respectively (p= 0.036). However, more patients in the RT vs. S±RT group had axially located tumors

(15/25 of which 12 pelvic). In localized disease all local recurrences occurred within 2½ yrs. Distant recurrences, however also occurred later, with 6 patients recurring after 2 yrs having a significantly prolonged survival after recurrence.

Conclusions: In this single institution study survival seemed to improve with subsequent treatment protocols; results were not significant, most likely due to small subgroups. Local treatment with S±RT had a favorable local control compared to RT, however more patients in the RT group presented with axially and pelvic located tumors. Distant recurrences are still seen after 2 yrs, these patients have better survival chances after recurrence compared to those who experience a recurrence within 2 yrs.

999 poster

ALGORITHM FOR AUTOMATIC OFFLINE DETERMINATION OF THE RESPIRATORY PHASES IN FOUR-DIMENSIONAL COMPUTED TOMOGRAPHY

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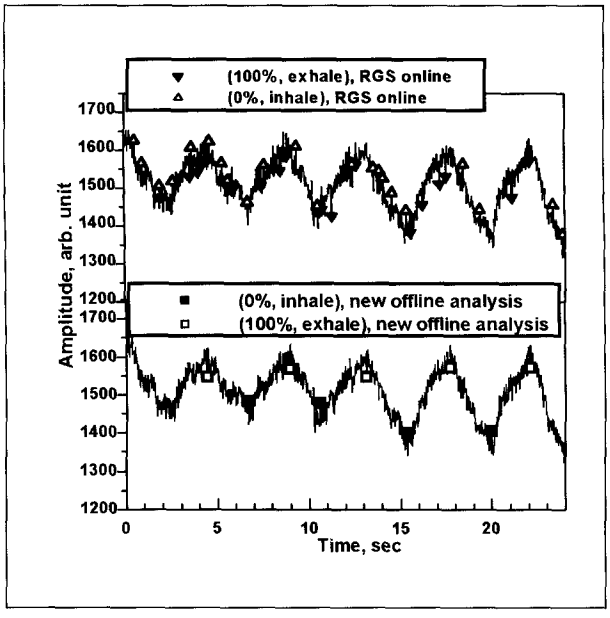
Purpose/Objectif: The respiratory correlated CT (RCCT) is widely used to take into account the displacement of the internal organs due to respiratory motion and thereby to reduce motion artefacts. Several devices for RCCT are available for clinical usage. One of them is the Respiratory Gating System (RGS) AZ-733V (Anzai Medical, Tokio, Japan). The purpose of the presented work is to improve the accuracy and reliability of the RGS online respiratory phase determination using offline analysis.

Materials/Methods: More than 50 lung cancer patients were investigated at the University Clinics for Radiooncology Tuebingen since August 2005 using Somatom Sensation Open 4D CT scanner (Siemens Medical Solutions, Germany) equipped with RGS. RGS uses for the image data synchronisation a signal from the pressure sensor fixed in the abdominal region with a special elastic belt. RGS determines online two characteristic amplitude-phase points corresponding to the beginning of the rising slope of the signal (0%, inhale) and of the falling slope of the signal (100%, exhale). Phases in between are calculated using these two by linear scaling. RGS uses unfiltered unsmoothed raw respiratory signal for the online analysis. Due to this fact several (0%, inhale) and (100%, exhale) phase-points for one respiratory period were determined for most of the investigated patients. An example of the RGS online analysis is shown in the upper part of the Figure. The odd phase-points had to be edited manually offline what is not convenient for the clinical practice. To solve this problem an algorithm for the offline phase-points determination was developed. This algorithm is based on the individual analysis of the Fourier-transformed and filtered with a low-pass filter signal for every respiratory period. (0%, inhale) and (100%, exhale) phase-points are defined in terms of the analytic features (extrem points) of the filtered signal.

Results: The respiratory curves of more than 50 patients were successfully analysed with the same version of the developed offline algorithm. It demonstrated good stability and reproducibility in phase-point determination even for complicated peak shapes. An example of the offline analysis with the new algorithm is presented in the lower part of the Figure. The execution time of the code is much less than time needed for the manual phase-points determination.

Conclusions: The developed algorithm can be successfully used for the analysis of noisy and distorted signals. No relevant difference between the images reconstructed using manually and automatically determined phase-points has been found. This means that the offline analysis procedure does not influence the accuracy of the reconstruction results but allows to decrease the dependency of the whole procedure on the human factor and makes it much faster. Use of the developed algorithm for the offline phase-points determination can make the 4D CT procedure more convenient for the clinical routine.



1000 poster

AN INTERACTIVE AND DIDACTIC TOOL FOR RADIOBIOLOGICAL ANALYSIS OF DIFFERENT FRACTIONATION SCHEDULES AND TIME EFFECT IN RADIOTHERAPY

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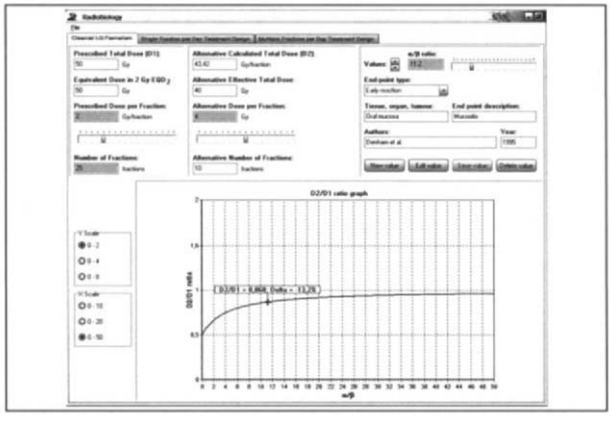
Purpose/Objectif: The radiobiological evaluation of different fractionation schedules in radiotherapy can be realized by using the Linear-Quadratic formalism. It offers an affordable tool to directly analyze the different contribution in radiobiological effects of different fractionations in the same anatomical district, due to the variability in alfa/beta ratio parameter for the different tissues and tumours. But the practical use of Linear-Quadratic formulas and the teaching of these kind of formalism can be hindered by the intrinsic difficulties in mathematical didactical approach of radiobiological topics.

Materials/Methods: In order to provide a simple and prompt tool to analyze radiobiological features of different fractionation schedules and to observe the influence on effective total delivered dose due to different timing in delivery, a software was realized that encloses all the mathematic formulas of Linear/Quadratic formalism, multi daily fractionation treatment formalism and time effect in delivery. The software has been designed in order to provide a graphical interface that allows the user to simply modify the different parameters that are used in the different formulas. Moreover it provides a graphical output (fig. 1) that puts in comparison the fractionations analyzed in terms of alfa/beta ratios and different dose per fraction put in. It is also possible to see the effect of multiple fractions per day and finally the effect of delay or interruptions during treatment can be analyzed.

Conclusions: The current application in daily clinical practice of many important issues of radiobiology is often hindered by problems that can be roughly divided into two different types: first, the lacking of affordable radiobiological data regarding the most important human body tissues and anatomical structures strictly classified and ordered basing on systematic experimental protocols; this

fact leads into a substantial difficulty in the clinical application of radiobiological models for daily practice. Second, the application of radiobiological models often requires a wide mathematical use of the really common formulas that can distract the clinicians from the clinical effects of changes introduced in fractionations and effective biological dose delivered. So we think that the use of a software designed in order to simplify these aspects of radiobiology could be useful in order to be used in the didactic of the radiobiology, for the comparison of biological value of different fractionations and fast analysis of radiobiological data collected from experimental trials.
Fig. 1. Main form of software.



1001 poster

ASSESSMENT AND COMMISSIONING OF A NOVEL DEVICE FOR THE TREATMENT OF WET MACULAR DEGENERATION

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Purpose/Objectif: A new device (eXsight™ Macular Irradiation System (MIS)) designed for the treatment of wet macular degeneration has been investigated. The treatment involves applying a concentrated dose of radiation from six beam directions to the macular lesion. The 6 fields are highly collimated elliptical shapes, which project a circular-shaped field on the macula while avoiding the lens. The MIS is attached to Varian linacs by the collimator mount and a tertiary collimator produces a field of 10mm diameter at 100 cm. A Virtual Alignment process defining the field centres reduces any variability in mechanical anisocentricity and allows an optimal overlap area for all six fields. Two orthogonal cameras (one anterior and one lateral) provide exact alignment of the patient's corneal surface and pupil position.
Materials/Methods: The MIS was used on a number of different Varian 600C/D and 2100C/D linacs to investigate the reproducibility and variability in set-up. The dosimetry of the MIS was assessed by scanning a PTW diode in a water tank to obtain percentage depth dose and beam profiles at a depth of 2.5cm, as well as output factors for various field sizes with and without the MIS. Beam profiles were also measured with Kodak X-Omat V film placed at isocentre, which was then read using a Vidar film scanner. The dosimetry was further assessed by delivering a 'dummy' treatment to a Rando anthropomorphic phantom with TLD pellets placed at the macular level (approximately 2.5cm deep) beneath wax to approximate for the eye.
Results: The output factors were comparable to those measured for equivalent stereotactic field sizes as published in the literature. The profile measured for all six fields compared to the profile for a single field was indistinguishable except at the low dose level (<10%). A table of MU settings for measured SSD was created for use in a phase I clinical trial.

1002 poster

COMPARISON OF DIFFERENT IMRT TREATMENT PLANNING SYSTEMS ON PEDIATRIC CASES

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Purpose/Objectif: To evaluate the performance of seven different treatment planning systems when intensity modulated (IMRT) plans are designed for pediatric tumour treatments. Systems analysed were: Corvus, Eclipse, Hyperion, Konrad, Oncentra-Masterplan, Pinnacle and PrecisePlan.
Materials/Methods: A dataset of four patients (CT images and volumes of interest) was distributed to design IMRT plans. The tumour types analysed were: one extraosseous, intrathoracic Ewing Sarcoma; one mediastinal Rhabdomyosarcoma; one Rhabdomyosarcoma of the anus with intrapelvic, inguinal and osseous metastases; one Wilm's tumour of the left kidney with multiple liver metastases. To minimise biases, the same geometry and clinical planning aims were imposed to all planning systems for the individual patients. Centres were invited to set all the needed tools to achieve the three following main topics: i) target coverage, ii) organs at risk sparing below the stated tolerances (mainly derived from the National Cancer Institute), iii) healthy tissue sparing. Results were analysed in terms of dose distributions and dose volume histograms.
Results: Over all cases, it is predicted that the use of IMRT could lead, in average, to acceptable treatments in terms of conformal avoidance since most of the dose objectives on OARs where respected and Conformity Index, averaged over all TPS and patients ranged from 1.14 to 1.58 on large volumes and from 1.07 to 1.37 on boost volumes. The objective of minimising the healthy tissue involvement was also measured in terms of several parameters, and for example the average mean dose ranged between 4.6 and 14. Gy (depending on patients). A global scoring method was developed to rank plans according to their degree of success in respecting dose objectives. For OARs the range of scores was between 0.75 ± 0.15 (Eclipse) to 0.90 ± 0.13 (Oncentra Masterplan) lower values being better than higher ones. Similarly for target volumes the range of scores was from 0.06 ± 0.05 (Hyperion) to 0.19 ± 0.05 (Corvus).
Conclusions: Interesting findings were reported on a set of highly complicate pediatric patients planned for IMRT treatment. Within a large spread of results, due to the heterogeneous nature of indications, it was generally found that commercial inverse planning systems are capable to offer promising results with IMRT allowing to widen the treatment strategies for this very sensitive class of patients.

1003 poster

COMPARISON OF TWO VERSIONS OF GEANT4 WITH RESPECT TO BETA RADIATION

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Purpose/Objectif: Monte Carlo codes play an important role in medical physics. Sometimes it is not possible to achieve dose infor-

mation except by applying Monte Carlo simulations. Especially if the structures of different materials are small (of the order of the mean path length of low energy particles). As measured data is not available for such problems usually either some Monte Carlo codes are compared to each other or parameters in a code are optimised until a mathematically predictable result is reproduced within a certain accuracy.The Monte Carlo code GEANT4 is under permanent development. Therefore the defaults and program routines may change from version to version. The two latest versions of GEANT4 were investigated in this work.

Materials/Methods: The geometry of a Sr90/Y90 source train for intravascular brachytherapy was used as input for simulations with GEANT4. GEANT4 input data is a C++ source code which is linked to the applied GEANT4 version. Therefore it is very simple to exchange the input between different versions. The input data was used for simulations with GEANT4 8.0p1 with CLHEP (a Class Library for High Energy Physics) 1.9.2.2 and GEANT4 7.1p1 with CLHEP 1.8.2.0. The simulations used the same data libraries. The only adjustments accounting for the small structures were a secondary particle generation threshold of 25 µm (particles with a lower remaining path length are not allowed to produce secondary particles) and choosing the physics processes adopted for such problems.

The simulated dose was compared to data measured by micro MOSFET dosimeters.

Results: The comparison of the simulations with measured depth dose data shows that version 8.0p1 generates results closer to the measurement than version 7.1p1 does.Further simulations for a stent showed that in areas where small structures (i. e. stent wires) are present version 7.1p1 generated extreme dose peaks that cannot be found in simulations with 8.0p1.

Conclusions: Simulations with GEANT4 version 8.0p1 and 7.1p1 give different results. The results from version 8.0p1 are closer to measured data.

1004 poster

CONSERVATIVE TREATMENT FOR SOFT TISSUE SARCOMAS OF THE EXTREMITIES: INFLUENCE OF TOTAL DOSE OF RADIOTHERAPY FOR LATE NERVOUS TOXICITY

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Purpose/Objectif: The aim of the study was to analyse local results (local control and late toxicity) in a consecutive and homogeneous series of 77 patients with soft tissue sarcomas of the extremities treated by surgery and postoperative radiotherapy in the same institution, from January 1996 to December 2000.

Materials/Methods: Median follow up was 56 months (17-89 months). Analysis of local control was performed according to quality of surgical resection, modalities and dose of radiotherapy, analysis of late toxicity using LENT SOMA criteria for skin, muscles, soft tissue and peripheral nerves scales. Nevertheless, only toxicities of level 3 and 4 were registered and analytic criteria were not systematically used due to retrospective analysis.

Results: After surgery, 52 patients (67%) had clear microscopic surgical margin (R0 resection), 23 (30%) had histological positive microscopic margin (R1 resection), 2 had a macroscopic residual disease (R2 resection). For most cases, an anatomical definition of the target volumes was used for conformal treatment. The mean dose was 50 Gy in 25 or 28 fractions. Twenty-three (23) patients received a boost (10-15 Gy) restricted to the tumor bed: 13 with external beam radiotherapy, 10 with HDR brachytherapy. Thirty-four (34) patients had adjuvant chemotherapy. The overall 5 year local control rate was 90%. Seven local relapses were described in which five had high grade tumours and five patients had positive margins. In univariate analysis, quality of surgery showed a significant effect for local control (p=0,03).

By using LENT-SOMA scales, the main toxicities were described as follow. For cutaneous toxicities, we noticed 4 skin ulcerations (requiring surgical graft in 3 cases), 6 fibrosis and 12 major oedemas. For muscular toxicities, 12 patients had painful toxicities associated with muscular fibrosis and reduction of muscular force. For nervous toxicity, 3 peripheral deficit were observed and 7 patients required long term treatment with gabapentine for neurogenic pain. When comparing patients receiving a radiation boost to patients who did not, a significant difference in neurological complications was noticed (p=0.03), as well as a near significant difference for muscular complications (p=0.06). However, no significant difference was observed for cutaneous complications (p=0.25).

Conclusions: The results of the series validate the concept of defining the target volume to be treated by a radiation dose of 50 Gy with a conformal treatment. A boost should be administered when treating sites with positive margins and may be needed for high grade tumors. Neurological toxicity must be considered when determining the prescription dose.

1005 poster

DOSE BUILD-UP BEHIND AIR?CAVITIES FOR CO-60, 4, 6, AND 8MV. MEASUREMENTS AND MONTE CARLO SIMULATIONS.

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Purpose/Objectif: It has been shown in several studies that the build-up in photon beams behind air-cavities (such as in the head and neck) increases with energy. There is a risk of under-dosing part of the target volume if the target volume is in the build-up region. This is the first study to investigate this effect over a broad range of energies that have been used for treating head and neck tumors. The study addresses the question whether an energy lower than 6MV is desirable and is based on measurements and Monte Carlo (MC) simulations. In many hospitals, 6MV is the lowest available photon energy. This is partly due to the design of many medical accelerators making 6MV the lowest possible energy if one also wants a high energy (15-18MV) on the same accelerator.

Materials/Methods: In a PMMA phantom containing an air-cavity ($3x16x3cm^3$ at 3cm's depth) an ionization chamber (Capintec PS-033, with a window of only $0.5mg=cm^2$ corresponding to less than 0.005mm PMMA or water) was used to measure the dose build-up behind the cavity for 4, 6 and 8MV beam qualities for different field sizes (from $3x6cm^2$ to $8x8cm^2$). MC simulations were made using the EGSnrc code for the same geometry and energies as well as for Co-60.

Results: Measurements and MC simulations agree well when the fixed-separation plane-parallel chamber measurements have been corrected for the expected over response in the build-up region.

Figure 1 shows an example of the MC simulations for a $3x6cm^2$ field (the data are normalized to 100% at a depth of 15mm below the air-cavity).

Conclusions: This work demonstrates that the build-up effect of 6MV is "closer" to the build-up effect of 8MV than that of 4MV. This suggests that if the build-up effect is of concern when the target volume is in the vicinity of air-cavities, 4MV should be preferred over both 6MV and 8MV. This work also shows that the build-up effect for Co-60 is significantly smaller than that of 4MV. Moreover, the build-up effect increases as the field size decreases. With the increased use of IMRT (and radiosurgery), small fields are used more frequently making these issues even more relevant. This should be taken into consideration when choosing the accelerator energies for a radiotherapy department.

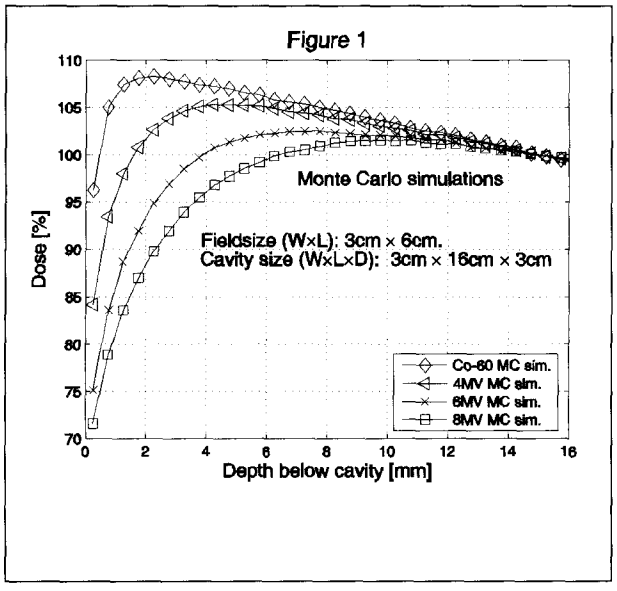

Figure 1
Monte Carlo simulations
Fieldsize (WxL): 3cm x 6cm.
Cavity size (WxLxD): 3cm x 16cm x 3cm
Co-60 MC sim.
4MV MC sim.
6MV MC sim.
8MV MC sim.
Dose [%]
Depth below cavity [mm]

1006 poster

ENHANCING QUALITY AND COST-EFFECTIVENESS BY DIGITALISATION OF THE WORKFLOW IN A RADIATION ONCOLOGY DEPARTMENT: A CHALLENGE LIKE NO OTHER ?

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Background & Rationale: The transition from a paper to a digital environment encounters many challenges. Software vendors offer pricey yet only partial solutions to implement electronic patient files and workflow management (WFM). Non-customised WFM systems frequently follow rigid concepts leading to the need for separate protocols to incorporate every single exception. Treating over 3000 patients yearly, referred by 9 major hospital locations, we defined our own needs to obtain a flexible backbone upon which an electronic patient file and tools for patient logistics can be established.
Materials/Methods: From February to May 2005, we revised and described all procedures by means of existing documentation and interviews with key persons from our department. This led to a complete description from referral to final follow up, including all steps involved in patient contacts and treatment prescription and execution.
From June to October 2005, the total process was analysed to omit all duplications. We redesigned it, using administrative support software (Protos, Pallas Athena BV), into one major and consistent care protocol, discerning several modular sub-processes. At crucial points tasks and authorisations were defined. Sub-processes like reporting, making appointments, requesting/processing of incoming data and invoicing were lifted from the basic process and described as separate generic processes which can individually be started up at each moment in the chain, contributing to the flexibility of the whole.
Results: In January 2006, we initiated the building of a WFM system (FLOWer, Pallas Athena BV) based upon this concept, to be implemented by the end of 2006. Its case-handling concept answers the need to suit workflow to individual patient care, and contributes to transparency by enabling doctors and paramedics, if authorised, to keep track of patients along the process.
Discussion & Conclusions: Workflow through case-handling puts in the centre the case, i.e. the patient, instead of the process, and provides an essential tool for tailored service for patients undergoing a complex and often multidisciplinary treatment. Apart from being a powerful tool to manage the primary care process from the medical as well as from the business point of view, we estimate that a cost reduction of the management process of 30 % can be achieved.

1007 poster

INFLUENCE OF THE CENTRAL ELECTRODE IN IONIZATION CHAMBERS - A MONTE CARLO SIMULATION BASED INVESTIGATION OF FANO'S THEOREM

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Purpose/Objectif: According to the fundamental theorem of Fano (Fano 1954), a central electrode made of graphite in a thimble ionization chamber should not alter the electron fluence and thus the measured dose. Though, in some chambers other materials are used, which generally violates the theorem and makes energy dependent corrections necessary - as found in current dosimetry protocols (e.g. IAEA TRS391) -, which are hard to quantify via measurement. The Monte Carlo (MC) Method gives insight to all relevant processes in particle transport through matter and makes it possible to analyze the influence of different components of an ionization chamber on measured dose.
Materials/Methods: Based on the established MC-code 'EGSnrc' (Kawrakow et. al. 2001) an interface to the underlying transport-algorithm was developed which brings access to various quantities of interest. Particles are marked regarding to their background, which gives chance to calculate the fraction of dose in the sensitive air-volume by electrons that are result of an interaction in the central electrode. For the simulation a simple cylindrical model of a chamber including a build-up cap was chosen, whose central electrode was varied between air, graphite, aluminium and steel. The chamber model was irradiated from side with a parallel beam of monoenergetic photons with 1.25MeV.
Results: In column 2 of the table the change in cavity dose (D) is shown, relative to the ideal case of an electrode made of air ($D_{air-electrode}$). As expected, the influence of a graphite electrode is negligible at this energy range. Column 3 shows the fraction of total cavity dose that is caused by those electrons that origin in the central electrode after an interaction of incident photons or electrons (D_{SE}). The fact, that this fraction is much larger than zero, although the cavity dose itself is not changed compared to the air-electrode case, can only be explained by absorption of electrons in the electrode. Hence, a balance of secondary electrons is achieved, irrespective of materials density as long as the chemical composition is the same. That is exactly the prediction by Fano's theorem. Using other materials for the central electrode leads to a higher fluence of secondary

electrons and a corresponding higher energy deposition in the sensitive air volume.

electrodematerial	$D/D_{air\text{-}electrode}$	D_{SE}/D
air	-	0.1
graphite	0.07 %	4.7 %
aluminium	0.76 %	5.8 %
steel	1.5 %	6.7 %

Conclusions: The presented results show the principle influence of a central electrode and the violation of Fano's theorem. This violation yields in a necessary appliance of an energy dependent correction factor as earlier calculated by MC simulations by other authors, which are part of current dosimetry protocols. The developed interface can further deliver energy-spectra of particles that leave a certain region and could help to improve the design of ionization chambers, concerning a flat response over the energy range used in radiation therapy.

1008 poster

MEDICO-ECONOMIC AND SPATIAL MODELIZATION FOR DECISION MAKING IN INNOVATIVE THERAPIES: APPLICATION TO LIGHT IONS THERAPY PROJECTS IN EUROPE

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Purpose/Objectif: Innovative therapies are characterized by major uncertainties regarding clinical benefit, cost and medico-economic benefit compared to standard therapies, but also for the estimation of the demand, as to define the offer.
Due to the lack of reliable data, and as to simulate the consequences of different scenarios, we have developed an "integrated medico-economic and spatial model" as a tool for decision making in innovative therapy. This model has been developed and applied for light ion therapy projects in Europe in the framework of the European Network for Light Ion Radiotherapy leaded by ESTRO.
Materials/Methods: Three independent but complementary models have been developed:
- A spatial model, to calculate the recruitment of each centre taking into account the quantitative and qualitative parameters of the demand (potential indications) and the offer (concurrent centres for hadrontherapy or other alternative therapies). The accessibility in terms of distance was modelized, as to test the consequences of several scenarios for the spatial location of the facilities.
- A cost model with the objective to assess the initial treatment complete cost per each therapeutic protocol with the hospital point of view, taking into account the specificities of each protocol and different operating scenarios for a given.
- A medico-economic model as to compare different treatment strategies for a given indication integrating both the clinical expected benefit and costs in a societal perspective, including not only the initial cost, but also the avoided cost.
Results: Numerous scenarios have been designed and applied to the French ETOILE project for each model. The main conclusions that will be detailed in the presentation are:
- The qualitative recruitment (repartition of the indications prioritised according to the expected clinical benefit) is very sensitive to the capacity of the centre, the extent of the area for pts recruitment (i.e. national vs. European) and the competitive context. The spatial location of the centre may have some consequences according to the structure of the recruitment. The qualitative recruitment in terms of pts or sessions is directly linked to the centre capacity and the protocols characteristics.
- The cost per protocol is directly linked to the treatment modalities (number of sessions and their mean duration, technical requirements...) and to the capacity of the centre (operating scenario). The lack of adequacy with several financing system was quantified.
- Medico-economic comparative simulations between several scenarios were performed for base of skull chordoma, showing that light ion therapy can be much cost-effective than conventional irradiation according to several hypotheses for the expected benefit.
Conclusions: Modelization can be used as a major tools for decision making in innovative therapies .

1009 poster

PHANTOM INVESTIGATION OF THREE-DIMENSIONAL, MOTION DEPENDENT VOLUME ALIASING DURING CT SIMULATION FOR RADIATION THERAPY PLANNING

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2 - University of Texas Health Science Center/Cancer Therapy and Research Center, *Radiation Oncology, San Antonio, Texas, USA,*
3 - Computerized Imaging Reference Systems, Inc., *Medical Physics, Norfolk, Virginia, USA,*
4 - University of Texas Health Science Center/Research Imaging Center, *Radiology, San Antonio, Texas, USA,*
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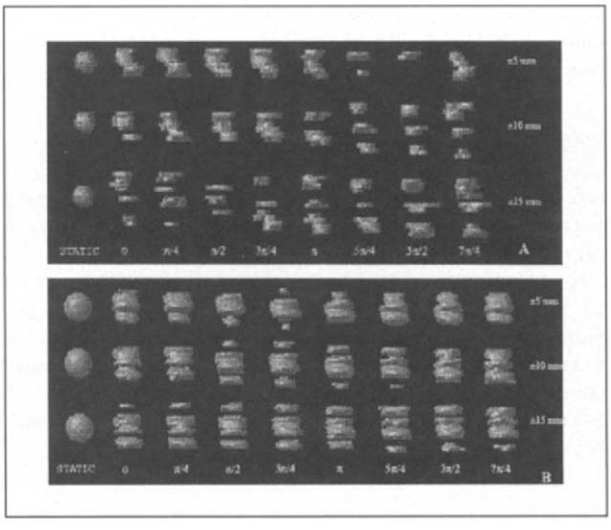
Purpose/Objectif: To quantify volumetric aliasing during non-gated fast and slow scan CT techniques due to 3 dimensional target motion.
Materials/Methods: A series of spiral CT scans were acquired using 1) single-slice fast (1-sec), 2) single-slice slow (4-sec), and 3) multi-slice fast (1-sec) scanning techniques on known dynamic, spherical targets (1 and 3.15 cm in diameter), embedded in a prototype of a commercially available dynamic anthropomorphic phantom (CIRS Inc., Norfolk, VA, USA). Target motions typical of clinically observed 3D tumors were investigated. Target motion excursions included ±5 mm, ±10 mm, and ±15 mm displacements in the S-I direction synchronized with constant displacements of ±5 mm and ±2 mm in the A-P and lateral directions, respectively. For each target, scan technique, and motion excursion, eight different initial target motion-to-scan phases were investigated. In addition to the single slice image acquisition times of 1 and 4 seconds, scans with image acquisition times of 1.5, 2, and 3 seconds were also acquired, and each reconstructed with slice widths 1.5, 2, 3, 4, 5, 8, and 10 mm.
Results: An anticipated, general trend of target volume overestimation, in the presence of 3D target motion, was observed during spiral CT imaging. The mean percentage overestimation of the true physical target volume typically increased with target motion amplitude and decreasing target diameter (Fig 1). Slow-scan percentage overestimations were larger, and better approximated the time-averaged motion envelope, as opposed to fast-scans. Motion induced centroid misrepresentation was observed, and was greater in the S-I direction for fast scan techniques, but smaller in the same direction for the slow scan technique. The smaller target was more suscepti-

ble than the larger target to aliasing due to motion-amplitude and initial-motion-phase changes, as well as to motion-induced artifacts. Finally, overestimation is fairly uniform for slice widths less that 5 mm, beyond which there is gross overestimation.
Fig 1: Distortion of a 10- (image set A) and 31.5-(image set B) mm diameter targets as a function of motion amplitude and initial motion phase for a multi-slice fast (1-sec) scan technique. The first column was reconstructed from a scan of a static target, and subsequent columns from 8 known equally spaced motion-to-phase synchronization schemes (columns) and 3 known motion amplitudes (rows). Tables of specific values for volume distortion will also be presented.
Conclusions: Non-gated CT imaging of targets describing clinically relevant, 3D motion results in aliased overestimation of the target volume and misrepresentation of centroid location, with little or no correlation between the physical target geometry and the CT-generated target geometry. Slow scan techniques are a practical method for characterizing time-averaged target position. Fast scan techniques provide a more reliable, albeit still distorted, target margin.



1010 poster

PHOTON SPECTRA OF A LINEAR ACCELERATOR IN A WATER PHANTOM: INVESTIGATION OF THE FIELD SIZE DEPENDENCE VIA MONTE CARLO SIMULATION

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Purpose/Objectif: In the last years several authors published measurements of output factors OF = $D_w(z, FG) / D_w(z, FG_{ref})$, with several types of ionisation chambers in high energy photon beams [1]. R. Kranzer, Z. Zink 2003, [2] F. Haryanto et. al. 2002. These measurements showed discrepancies especially in large field geometries (field size FZ =40x40cm²) for different chambers up to 15%. These discrepancies are caused by the different material of the central electrode witch was used in the different chambers. To gain a better understanding of the processes involved it is necessary to know the spectral photon- and electron fluence at the point of measurement and the resulting water/air mass-stopping-power-ratios (w/a MSPR) as a function of field size.
Materials/Methods: The head of a linear accelerator was modelled with the Monte Carlo software BEAMnrc and adjusted with cross section profiles and depth dose measurements of a Varian Clinac 2100C in 6MV photon mode as described by J. Pena et. al. 2004. This model was used to determin photon spectra in a depth of 10cm in a water phantom for different field sizes. Afterwards the restricted w/a-MSPR was calculated on the central axis with the EGSnrc user code sprrznrc for each field.
Results: As expected, the photon spectra show a strong fluence increase in the lower energy parts of the spectra (Fig 1) The resulting mean energies are varying between E_{med} = 0,89 MeV at 40x40cm² and E_{med} = 2,13 MeV at 2x2 cm². Nevertheless it has only a slight influence on the resulting secondary electron spectra and to the restricted w/a-MSPR, for the photon spectra shown in Fig. 1 it is merely shifted by 0,7 %.
Conclusions: The results presented in [1, 2] lead to the assumption, that the discrepancies between the different ionisation chambers are related to chamber dependent correction factors. However the chamber independent factors (photon- and electron spectra, w/a-MSPR) should be investigated in detail. The results of the Monte Carlo simulations show strong field size dependence of the spectral photon fluence at the point of measurement. The resulting change in MSPR to the value at 10x10cm² however is less than 0,5%. If these results are added to the results of Sánchez-Doblado et. al. 2003, it seems warrantable to use the value for the restricted w/a-MSPR under reference conditions for all field sizes since the errors made are within the limits of ±0,4%.

1011 poster

POPULATION BASED DATA BASES, HOW REPRESENTATIVE IS A REPORTED EXPERIENCE IN TEH LITERATURE.

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Purpose: Much of medical practice is based on center experiences and retrospective evaluations. Randomized controlled trials are only available for limited situations and common diseases. In addition to known and reported biases, the results of these surveys are also limited by the fact that reported experiences are only a small proportion of the total population. Looking carefully at statistical reports in many published studies reveals that usually only a proportion of the total are used for outcome analysis, which introduce further biases.
Objectives: To quantify the actual correlation between total data base statistics and the reported experience in a population based cohort of patients.
Materials/Methods: Computerized data capturing was created in access inter-relational database.Institutional database was available with limited information including demographics, treatment and survival statistics. Patients' charts registered in the period from 1960 to 2005 were reviewed. All the Head and Neck data base listings were reviewed to ensure that all patients names were captured. Data captured included Age at diagnosis, Gender, Presenting Symptoms & Signs, Investigations (findings), Living/disease status at last F/U (+ cause of death), Tumour location, size, Histology, Grade, TNM classification, Treatment modality such as surgery, chemotherapy, radiotherapy, its dose and intent (radical/adj/palliative), Treatment Toxicities, Social Habits (tobacco, EtOH) and occupational exposure Quality assurance audits were carried out on the charts. Data were entered into the computer. A Sass Statistical package was used for analysis.
Results: During the period of 1960 to 2005 a total of 6727 patients were registered. 1137 arisen in the Oral Cavity (excluding Lips), 635 in the Lips, 256 Nasopharynx, 1272 in the Oropharynx, 379 in the Hypopharynx, 1890 in the Larynx (Supraglottis - 581 , Glottis - 1279, Subglottis - 30) 300 in the Salivary Glands, 231 in the Sinuses, 6 in the Ear , in 626 site unspecified. Reported incidence of second tumours were 6 primary tumors in 1 patient, 5 in 4 patients, 4 in 15 patients, 3 in 68 patients, 2 in 523 patients(8%) and 1 in 6114 patients (91%). On further review of the data only 1600 (24%) patients had adequate information to allow reliable outcome analysis. Detailed analysis will be presented.
Discussion: That study in addition to review of the literature highlights the added deficiency in retrospective evaluations which forms the bulk of the medical evidence that support our pattern of practice. In our study a mere 24 % of the patients had well documented

data to support reliable toxicity and outcome analysis
Conclusions:A well-thought and carefully designed prospective data base is a must for developing further reliable scientific evidence particularly in rare conditions.

1012 poster

RADIOTHERAPY SOFTWARE FOR DEPARTMENT MANAGEMENT AND ORGANISATION

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Purpose/Objectif: A radiotherapy department has a complex organisation due to multidisciplinary (physicists, doctors, nurses, engineers) and sequential process of working. As in a team work, we need a very good organisation and management. In the idea of "process improvement" we have developed in our center a software to upgrade the organisation, to have a better transfer of information between the different teams. Finally, it gives a global overview of all the tasks we have to do.
Materials/Methods: We have made a study of what is the job of everyone in a radiotherapy department. The result is a checklist of all the things to be done. From the consultation to the first treatment day of the patient, trough the first simulation, planning, realisation of cerrobend blocks, ... Each checklist is customised for each different patient planning. It is a modular system depending on the treatment.Practically, the main page of this software is the list of the different patients names to be treated in different background colours. Each colour belongs to one trade (red for physicists, blue for nurse, ...). When the stage is finished the background colour of the patient name will change to the next one. Therefore, someone else can deal with the continuation of the treatment preparation.
Results: From a technical part, the "radiotherapy Intranet" is working like a website. The database is running on a local web server, each computer can access to it via a web browser like Internet Explorer, Mozilla Firefox, ... as well under Windows, Linux or Macintosh, and, a big advantage for a radiotherapy department, without any installation on each client. It is an internal website, confidentiality is 100% guaranteed. This software can be connected to VISIR (Record & Verify), TomoTherapy or any TPS to get some information from their database. Like a "classical" intranet, we have a calendar, phone book, mailing list, ... We have also our linacs failure database to automatically get the downtime statistics.
Conclusions: This "Intranet" can't work if everyone involved does not use it correctly. But now, after one year of use, we can say that it became difficult to work without this huge information database. Moreover, we are able to get some statistics on the time needed for a particular activity, on the improvement of organisation, on the time lost in the procedures, number of patients (by date, pathology, region, ...), ... We have now a better organisation with no more delays in the treatment preparation. It is really helpful during all the workflow.

1013 poster

RENAL TOXICITY IN CHILDREN UNDERGOING TOTAL BODY IRRADIATION FOR BONE MARROW TRANSPLANT

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2 - Emory University, Medicine, Atlanta, USA, μ3 - Baylor College of Medicine, Radiaion Oncology, Houston, USA

Purpose/Objectif: This institutional retrospective study evaluates the frequency of renal dysfunction in children after total body irradiation (TBI).
Materials/Methods: Between 1995 and 2002, 62 children (median age 9, range 1-18) underwent TBI as part of a conditioning regimen before allogeneic bone marrow transplant (BMT). Patients received between 10 and 14 Gy at 1.75 to 2 Gy per fraction in 6 to 8 fractions. Lung shielding was used in all patients to limit lung dose to less than 10 Gy; renal shielding was not used. Most patients underwent glomerular filtration rate testing prior to TBI. Renal dysfunction was evaluated on the basis of serum creatinine levels at acute (0-90 days) and chronic (< 90 days) intervals after completion of BMT.
Results: Acute renal dysfunction was documented in 27 patients (43 %); 18 of them had concurrent diagnosis of veno-occlusive disease (VOD) or Graft-versus-Host Disease (GVHD) and 15 had other potential causes (sepsis, anbtibiotic or chemotherapy related). Six patients developed chronic renal failure; one died of this complication and one required hemodialysis and eventually a kidney transplant. None of these patients had other documented potential causes of renal failure. There was no significant relationship between TBI doses of 10-12.5 Gy and 13-14 Gy in terms of development of acute or chronic renal failure.
Conclusions: The overall frequency of renal dysfunction in this pediatric BMT population is alarmingly high: 10% of patients developed chronic renal insufficiency, of which two suffered organ failure. As these patients did not have other potential causes of renal dysfunction, this may be attributed to radiotherapy. Further analysis of radiation exposure to the kidney during TBI in this population is warranted. These data support consideration of partial transmission kidney blocks with TBI regimens to minimize renal dose and potentially reduce renal toxicity.

1014 poster

SHIELDING CALCULATIONS FOR HELICAL TOMOTHERAPY

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2 - Radiation oncolgy department, CHUV, Lausanne, Switzerland

Purpose/Objectif: Helical tomotherapy presents new radiation protection challenges related to the shielding design of the unit, particularly due to the increased beam-on-time. A conservative model has been developed for the shielding of the Hi-Art II tomotherapy system.
Materials/Methods: The protection thickness is calculated using formula: $s_i=z_i \log(WUTR_i/H)$ where i: radiation component index; s: required shielding thickness; z: tenth-value layer; W: weekly workload; U: direction factor; T: occupation factor; H: allowable ambient dose; R: reduction factor (see table, where A_0: reference distance; A_n: distance between place to protect and source; A_s: distance between place to protect and entrance point; D_d/D_r: ratio between leakage and reference dose rates; F_n: maximal field surface). For tomotherapy, all these formulas have to be reassessed.
Results: For tomotherapy, a conservative workload of 10 kGy/week was used instead of 1 kGy/week. The reference point was set to the isocentre at 0.85m from the source. Shielding calculations were performed for primary, leakage and scatter radiation.
Primary: The attenuation factor of the beam stop was estimated to be 285. Since the gantry constantly rotates, the reduction factor R_r is corrected by a factor of 10 (see table, where A_p: distance between place to protect and isocentre).
Leakage: As the source is not punctual, a reformulated distance correction is necessary for the leakage radiation component. The dose rate does not decrease with the square of the distance. Therefore a mean radius, A_{mean}, varying inversely with the square of the distance from the isocentre and an experimental normalization factor K(t) were introduced to determine the reduction factor R_d (see table, where t: angle relative to rotation axis).
Scatter: Since scatter radiation is produced at the isocenter, the in-

verse square law of the distance is applicable. The maximum value of 2% for scatter radiation fraction (depending on t angle) was adopted to establish the reduction factor R_s (see table).

Conclusions: A conservative shielding method for tomotherapy units was proposed. An analytical model was developed to determine the leakage radiation contribution as a function of the angle relative to the rotation axis and the distance from the isocentre. Leakage radiation yields the main contribution. However, although the contribution from the primary beam is less than the contribution from leakage radiation, it must be taken into account for determining the shielding thickness. Scattered radiation is negligible.

RADIATION COMPONENT	LINAC	TOMOTHERAPY
PRIMARY	$R_1 = \frac{A_0^2}{A_s^2}$	$R_1 = \frac{A_0^2}{(A_0 + A_s)^2} \cdot \frac{1}{250} \cdot \frac{1}{10}$
LEAKAGE	$R_2 = \frac{D_0}{D} \cdot \frac{A_0^2}{A_s^2}$	$R_2 = K(t) \cdot \frac{1}{A_{max}^2}$
SCATTER	$R_3 = 0.01 \cdot F_1 \cdot \frac{A_0^2}{A_s^2}$	$R_3 = 0.02 \cdot F_0 \cdot \frac{A_0^2}{A_s^2}$

1015 poster

THE USE OF ELECTRONIC COMENSATORS TO OPTIMIZE DOSE DISTRIBUTIONS IN BREAST AND HEAD AND NECK TREATMENTS: A FEASIBILITY STUDY AND FIRST TREATMENTS

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Purpose/Objectif: To replace the use of conventional wedges in breast treatments and head and neck (H&N) treatments with electronic compensators generated by dynamic multileaf collimator in an attempt to improve dose homogeneity. The use of electronic compensators also allows single isocentric set-ups for both types of treatments.

Background: Breast and H&N patients in the Radiotherapy Department of Namur were routinely planned - by using a 3D CT-scan with conventional (hard and dynamic) wedges in the medio-lateral direction combined with - in some cases - in the cranio-caudal direction. The development of IMRT has opened the possibility to "redesign" the concept of missing tissue compensators to further improve the dose inhomogeneity. Varian has recently implemented such electronic compensators ("irregular surface compensator") into the Eclipse TPS. Standard IMRT requires contoured volumes for the planner to run the optimization on. Electronic compensator modules, on the contrary, require no other contouring than the body outline and automatically generate the surface on which the dose volume optimizer aims to deliver a homogenous dose. The optimal fluence produced as such is converted into dynamic leaf motion files for delivery. Hence, the former mechanical compensators are mimicked by the dynamic multileaf collimator.

Materials/Methods: For a cohort of breast and H&N patients (<50), electronic compensator plans were compared with optimized conventional wedged plans with regard to: DVH and planning time. If the electronic compensator plans were deemed dosimetrically superior to the conventional wedged plans, obviously the patients were treated with the electronic compensators.

In a second phase, breast and H&N treatments with electronic compensation were delivered in a single isocentric set-up; this allowed a further improvement in dose homogeneity by using junctions of half beams and using the electronic compensators in asymmetrical beams where hard or dynamic wedges can not be used.

Results: Especially for large breast and/or asymmetric breasts, the electronic compensation in a single isocentric set-up leads to better target coverage. Also, energy mixing (6MV and 18MV) was no longer necessary for many of the cases. Planning time was also substantially reduced. For small breasts with a single wedge in the medio-lateral direction, no substantial gain was observed with the electronic compensation. For the H&N treatments, the use of electronic compensation in a single isocentric set-up improved the dose homogeneity in the target volume and eliminated the junction problems between the lateral fields and the supra-clavicular field.

Conclusions: The new modules for the irregular surface compensators (Eclipse, VMS) allow fast and flexible planning and delivery of a missing tissue compensator with the dynamic MLC. This is a natural extension of using IMRT tools to improve dosimetry of conventional 3D plans.

1016 poster

UNSUSPECTED ABNORMALITIES ON RADIOTHERAPY TREATMENT PLANNING CT SCANS REVEALED AFTER IMPLEMENTING ROUTINE DIAGNOSTIC REVIEWING.

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Purpose/Objectif: To document the frequency of clinically important, unsuspected abnormalities revealed by diagnostic review of radiotherapy treatment planning CT scans.

Materials/Methods: Starting February 2006, radiotherapy treatment planning CT-scans were routinely reviewed by radiologists and reports were available after one day. The frequency of unsuspected abnormalities was noted retrospectively for the first consecutive 93 scans. In all patients, diagnostic imaging was performed according to national guidelines. Furthermore, we classified these abnormalities as benign or malignant, and whether these findings had influenced clinical decision-making.

Results: On the 93 scans that were reviewed, 18 (19%) unsuspected abnormalities were found: 8 (9%) malignant, 8 benign and 2 uncertain malignant. Of the 8 malignant abnormalities, 5 (5%) altered treatment decisions: in 3 cases post operative radiotherapy with curative intent had to be replaced by chemotherapy for disseminated disease; in 2 cases additional surgery was undertaken and radiotherapy postponed. Of the 8 benign abnormalities, 4 findings led to an additional treatment planning CT to adjust clinical target volume. Two abnormalities were uncertain malignant and are currently further investigated. Nine of the 18 unsuspected abnormalities were found in patients treated for breast cancer, of which 4 findings were malignant and altered treatment regimen.

Conclusions: Routine diagnostic reviewing and reporting of radiotherapy treatment planning CT scans by the department of radiology proved to be feasible at our institution. Most important: 19% unsuspected abnormalities were found (9% malignant) and in 5% treatment decisions were altered based on the additional information provided. Furthermore, in 4% additional imaging to adjust treatment was performed. We recommend routine diagnostic reviewing of radiotherapy treatment planning CT-scans.

Posters Modelling TCP/NTCP

1017 poster

STATISTICAL METHODS FOR DETERMINATION AND VALIDATION OF DOSE-RESPONSE RELATIONS FROM CLINICAL PATIENT DATA-SETS

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Purpose/Objectif

Radiobiological treatment plan evaluation is achieved by quantifying the predictive strength of the different radiobiological models and the validity of their parameters for tumor control and normal tissue complications using a series of statistical methods. In the optimization of prostate cancer radiotherapy it is important to estimate the parameters that describe the dose-response relations of the tumors and involved organs at risk.

Materials/Methods

A popular method for determining the best parameter estimates of different radiobiological models is the maximum likelihood fitting. Furthermore, the statistical methods of the error distribution, regression analysis, receiver operating characteristic curve (ROC) and Pearson's test are utilized to assess the agreement between the pattern of the model predictions with that of the follow-up results. The estimated, with these methods, model parameters should be validated clinically by predicting the treatment response probabilities in an individual patient group. Finally, a Markov chain method can be initiated to maintain and update the clinical validity of the model parameters in relation to the applied clinical methodology. In this study, these statistical methods were applied to 80 patients who received radiation therapy for clinically localized prostate adenocarcinoma.

Results

Parameter sets of the prostate tumors were estimated for the radiobiological models of Relative Seriality, LKB and Parallel. For the organs at risk, published reference parameters (bladder: D_{50} = 80.0 Gy, **g** = 3.0, s = 0.3, rectum: D_{50} = 75.0 Gy, g = 2.5, s = 0.7, anal sphincter: D_{50} = 70.2 Gy, γ=1.22, s=0.35) were validated for tehir suitability in reproducing the treatment outcome pattern of the patient material studied (through the probability of finding a worse fit, area under the ROC curve and X^2-test). For every tissue and clinical endpoint, the biologically effective uniform dose (D) was specified to serve as a more p roper dose prescription unit.

Conclusions

Dose-response parameters derived by a maximum likelihood fitting can be used as a reference to evaluate their compatibility with a given treatment methodology. The examined dose-response parameters can predict the tissue response for the studied treatment methodologies with a good accuracy. Finally, the demonstrated statistical methodology is recommended for clinical verification of dose-response relations before their gradual introduction in the clinical practice.

1018 poster

TREATMENT PLANS EVALUATION USING ELABORATED PARAMETERS FOR ORGAN AT RISKS IN THE PROSTATE CANCER

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Purpose/Objectif

Comparison of treatment plans based on DVH or/and TCP, NTCP parameters is a useful tool applied to verification of new developed techniques. In clinical practice these parameters provided no sufficient information for selection of the best technique for specified patient. The aim of this study was evaluation of the three elaborated parameters describing patient's anatomy on the process of technique selection in clinical practice.

Materials/Methods

Fifty patients with prostate cancer irradiated in supine position with knee support were chosen for the analysis. The prescribed dose was 72Gy. One 3-beam and two 4, 5, 6 beams IMRT and 3DCRT plans were made for each patient. The same beam configuration for IMRT and 3DCRT were used. Three anatomy-dependent parameters were chosen for each patient, respectively:

1/ volume-dependent parameter defined as: VD=V(OAR)/V(PTV) where V(OAR) is the volume of organ at risk and V(PTV) is volume of PTV; 2/ length-dependent parameter: LD = L(OAR)/L(PTV) where L(OAR) is a length of organ at risk and L(PTV) - length of PTV in cranial-caudal orientation; 3/ distance-depended parameter (DD) defined as a distance between geometrical centre of PTV and centre of OAR. The plans were compared using TCP and NTCP, conformity index and means of organ at risk volumes irradiated to the dose above 60Gy for bladder and rectum) and to above 50Gy for femoral heads, respectively. Comparisons were performed with and without anatomy-dependent parameters. The comparison included anatomy-dependent parameters was performed after correlation tests where choice of the best parameter for specified OAR was performed.

Results

The comparison where anatomy-dependent parameters were not take into the consideration showed only trends of dose differences between distributions obtained from analyzed plans ($p>0.1$). For example, range of NTCP in rectum was between 4.1% and 7.2% with standard deviation between 1.1% and 3.0%.

The correlation between anatomy-dependent parameters and OAR's revealed that for bladder the best is VD (R=0.874), for rectum - LD (R=0.901) and for femoral heads - DD (R=0.843) ($p<0.001$).

Using above parameters for the treatment plan comparison, patients were divided into groups. Respectively, for NTCP analysis in rectum, patients were grouped by LD parameters and for group where LD was higher than 1.5, mean value of NTCP enclosed in range from 3.0% to 5.0% with standard deviation from 0.9% to 1.5%. Smaller standard deviation leaded to selection best techniques (in this situation: rectum analysis in group of patients with LD=1.5 - 5 fields 3DCRT - developed by St Luc Brussels and 6 field IMRT - developed by MSK New York techniques were the best).

Conclusions

Anatomy-dependent parameters effectively facilitated the process of selection of the accurate technique for specified patient in clinical practice.

Posters Molecular Oncology

1019 poster

COMBINATION OF IRRADIATION AND KNOCK DOWN OF SURVIVIN VARIANTS IN TWO SOFT TISSUE SARCOMA CELL LINES UNDER HYPOXIC CONDITIONS

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Purpose/Objectif: Survivin is an essential protein for regular mitosis. The inhibitor of apoptosis survivin is overexpressed in several tumors and is a prognostic marker for soft-tissue sarcoma. The downregulation of survivin full length and survivin variant delta 3 and 2B expression via variant specific siRNA could be a suitable target for gene therapy approaches.

Materials/Methods: To test the impact of survivin expression for the hypoxic radiosensitivity we treated two soft tissue sarcoma cell lines (A 204, US 8-93) with different p53-gene status under hypoxic conditions. After siRNA application and a dose of 2-14 Gy we analyzed the clonogenic cell survival and applied quantitative real time PCR and western blot technique to detect the RNA and the protein expression levels after combined treatment.

Results: In both cell lines A204 (wt-p53) and 8-93 (mt-p53) hypoxia lead to an increase of radioresistence by the factor 2 to 4 (2 Gy until 6 Gy). The siRNA construct targeting full length survivin and 2B survivin caused a decrease of full length survivin mRNA and 2B mRNA as well as an decrease of survivin protein after hypoxia. The clonogenic cell survival was decreased up to 70 % in both cell lines. Only in the cell line A204 the survivin knock down caused a radiosensitisation with an enhancement factor of 1.9 (2 Gy) and 3.3 (4 Gy), respectively. At variant specific siRNA targeting the variants delta 3 and 2B induced a decrease of mRNA expression of the specific target mRNA. Both constructs reduced the clonogenic cell survival up to 25 %. The delta 3 specific construct lead to a higher radiosensitivity with an enhancement factor of 2.6 at a dose of 4 Gy, whereas at using the 2B construct the radiosensitivity was not changed under hypoxic conditions.

Conclusions: Altogether, we could show that the knock down of full length survivin lead to a radiosensitization in the wild type p53 cell line A204 under hypoxic conditions. The reduction of the other survivin variants delta 3 and 2B caused not a massive reduction of cell survival or a radiosensitization.

1020 poster

HYPERMETHYLATION OF GENES INVOLVED IN CELLULAR RESPONSE AFTER RADIOTHERAPY: INFLUENCE ON RADIOSENSITIVITY OF HNSCC CELL LINES

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Purpose/Objectif: Although the research of epigenetic phenomena such as promoter hypermethylation is a booming field in HNSCC among other tumor types, an influence on radiosensitivity has not been investigated yet. The present study aimed to explore the effects of hypermethylation of genes involved in cellular response after radiotherapy on the radiosensitivity of HNSCC cell lines.

Materials/Methods: Sensitivity of HNSCC cell lines to radiotherapy +/- demethylating agents +/- HDAC inhibitors was determined by sulforhodamine B and colony assays. Hypermethylation of genes involved in cellular response after radiotherapy was assessed by methylation-specific PCR (MSP) in these cell lines. This was performed for genes known to be possibly hypermethylated as well as for newly in silico selected candidate genes.

Results: The cell survival experiments revealed a possible radiosensitising effect of the HDAC inhibitor Trichostatin A for SCC-61.

So far, only SCC-61 showed a consistent methylation of $p16^{INK4a}$ by MSP. This hypermethylation has to be confirmed at the RNA and protein level and by demethylating experiments.

Conclusions: Trichostatin A may radiosensitise SCC-61, in which $p16^{INK4a}$ seems methylated as detected by MSP. After confirmation of this methylation, knock-out and knock-in experiments will have to evaluate the effect of $p16^{INK4a}$ methylation on radiosensitivity of SCC-61.

In addition, the methylation status for the selected cellular response genes, as well as the radiosensitising capacity of several demethylating agents and HDAC inhibitors will be assessed in other HNSCC cell lines.

These results will be presented at the time of the meeting.

1021 poster

LYMPHOCYTE RADIATION-INDUCED APOPTOSIS AS A PREDICTOR FACTOR OF POST-IRRADIATION TOXICITY IN IRRADIATED PROSTATE CANCER PATIENTS.

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Purpose/Objectif: Prediction of individual radiation sensitivity can be helpful to select which patients could receive higher doses of radiotherapy at acceptable risk and which patients should not receive doses over the standards. It can be particularly useful in those prostate cancer patients whose treatment objective is dose scalation. The aim of this work is to study CD4, CD8 and CD19 lymphocyte apoptosis in prostate cancer patients submitted to curative irradiation as prediction factors of post-irradiation toxicity, and their statistical significance.

Materials/Methods: Two blood samples were obtained from each patient. One of the tubes was irradiated with 6MV X-Rays at a single dose of 8 Gy. After irradiation, mononuclear cells from each blood sample were isolated and cultured in appropriate medium (RPMI, 10% FBS, 2 mM glutamine) for 48 hours. Apoptosis was measured by surface annexin V staining as previously described (Campàs et al. Blood 2003). To analyze apoptosis in B lymphocytes, 5 x 10^5 cells were collected from the culture, washed in PBS, and incubated in 50 mL annexin-binding buffer with and phycoerythrin (PE)-conjugated anti-CD19 for 10 minutes in the dark. Cells were then diluted with annexin-binding buffer to a volume of 150 mL and incubated with 1 mL annexin V-FITC for 15 minutes in the dark. To analyze apoptosis in TCD4+ and TCD8+ lymphocytes cells were incubated with both CyPE-conjugated anti CD3 plus PE-conjugated anti-CD4 or PE-conjugated anti-CD8, respectively. Data were analyzed using Cell Quest software (Becton Dickinson, Mountain View, CA). Acute toxicity was evaluated in all patients using the RTOG scale.

Results: Between March 2005 and April 2006 126 consenting patients with prostate cancer treated by curative radiation therapy were included in this study. We statistically analyzed lymphocyte toxicity and acute radiotherapy-induced toxicity data from 50 patients. Median age was 70 +- 4.89 years. The median dose was 72+-

3.38Gy. The toxicity GI were: 12% grade I, 48% grade II, 20% grade III, 20% no toxicity, and GU were 20% Grade I, 46% grade II, 12% grade III and 22% no toxicity. Following 8 Gy irradiation, median CD4, CD8 and CD19 apoptosis were 28,6% (range 3 to 49), 55,2% (range 15 to 79) and 72,7% (range 28 to 95). The relationship between acute toxicity and CD4, CD8 or CD19 apoptosis is shown in table 1.

Conclusions: Our results were similar to the bibliography. No statistically significant correlation was found between early toxicity and radiation-induced apoptosis in CD4- CD8 -or CD19- lymphocytes. Further investigation is required to analyze the correlation between chronic toxicity and sensitivity of lymphocytes to radiation

	Gastrointestinal				Genitourinary			
Acute toxicity	No toxicity	Grade I	Grade II	Grade III	No toxicity	Grade I	Grade II	Grade III
CD4 apoptosis %	28	27	30	27.3	21	29.3%	33.2	26.5.
CD8 apoptosis %	53.7	55	56	54.3	49.3	53.5	60	51.7
CD19 apoptosis %	74.4	71	70	77.5	67.6	72.6	74.8	75

1022 poster

MOLECULAR MARKERS IN CERVICAL CANCER PATIENTS TREATED WITH RADIOTHERAPY

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Purpose/Objectif: To evaluate a panel of molecular markers associated with different aspects of tumor biology in patients (pts) treated with radiation for cervical cancer.

Materials/Methods: Upon revision of medical records, 82 women who received radiotherapy at our institution between 1996 and 2004 as treatment for cervical cancer (predominantly FIGO stages IB2-III) were identified. 56 pts received concomitant chemotherapy. RACK1, p-Akt and MAPK were evaluated by immunohistochemistry in pre-treatment diagnostic cervical biopsies. The extent and intensity of staining were measured and an immunohistochemical score determined. Time to progression (TTP) was calculated from the date of diagnosis until the date of the first failure/progression. Survival curves of TTP as a function of pathologic characteristics, histologic type and IHC were compared by the log-rank method.

Results: 78 pts were analyzed: median follow-up was 19 months (3.2-97.1 months) and median age 62 years (31-89 years). Histology was squamous cell (SCC), adenocarcinoma (ADK) and other in 54, 22 and 2 pts, respectively. 57 pts achieved complete response. A low RACK1 IHC score was significantly associated with shorter TTP in the overall group (p=0.019). Following stratification by distant metastases and local recurrences as the first site of failure/progression, significance only remained for TTP(metastatic) in ADK (p=0.04). Local control was not affected by RACK1 expression. There was a significant correlation with higher p-Akt IHC score (p=0.024) for TTP(local) in the overall group. However, it was lost after segregating for histological subtype, presumably due to sample size. A weak MAPK IHC score was significantly associated with shorter TTP in the overall group.

Conclusions: The evaluation of a panel of biomarkers may strongly predict cancer pts outcome and overcome the limited ability of individual marker evaluation. Our preliminary data suggest that low RACK1 expression is significantly associated with distant failure in ADK-type cervical cancer treated with radiation therapy. However, p-Akt expression is statistically associated with local control in cervical cancer. Updated information including additional potential biomarkers will be presented at the meeting. Prognostic subgroups may be treated accordingly in risk-adapted protocols.

1023 poster

PROGNOSTIC SIGNIFICANCE OF IMMUNOHISTOCHEMICAL EXPRESSION OF CYCLIN B1 IN ORAL CAVITY CARCINOMA TREATED WITH SURGERY AND POSTOPERATIVE RADIOTHERAPY

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Purpose/Objectif: To assess the prognostic value of immunohistochemical cyclin B1 expression (CB-1) in 163 oral cavity carcinomas treated with radical surgery and postoperative radiotherapy.

Materials/Methods: Representative slides of surgical specimens were stained with a monoclonal antibody directed against CB-1. Slides were independently scored by two investigators, blinded for clinical outcome. In the univariate analysis with regard to locoregional control (LRC), distant metastases free interval (DMFI), disease-free survival (DFS) and overall survival (OS), curves were estimated using the Kaplan-Meier method. For the multivariate analysis, Cox-regression was used.

Results: Overexpression of CB-1 was present in 68 patients (42%). No significant associations were found between CB-1 expression and other pre-treatment variables, except for perineural invasion (48% in case of no vs. 27% in case of yes (p=0.01)). The 5-years LRC in the CB-1 positive cases was 82% versus 70% in the CB-1 negative cases (p=0.20). The 5-years DFS in the CB-1 positive cases was 48% versus 55% in the CB-1 negative cases (p=0.64). No difference between the CB-1 negative and positive cases was noted with regard to overall survival which was 51% and 57%, respectively. In the multivariate analysis, no significant associations were found between the expression of CB-1 and any of the endpoints.

Conclusions: Immunohistochemical cyclin B1 expression does not predict outcome in oral cavity carcinomas treated with radical surgery and postoperative radiotherapy.

Posters Monitor Unit Calculations

1024 poster

AN INDEPENDENT VERIFICATION OF MONITOR UNIT CALCULATION FOR STEREOTACTIC RADIOSURGERY PLANNING USING DYNAMIC CONFORMAL ARC TECHNIQUE

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Purpose/Objectif: A spreadsheet based method is implemented in our department to perform an independent monitor unit (MU) calculation verification for the Quality Assurance of stereotactic radiosurgery (SRS) planning using Dynamic Conformal Arc (DCA) technique.

Materials/Methods: A Varian Clinac 2100CD linac (Varian Inc, Palo Alto, CA) with an add-on micro- multileaf collimator (m3, BrainLAB AG, Heimstetten, Germany) was the system used to deliver SRS treatments (6MV), previously calculated them by the treatment planning system (TPS) BrainScan 5.3 (BrainLAB AG). DCA was the irradiation technique used consisting of a dynamic field shaping rotation therapy. Isocenter of the calculated plan was the reference

point selected to perform the verification of MU given by BrainScan. An independent MU calculation program (MUVerif) was designed using Excel software (Microsoft, Redmond, WA) requiring a number of input data taken from the plan in order to recalculate the dose predicted by the TPS: relative weigth, averaged equivalent depth of isocenter and the effective equivalent square of each arc involved in the plan. In addition, values of percent-depth dose distributions, scatter factors and absolute calibration extracted from the commissioning data of the SRS system were needed for the calculation.A verification of MUVerif was performed for the case of a cylindrical phantom with an embeded ion chamber by comparing the measured dose to isocenter (localizated at the center of the detector air cavity) with the corresponding calculated dose with MUVerif when it´s treated with the arrangement of a DCA plan calculated by BrainScan and delivering the MUs given by MUVerif program.
Results: The independent MU calculation verification was performed for 121 DCAs corresponding to 29 SRS treatment plans designed with BrainScan 5.3 TPS. The percent differences between the MU calculated by the TPS and the MU computed by the spreadsheet program were calculated for each one of the DCA involved in a same treatment plan. Over all the plans, the mean percent MU difference per arc was -0.6% with a SD of 1.1% (range -6.4-1.6%). The phantom based verification of MUVerif program was better than 1%.
Conclusions: From the mean difference and standard deviation found between the MU calculated by the spreadsheet program and the MU computed by the TPS for a considerable number of checks (121), a confidence limit of 3.0% can be establish in our routine practice in order to verify the MU calculation given by BrainScan for DCA treatments.

1025 poster

MONITOR UNIT CALCULATION USING THE MONTE CARLO-BASED ONCENTRA MASTERPLAN PLANNING SYSTEM

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Purpose/Objectif: One of the most important features of planning systems is the monitor units calculation. So far, these calculations were not precise enough for electrons, but with the introduction of Montecarlo algorithms an important improvement is expected. The aim of this work is to check the accuracy of Oncentra Masterplan to calculate monitor units of clinical electron fields.
Materials/Methods: 6, 9, 12, 15, 18 and 21 MeV electron beams of a Siemens Primus linear accelerator were studied. Oncentra Masterplan v 1.4.1.2 sp3 was used for calculations. This planning system uses a Coupled Multi-Source electron beam model for the space phase and a VMC++ algorithm for dose calculation.
Accuracy of calculations for different combinations of slices separations (2, 5 and 10mm) and number of histories per cm^2 (10000, 20000, 30000, 50000, 100000 and 200000) were studied. Calculation matrix was 2x2xslice thickness mm^3 . The calculation time was also stated.
Results: Results for more than 20000 histories did not show clear dependence with slice thickness and energy, but the lowest differences were found at 100000 histories. With this number of histories and in the whole range of slice thickness, the lowest error found in calculations was at 6MeV (0.2%), and the highest at 12MeV (1.1%).
10000 and 20000 histories did not show clear dependencies with slice thickness or energy, but their range of deviation was the highest between different values of slice separation (up to 2.5%).
The range of absolute deviations in monitor units calculations was a 0.15% for a number of histories of at least 30000.
The calculation time increased with energy and linearly with the number of histories, but did not show significant changes with the slice thickness.
Conclusions: A combination of a low number of histories (less or equal to 30000) and slice thickness of 2mm seem not to be good for accurate calculations of monitor units. For high energies, where calculation time is increased, a low number of histories can be used, but at least 30000 are needed. A balance of number of histories and calculation time must be considered in clinical situations. For clinical dosimetry, slice separations of 2mm are not needed, and the lowest differences were obtained with 5 and 10 mm.

1026 poster

SATURATION EFFECTS IN ION CHAMBER DOSIMETRY FOR TOMOTHERAPY

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Purpose/Objectif: Commissioning and QA checks of a TomoTherapy HiArt machine include dosimetry based on measurements with an Exradin A1SL ion chamber. Tomotherapy recommends a polarising potential to be applied to this chamber of -300 V with a corresponding correction factor to account for the effects of ion recombination of 1.01. Our goal is to investigate the ion recombination effects for 3 ion chambers: the exradion A1SL, the NE2571 and the NE2611, the two last ones being reference ion chambers in Europe.
Materials/Methods: Ion recombination measurements for these 3 ion chambers have been performed in a static Tomotherapy beam, in a continuous 60-Co gamma beam, and in the pulsed beam from the NPL linear accelerator.
Results: We find good agreement between the measured saturation and a theoretical model only if the effects of charge multiplication are taken into account as well as initial and general recombination. Charge multiplication becomes apparent in the A1SL measurements when the polarising potential increases beyond -100 V. Charge multiplication is negligible for the NE2571 and NE2611 chambers when used at their recommended polarising potentials, respectively -250 V and -200 V, however becomes apparent when the NE2571 is used at a polarising potential of -300 V. We note that this and other Farmer-type chambers are sometimes used at a polarising potential of -400 V, and would expect charge multiplication effects to be significant in that case.
Conclusions: Charge multiplication is essentially independent of dose rate, and is liable to confuse the interpretation of measurements made using the two-voltage technique. This risk is increased when measurements are made using an electrometer that cannot provide more than two distinct polarising voltages. From our experimental and theoretical investigation we conclude that the saturation correction factor for measurements made in a Tomotherapy beam should be not more than 1.003, 1012 and 1.015 for the A1SL, NE2571 and NE2611 chambers with polarising voltages of -300 V, -250 V and -200 V respectively.

Posters Monte Carlo Methods in Treatment Planning

1027 poster

EFFECT OF THE GEOMETRY ON THE DOSIMETRIC PARAMETERS OF THE ^{125}I BRACHYTHERAPY 6711 SEED

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Purpose/Objectif: In the past few years, Monte Carlo (MC) simula-

tions have appeared as a powerful tool to assess the details of dose deposition processes both in external radiotherapy and in brachytherapy. However, the accuracy of results obtained by this method highly depends on the accuracy of the geometrical parameters used in the simulations. This is particularly significant when seeds, used in brachytherapy prostate permanent implants, are simulated. It is known that different seeds from the same model may have geometrical parameters slightly different due to the fabrication process. This can explained why various MC and experimental studies reveal quite large differences regarding the dosimetric parameters as observed in one of the most studied type of seed: the ^{125}I model 6711 from Amersham.

Materials/Methods: The MC code Penelope 2005 was used in the simulations. In order to observe the effects of the seed geometry on the dosimetric parameters, some of the 6711 geometrical parameters were modified such as the length and radius of the silver rod and the titanium capsule, resulting then in various 6711 sub-models to simulate. In all sub-models the source distribution is the same (TG43 update spectrum). Radial and anisotropy dose functions were calculated using a simulated water phantom. Finally, dose rate calculations were performed using simulated spectra determined in vacuum at 1m from the seed center.

Results: Simulations showed that the dose rate constant does not vary significantly when varying the geometrical parameters (less than 1%). The most significant differences were found in the anisotropy dose function results, in particular for small polar angles where differences can reach up to 15% at 1cm.

Conclusions: This study has shown that even small variations in the geometrical parameters of the 6711 seed model can have a great influence in the anisotropy dose functions at small polar angles. Combined with the fact that most of the actual treatment planning systems used in seed prostate implants do not take into account the 3D seed orientation, the delivered dose distribution in the patient can be substantially different from the planned one. More investigation is necessary to solve this type of issue.

1028 poster

IMPLEMENTATION AND VALIDATION OF AN ADD-ON MLC FOR MONTE CARLO DOSE CALCULATIONS IN CONFORMAL STEREOTACTIC RADIOSURGERY

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Purpose/Objectif: The objective of this study was the implementation and validation of an add-on MLC, with 40 leaves of 2.5 mm width in the isocentre, for an Elekta SL25 accelerator into the monte carlo BEAM code and MCDE Monte Carlo dose engine for 6MV quality photon beams. For the stereotactic radiosurgery of intracranial tumors, a spatial accuracy of 2mm and dose delivery of 2% is required. This can not be realised by a standard MLC with leaf width of about 1cm (isocentre). Therefore an add-on mini MLC with a leaf width of about 2.5 mm (isocentre) is recommended, following the considerations and results in the literature [1,2].

Materials/Methods: The monte carlo calculations were made in the EGSnrc BEAMnrc/dosxyznrc and MCDE code [3]. The accelerator head is modelled in BEAMnrc and the dose deposition in the phantom is handled in dosxyznrc. MCDE is an in-house developed calculation engine which combines the BEAMnrc and dosxyznrc code for the beam delivery calculation of clinical patient treatment plans. The add-on MLC component, which has a design without tongue and groove, is based on the MLCE component module. Starting from the technical data, several approximations concerning leaf geometry were made in the simulated geometry to obtain optimal correspondence with the measured results. The calculations in the clinical treatment planning system Pinnacle 7.4f are based on a collapsed cone convolution algorithm. The profiles were measured with a diamond detector, as larger cylindrical chambers do not have adequate spatial resolution for the smallest fields. Depth dose curves were measured with a cylindrical chamber.

Results: An integrated transmission of 1.13% was measured and reproduced in the calculations. Several half beams and irregular shaped fields have been measured and reproduced within 2% and 2mm. The measured square field output factors of the fields ranging from 10x12cm to 0.5x0.5cm are also reproduced in the calculations within 2%. The device was implemented in the MCDE dose computation code for quality assurance of the clinical planning system, for which the results will be presented.

Conclusions

An add-on MLC for conformal stereotactic radiosurgery was implemented and validated in the MCDE Monte Carlo dose engine code. This has been done for quality assurance of the clinical treatment planning system, and quantification of the dosimetrical advantages of the add-on MLC.[1] Bortfeld et al (2000) Med. Phys. 27, 11, 2494-2502[2] Ramaseshan (2003) Phys. Med. Biol. 48, 14, N199-N205[3] Reynaert et al (2004) Phys. Med. Biol. 49, 14, N235-N241

1029 poster

MONTE CARLO SIMULATION OF THE TOMOTHERAPY TREATMENT UNIT IN THE STATIC MODE USING MC_HAMMER, A MONTE CARLO TOOL DEDICATED TO TOMOTHERAPY

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Purpose/Objectif: Tomotherapy treatment unit is designed to deliver highly modulated IMRT treatments. Because of the complexity of the treatment, inaccuracies may occur for convolution/superposition based algorithms, specially in inhomogeneities. Monte Carlo (MC) calculations' validity, instead, is not limited by the complexity of the treatment and it is therefore a tool of choice to calculate accurately dose distribution provided by IMRT treatments, specially in a highly heterogeneous media (head and neck tumors, ...). Helical Tomotherapy is a relatively new technique for delivering IMRT. Tomotherapy "HI-ART" has several engineering aspects which are different from conventional C-arm linear accelerators. The 6 MV photon beam rotates around the patient on a gantry similar to a CT scanner gantry. A binary multi-leaf collimator is capable of delivering the most complex treatment plans. This concept of Tomotherapy provides new challenges in MC simulations, since simultaneous movement of the gantry, the couch and the multi-leaf collimator (MLC) must be simulated accurately. However, before accounting for gantry and couch movement, high accuracy must be achieved while simulating the static mode (gantry and MLC are not moving during irradiation).

Materials/Methods: MC_HAMMER is a graphical user interface allowing MC simulation for various configurations of the Tomotherapy treatment unit. MC_HAMMER code has the possibility to simulate beam generation, all the jaw openings and any configuration of the multi leaf collimator (MLC). It is based on the PENELOPE code, which can simulate any geometry configuration, provided that the different elements of the geometry are delimited by quadric surfaces. Since we have very precise knowledge of the geometry of the different elements and materials involved in the beam generation, negligible approximations are made in our MC geometry input file. The only parameters that can be tuned on are therefore electron source spot size and electron energy. Electron energy is determined matching calculated and measured depth dose for the wider field size whereas electron spot size is determined in first approximation

by matching measured and calculated profiles. The simulation is divided into three parts. Firstly, we run a simulation through the target and the jaws for three different field sizes (1, 2.5 and 5 cm field width, 40 cm length), providing one phase space file. Secondly, the particles of this phase space are transported through the MLC, giving another phase space below the MLC, which may be used then to calculate dose distributions into water phantoms (and, in the future, CT scans).

Results: The first results show good correspondence between MC results and measurements. Nominal energy has been found to be equal to 4.8 MeV. We determined also precisely the opening of the jaws with respect to the MLC model in order to give good results whatever the positions of the leaves are. As soon as the static mode is commissioned, gantry's rotation and couch's movement will be simulated by changing the origin of the phase space files, each one being calculated for a specific configuration of the MLC.

1030 poster

SHOULD MONTE CARLO BECOME THE STANDARD POST-IMPLANT DOSE CALCULATION METHOD?

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Purpose/Objectif

Available algorithms assume that the target volume and surrounding tissues consist of water, including the sources. This has profound consequences for the energy ^{125}I implants, as the interaction process is dominated by photoelectric effects. In this study, it is shown that clinical post-implant dosimetry using water-based AAPM TG43 leads to significant discrepancy compared to the Monte Carlo (MC) method.

Materials/Methods

This study looks at 21 patients with dose assessments based on CT exams conducted one month post-implant. Prostate, urethra, rectum and bladder were contoured by the treating physicians and the seed positions reconstructed. A commercial package, SPOT-PRO (Nucletron), was used for routine clinical dose calculation based on TG43. All CT images and structures (contours and seed positions) were exported from SPOT-PRO using DICOM-RT. The DICOM-RT files were input in a MC toolkit. The DVHs were evaluated for: 1- MC calculation in water, taking into account inter-seed attenuation only and 2- complete MC calculation, taking into account tissue density/composition from the CT scan and inter-seed attenuation. In the latter MC dose calculation, over 180 different materials (prostate tissue, muscle, ...) are utilized for each patient. MC DVHs and dose parameters for each organ were compared to clinical TG43 reported dosimetry.

Results

The inter-seed attenuation leads to statistically significant decreases of all dose parameters to the prostate and urethra. For CTV D90 this corresponds to an average attenuation of 4.6% (max 8.6%). Urethra V100 and V150 decrease by 3.4% and 4.7% respectively. When a complete MC dose calculation is considered, the decrease in D90 is even more pronounced and averages 13.8±0.9 Gy with a wide range of differences compared to TG43 going from 5.8 Gy to 20.7 Gy. In terms of relative differences, this corresponds to a mean change of 8.1%. For the urethra, V150 is reduced by 23% on average relative to SPOT-PRO, ranging from an increase of 5.7% to a decrease of 43%. These changes are significant based on paired Student t-tests. For the rectum and bladder, clinical parameters linked to toxicity, such as the absolute volume receiving large doses, are investigated. The changes in bladder (rectum) V100 are usually below 1 cm^3, but correspond to variations in volume going from an increase of 414% (174%) to a decrease of 98.9% (35%).

Conclusions: The differences between clinical TG43 and MC are significant. Almost half of the change in target D90 is due to inter-seed attenuation, the remaining difference is due to effective tissue density and composition. There are large variations between TG43 and MC pointing to variations in density of the organs from patient-to-patient. Moreover, small volumes of high doses to organs at risk are also strongly affected. These results point to potential deficiencies in the current clinical dose-outcome correlation studies. In this context, MC calculation should become the standard method for reporting clinical post-implant dose parameters.

1031 poster

STUDY OF R50, R85 AND PROFILES OF ELECTRON BEAMS CALCULATED BY A COMMERCIAL MONTE CARLO-BASED PLANNING SYSTEM

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Purpose/Objectif:

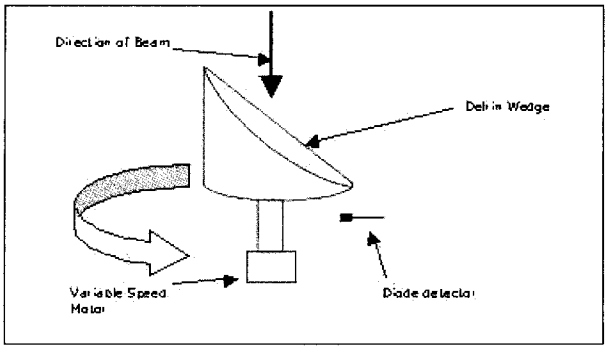
Energy parameters are critical when electron beams are used in radiotherapy. From IAEA TRS-398, the energy of the beam is described by R^{50}. Furthermore, from ICRU Report 71, R^{85} is used to decide which energy is the best to treat the PTV. New commercially available planning systems calculate this parameters using Montecarlo algorithms. The aim of this study is to check the accuracy and variations of both R^{50}, R^{85} and profiles, due to changes in the initial conditions of the calculation algorithm. These conditions are the number of histories by square centimeter and slice separation of the phantom.

Materials/Methods: 6, 9, 12, 15, 18 and 21 MeV electron beams from a Siemens Primus linear accelerator have been studied. Measurement of reference parameters was done by means of a semiconductor detector and Scanditronix RFA-300 3-D phantom and its software. The checked planning system was an Oncentra Masterplan, that uses a Coupled Multi-Source electron beam model for the space phase and a VMC++ algorithm for dose calculation. Differences in R^{50} and R^{85} depths obtained from depth dose curves were analyzed. The flat regions of profiles were compared using the mean of maximum observed differences. Phantoms of 2.5, 5 and 10mm slice separation were used for calculations and the number of histories varied in the range of 10000 and 100000 hist/cm^2. In all cases a calculation matrix of 2x2mm^2 was used.

Results

R^{50}: Observed variations in depth were less than 1 mm in all cases.
R^{85}: Results for 6, 9 and 12 MeV were independent of number of histories and slice separation. For higher energies, the maximum difference was 3mm for a low number of histories (10000). At least 50000 histories are needed to reach an error less than 1mm. Furthermore, differences were greater for low slice separations (2mm) and decreased when slice thickness increased. Profiles: Results were independent of slice separation but showed important variations with the number of histories. Differences for 10000 and 100000 histories were near to 4% and 2.5% respectively.

Conclusions: Calculation of R^{50} is very accurate independently of number of histories and slice separation. A low number of histories, between 10000 and 50000, minimizes calculation time and can be accurate enough for clinical dosimetry to find therapeutic range at low energies (6,9 and 12MeV) because calculation shows to be independent of all the parameters studied. For higher energies calculation of R^{85} should be performed with at least 50000 histories per cm^2. Where precision in isodose calculation is needed, at least 100000 histories should be used, independently of energy.



1032 poster

VIRTUAL PHOTON SOURCE DEFINITION IN MCNP4C MONTE CARLO CODE FOR DOSE CALCULATION

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Purpose/Objectif: The major drowback of clinical uses of Monte Carlo dose calculation is the time that is needed for particle transpotation through the Linac head, spatially generation of of bremsstrahlung photon beam. Definition of virtual photon source can reduce time of dose calculation in Monte Carlo method. the verification of this source is depending on accuracy of radial, angular and energy distribution photon fluence. defined virtual source must be efficient and procide accurate result.

Materials/Methods: Virtual source is defined by isocenter circles with increasing distance 0.5cm from the beam central axis up to 3.5cm under target and primary collimator. Radial, angular and energy distribution of bremsstruhlung photon beam is computed after complete stimulation of particle transpotation that is reached to scoring plates. Virtual source varities are derived from the different intervals of any distributions . as a result we intruduced minor and major for each distribution . Radial distribution s difined by two methods one by area ratio and the other by infuence ratio on each sub-source. 16 virtual sources are defined for each scoring plates totally. the method that is used for verification of each sources are defined for each scoring plates. the method that is used for verification of each source is based on absorbod dose comparisons of measuredand calculated depth-dose and dose- profile curves. the influence of MCNP4C Monte Carlo code parameters for production of bremsstrahlung photon beamand accuracy of definwd virtual source are also investingated. THe infuence of PHYS card on accuracy and efficiancy was investigated

Results: Depth dose and dose profile were affected by minor angular distributions than major ones spatially for source under taget. less influence was observed in depth dose profile or depth dose curves with respect to energy spread variations. Radial distibution that is defined by influence ratio is provided better results than area ratio. the accuracy of Monte Carlo results can be able to produce absorbed dose distribution with accuracy +_2% for depth dose and +-2 mm for depth dose profile.

Conclusions: The findings in this study indicated that we can define phase -space for MCNP4C with tally 1. we can use the resulted stimulation for defining of accurate and efficient virtual source.

Posters Normal Tissue Morbidity

1033 poster

3DRT OR IMRT IN PROSTATE CARCINOMA: HIGHER IMPACT OF INTERMEDIATE DOSES ON LATE RECTAL TOXICITY (LRT)

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Purpose/Objectif: Late rectal toxicity (LRT) represents the main limit for curative radiotherapy of prostate carcinoma. Different dose/volume constraints have been proposed to lower the incidence of this common complication. However, outcomes of the various studies differ for optimal dose-volume limits to be used. Aim of this analysis is to evaluate the impact of different dosimetric parameters on LRT in a population of patients consecutively treated with curative intent.

Materials/Methods: One-hundred consecutive patients with non-metastatic prostate carcinoma treated with 3D-RT (84) or IMRT (16) were included in the analysis. All patients received 1.8 Gy/fraction, with total dose ranging between 70.2 Gy and 73.8 Gy. Follow-up visits were scheduled every 6 months after radiotherapy. DVH were obtained (PLATO, Nucletron, The Netherlands) and for every patient rectal D_{max}, D_{mean}, V_{40Gy}, V_{50Gy}, V_{60Gy} and V_{70Gy} were recorded. Based on different cut-off values (median and incremental values with 10% steps) of these parameters, patients were compared for actuarial cumulative incidence of LRT (> grade 2, RTOG-EORTC scale), evaluated using the Kaplan-Meier method; curves were compared using the log-rank test.

Results: Two-year LRT ≥ grade 2 was 16.4%. No significant correlations were observed between V_{70Gy} and LRT, and between rectal D_{max} and LRT. However, both V_{50Gy} (using as cut-off values 70% [p=0.047] and 80% [p=0.043]) and V_{60Gy} (using as cut-off value 50% [p=0.044]) showed a significant correlation with LRT. Mean rectal dose, using as cut-off value the dose of 60 Gy, showed a significant relationship with the incidence of LRT (D_{mean} ≤ 60 Gy: 2-year LRT = 7.3%; D_{mean} > 60 Gy: 2-year LRT = 34.4%; p=0.018).

Conclusions: Significant differences in LRT incidence were observed using dose-volume rates in the range of 50-60 Gy. Furthermore, mean rectal dose > 60 Gy had a significant impact on LRT. Maximum rectal dose and V_{70Gy} did not show any significant impact on LRT. These data confirm the parallel functional organization of the rectum, and the predictive value of DVH on LRT.

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CARDIAC, PULMONARY AND SPINAL CORD DOSES AND RELATED NTCPS DURING 3D CONFORMAL RADIOTHERAPY OF OESOPHAGUS CANCER

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Purpose/Objectif: From 1996 we have used high dose (66Gy/33 fractions) conformal radiotherapy (RT) concomitant with chemotherapy as neoadjuvant or definitive treatment for cancer of the oesophagus. In this study, we have investigated the dose distributions and related normal tissue complication probabilities (NTCPs) for the heart, lungs and spinal cord for this RT procedure.

Materials/Methods: Since 1996, we have treated 81 patients. We have analyzed the results for 13 patients treated in 2005 and winter 2006. Dose-volume histograms were calculated for the first phase PTV prescribed 50 Gy (PTV1: 1.5 cm lateral and 3 cm cranial and caudal margins), the second phase PTV prescribed additional 16 Gy (PTV2: 1 cm uniform margins), heart, lungs and spinal cord. Both phases of the treatment were delivered in 2 Gy fractions, with 5 fractions/week without intervals using a CT-based 4-field conformal set-up with two opposing anterior/posterior fields and two posterior/anterior oblique lateral fields. NTCP calculations were performed using the probit NTCP model with parameters from Burman et al (IJROBP 21:123-135, 1991) for both the first phase to 50 Gy and for the total plan 66 Gy (endpoints: pericarditis and pneumonitis).
Results: The minimum PTV1 dose was on average 46.63 Gy, and ranged from 44.2 to 48.02 Gy, while the average maximum dose was 52.8 Gy (range: 51.6 - 53.9 Gy). On average 0.5% of PTV1 received < 95% of the PTV1 target dose (50 Gy). The minimum PTV2 dose average was 61.8 Gy (range: 59.6- 63.9) while the average maximum dose was 69.3 Gy (range: 67.4 - 70.8). On average 1.7% of the PTV2 volume received < 95% of the target dose (66 Gy). The overall mean cardiac dose was 31.8 Gy. About 43 % of the heart volume received ≥ 40 Gy (which is TD5/5 for the whole organ). The average dose to the right lung was 11.6 Gy, and 23.1 % of the right lung received ≥17 Gy (TD5/5 for whole lung is 17.5 Gy). The average dose to the left lung was 10.5 Gy, and 21.3% of the left lung received ≥ 17 Gy. The average maximum dose to the spinal cord was 45.1 Gy, and all patients had field lengths shorter than 20 cm (TD5/5 for 20 cm is 47 Gy). Further DVH parameters and NTCP predictions for the organs at risk are listed in the table.
Conclusions: The applied treatment technique gave good target volume coverage. The technique allowed for dose escalation up to 66 Gy with acceptable doses to the organs at risk, although the cardiac NTCPs may indicate that the treatment may induce an increased risk for cardiac adverse effects.

	Heart	Right lung	Left lung	Spinal cord
Rel volume ≥ 10 Gy (%)		40.2 (20.9-64.4)	40.1 (20.0-60.0)	
Rel volume ≥ 15 Gy (%)		27 (13.4-53.2)	25.7 (14.1-47.9)	
Rel volume ≥ 17 Gy (%)		23.1 (10.8-50)	21.3 (11.6-44.6)	
Rel volume ≥ 20 Gy (%)	63.7 (32.2-82.0)	17.2 (7.5-39.4)	15.2 (5.5-34)	
Rel volume ≥ 25 Gy (%)	59.3 (23.4-78.5)	12 (2.4-25.8)	10.2 (4.0-21.8)	
Rel volume ≥ 30 Gy (%)	54.9 (19.5-75.59			
Rel volume ≥ 40 Gy (%)	42.6 (11.8-68.1)			
Rel volume ≥ 50 Gy (%)	17 (7.5-24.8)			
Rel volume ≥ 60 Gy (%)	8.7 (3.0-13.5)			
Rel volume ≥ 70 Gy (%)	0			
Maximum dose (Gy)				45.1 (39.8-48.4)
NTCP 50 Gy dose (%)	0	0	0	
NTCP 66 Gy dose (%)	12 (0-35)	2 (0-16)	1 (0- 5)	

1035 poster

CHANGE IN THE EXPRESSION OF FIBRONECTIN, PAI-1, MMP BY RADIATION IN RAT GLOMERULAR EPITHELIAL CELLS

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Purpose/Objectif: Renal irradiation can lead to the development of radiation nephropathy, and this is characterized by the accumulation of extracellular matrix and final fibrosis. To determine the possible role of the glomerular epithelial cell, the radiation-induced changes in the expression of genes associated with the extracellular matrix were analyzed.
Materials/Methods: Rat glomerular epithelial cells (GEpC) were irradiated with a single dose of 0, 2, 5, 10 and 20 §í with using 6 MV LINAC (Siemens, USA), and the samples were collected 6, 24, 48 and 72 hours post-irradiation, respectively. Northern blotting, western blotting and zymography were done to measure the expression level of fibronectin (Fn), plasminogen activator inhibitor-1 (Pai-1), matrix metalloproteinases-2, 9 (MMP-2, 9), tissue inhibitor of metalloproteinase-2 (TIMP-2), tissue-type plasminogen activator (t-PA) and urokinase-type plasminogen activator (u-PA).
Results: Irradiation with 10 Gy resulted in a significant increase in Fn mRNA since 24 hours post-irradiation, and a significant increase in the Fn immunoreactive protein 48 hours post-irradiation. An increase in Pai-1 mRNA and protein was also observed by irradiation of 10 Gy and especially, the mRNA significantly increased 24 and 48 hours post-irradiation. The active MMP-2 measured 24 hours post-irradiation slightly increased in a dose dependent manner, but this increase did not reach statistical significance. The levels of MMP-9, TIMP-2, t-PA and u-PA appeared unaltered after irradiation.
Conclusions: Irradiation of the glomerular epithelial cells altered the expression of genes associated with the extracellular matrix, implying that the glomerular epithelial cell may be involved in the development of radiation nephropathy.

1036 poster

DELAYED ADMINISTRATION OF GROWTH FACTORS IN A MOUSE MODEL OF RADIATION-INDUCED KIDNEY DYSFUNCTION

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Purpose/Objectif: To test whether insulin-like growth factor-1 (IGF-1) or granulocyte colony-stimulating factor (G-CSF) stabilize or improve radiation-induced kidney dysfunction.
Materials/Methods: Animal experiments were conducted to test the role of delayed growth factor administration in a well-established C3H mouse model of unilateral single-fraction kidney irradiation (Andratschke N et al., Int J Radiat Oncol Biol Phys 2006, epub) and to assess the effects of IGF-1 and G-CSF. The kidney function was assessed prior to radiotherapy and in intervals of 6 weeks by means of 99mTc-dimercaptosuccinat scans (static scintigraphy). Growth factors were administered subcutaneously once daily incl. weekends to groups of at least 8 mice. Treatment started 49 weeks after irradiation, i.e. during progressive deterioration of the function of the irradiated kidney. At baseline, the irradiated kidney contributed 50-55% to the total kidney function in all mice. Before start of growth factor treatment, the remaining contribution was at least 25% in all but one animals.
Results: Follow-up from first growth factor administration was 12 weeks. Injection of IGF-1 improved kidney dysfunction in 25% of mice (stabilization in 33%, continuous deterioration in 42%). Injection of G-CSF improved kidney dysfunction in 38% of mice (stabilization in 25%, continuous deterioration in 38%). The difference between the two growth factors was not statistically significant. Improvement was defined as an increase of the contribution of the irradiated kidney to total kidney function by at least 4%, because deviations of up to 3% might occur when examining the same animal repeatedly with this method.
Conclusions: Administration of growth factors after radiotherapy might influence the progressive development of nephropathy. Further studies with earlier start of treatment are required to obtain a longer follow-up and to judge the durability of this effect.

1037 poster

DIRECT RADIOGENIC DESTRUCTION OF COLLAGEN

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Background: Fibrosis of vessels and soft tissue are side effects of radiotherapy. We assumed that there is an immediate direct radiogenic damage of collagen of bone, periosteum, teeth and skin. We set out to assess the concentrations of Hyp, HP and LP in the pulp and hard tissue of irradiated and non-irradiated human teeth and porcine jaws to clarify whether the collagen component was affected.

Materials/Methods: A total dose of 31.5 Gy was applied on 40 human third molar teeth in vitro (cobalt 60, single dose: 6.3 Gy/day), 40 further teeth remained untreated (group 2). We exposed 15 porcine jaw probes to a total dose of 60 Gy (cobalt 60, 2 Gy/day, 5 fractions/week). 15 jaw probes were stored accordingly (group 2, no irradiation, control). Collagen fragments (split collagen) of mineralized teeth tissue, pulp tissue, skin, bone and periosteum of the irradiated probes and none irradiated groups were isolated by ultrafiltration and pooled separately for each experimental group. Measurement of mature collagen cross-links hydroxylysylpyridinoline (HP) and lysylpyridinoline (LP) by high performance liquid chromatography (HPLC) was used to determine the ratio of the amount of collagen fragments of irradiated over non irradiated experimental groups. Collagen types were characterized by SDS-PAGE (Sodiumdodecylsulfate-Polyacrylamidegelelectrophoresis).

Results: The concentrations of HP, LP and Hyp (hydroxyproline) in ultrafiltrates of probes of irradiated of pulp, bone, periosteum and skin were significantly increased as compared to non-irradiated probes. No significant difference was found between the concentration of collagen cross-links in probes of mineralized teeth tissue. SDS Page did show Collagen types I and V in non irradiated bone, I and III in non irradiated skin and I in non irradiated periost samples. In irradiated samples smeared bands illustrated fragmentation of the collagen molecule.

Conclusions: Irradiation did not measurably affect the extent of collagen destruction of mineralized dental tissue, which may be due to relatively low concentration of this protein in dentin and enamel. The increased concentrations of HP, LP and Hyp in ultrafiltrates indicated increased concentrations of split collagen. Direct and instant radiogenic damage of (extracellular matrix) of pulp tissue, bone, periost and skin tissue collagen could be demonstrated. This is proof of direct and instant radiogenic damage of components of the extracellular matrix.

		Irradiation	HP [pmol/ml]	LP [pmol/ml]	Hyp [µg/ml]
Skin	pellet (non-split-collagen)	yes (group 1)	8500	1200	102700
		no (group 2)	8850	1250	103020
		Ratio	**0.96**	**0.96**	**1.00**
	ultrafiltrate (split collagen)	yes (group 1)	1700	230	35650
		no (group 2)	1097	144	15968
		Ratio	**1.55**	**1.60**	**2.23**
Periost	pellet (non-split-collagen)	yes (group 1)	12750	1000	21350
		no (group 2)	13250	1100	23850
		Ratio	**0.96**	**0.91**	**0.90**
	ultrafiltrate (split collagen)	yes (group 1)	2499	182	6708
		no (group 2)	1617	129	3792
		Ratio	**1.55**	**1.41**	**1.77**
Bone	pellet (non-split-collagen)	yes (group 1)	9614	3219	22017
		no (group 2)	9672	3219	18910
		Ratio	**0.99**	**1.00**	**1.16**
	ultrafiltrate (split collagen)	yes (group 1)	4786	763	11640
		no (group 2)	1297	415	3423
		Ratio	**3.69**	**1.84**	**3.40**

1038 poster

DOES RADIATION PREVENT 5-FLUOURACIL INDUCED COLITIS?

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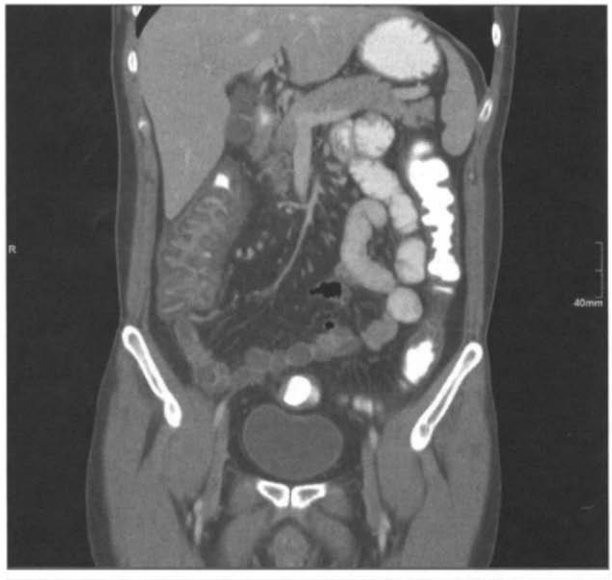
Purpose/Objectif: Preoperative radio-chemotherapy (RCT) for rectal cancer is usually well tolerated. Nevertheless, we observed a severe colitis in a patient receiving 5-Fluouracil (5-FU) and Mitomycin C (MMC) concomitant to preoperative radiation. Interestingly, only colon not irradiated showed signs of inflammation.

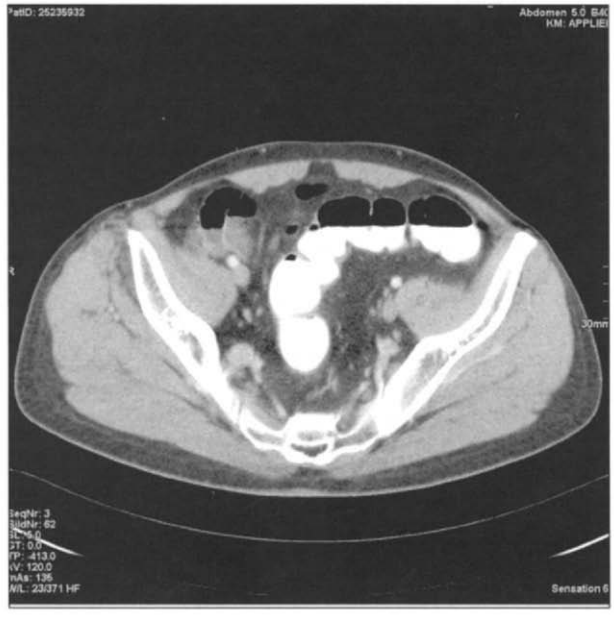
Materials/Methods: A 43-year old man in excellent general condition with an adeno-carcinoma of the lower rectum stage cT3 cN2 M0 was admitted for preoperative RCT. There was no history for stomach and for bowl disease. He was scheduled to receive 50·4Gy (5x1·8 Gy/week) to the pelvis. Concomitantly we administered 350 mg/m^2 5-FU over 24 hours and 200 mg/m^2 Leucovorin within one hour, both on days 1-5 and 8-12; 12 mg/m^2 MMC within one hour were given on days 5 and 12.

Results: On day 10 of the treatment course the patient complained of abdominal pain and developed severe diarrhea. Stool cultures, test for CMV-antigen and Dihydropyrimidin Dehydrogenase (DPD) mutation in the exon-14-section of the DPD-gene were all negative. Computed tomography showed a severe colitis involving ascendens, transversum and descendens (Fig. 1). This was confirmed by endoscopy and appropiate biopsies. Interestingly the colon sigmoideum and the rectum showed no signs of inflammation (Fig. 2). Thus, colitis was exactly restricted to unirradiated colon as confirmed by matching our CT-guided conformal radiotherapy treatment plan with all other diagnostic results. RCT was paused for six days and the patient received cefotiam (2 g BID), metronidazol (0·5g BID) for seven days. He recovered and radiotherapy could be continued. Surgery confirmed ypT3 ypN2 G2 adeno-carcinoma of the rectum that was resected with clear margins due to tumor regression by radiochemotherapy.

Conclusions: To our knowledge severe acute colitis sparing the irradiated parts of the colon has not been published before. Because there was no evidence for an infectious disease, the colitis was most probably induced by 5-FU. Severe colitis provoked by 5-FU is a rare side effect. The largest published series of which comprises only 6 patients.[1] Given a extremely complex mechanism of action and metabolism of 5-FU, its mode of action is not yet understood in full detail. Nor even less the pathogenesis of 5-FU induced colitis has been determined. For example one of the key enzymes in 5-FU metabolism is DPD, but missing evidence for a DPD-exon-14-mutation does not exclude other mutations and conditions leading to low enzymatic DPD activity as DPD-levels can vary six-fold in a population. Additionally, mutations of the p53 tumor suppressor gene and microsatellite instability can modulate 5-FU effects.[2,3] 5-FU has documented synergistic reactions with radiation including a moderate increase of side effects, but the exact mechanism of interaction remains unclear so far.[2] However, in this respect it is of particular interest that our patient experienced strong side effects out of the radiation field in the early phase of RCT in terms of an extensive mucosal inflammation, while no in-field side-effects occured. This may be explained by the well known anti-inflammatory nature of low dose radiation, including functional radiation effects and direct anti-inflammatory radiation effects.[4] As an example for functional anti-inflammatory effects by irradiation Forster et al. demonstrated a decrease of adhesion of peripheral blood leukocytes onto inflammatorily activated endothelial cells. This could be shown for doses of 0·3 up to 2 Gy.[5] A directly anti-inflammatory mechanism is the effect of low dose radiation on the intracellular nitric oxide (NO) production. NO as an important mediator of inflammation is produced by the inducible form of the NO synthase (iNOS).[6] This enzyme occurs at high levels not only in macrophages but also in the gastrointestinal mucosa in status of inflammation.[7] Hildebrandt et al. showed in an in vitro

model that the NO production in stimulated macrophages can be significantly decreased by low single radiation doses between 0·3 and 2·0 Gy, whereas it is increased by doses >2·5 Gy. The attenuated NO production lasted up to 30 hours.[8,9] Given these observations we hypothesize that in our patient the 1.8 Gy per fraction diminished 5-FU inflammation by attenuating NO production in early phase of RCT. However with an increasing cumulative dose this radiation effect is reversed.4 The fact that steroids develop anti-inflammatory activity in non-infectious enteritis by inhibiting the expression of iNOS in the ileum and colon may support our hypothesis.[7,10] From clinical point of view it appears worthwhile to separate side effects of RCT into radiation and chemotherapy induced. Ommitting distinct interpretation of our observations could led to the wrong assumption that the patient suffered during the early phase of RCT because he received a combined treatment with probably increased synergistic side effects. This differentiation seems to have an impact on planning individual therapy as we did not found any evidence for an increased radiosensitivity in our patient and therefore no reason to abandon radiotherapy in the preoperative setting of this patient. With respect to the current literature and to our clinical findings we suggest that iNOS may play a role in 5-FU induced colitis. Further, the anti-inflammatory effect of low dose irradiation may attenuate this colitis in the early phase of a RCT.





1039 poster

LATE GENITO-URINARY MORBIDITY AFTER 3D CONFORMAL RADIOTHERAPY FOR PROSTATE CANCER: ABSENCE OF DOSE AND DOSE-VOLUME EFFECT?

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Purpose/Objectif: To identify dose volume parameters and clinical factors predictive of a higher risk of grade ^{3}2 late urinary morbidity in patients with prostate cancer treated with three-dimensional conformal radiotherapy (3D-CRT) in a prospective dose escalation study.

Materials/Methods: A total of 213 evaluable patients with T1c-T3 prostate cancer treated with 3D-CRT to a dose of > 72.00 Gy and a minimum follow-up of one year were retrospectively analyzed. The mean ICRU reference dose was of 77.38 Gy, range 72.03 to 84.14 Gy. Urinary morbidity was grading according to the RTOG late radiation morbidity scoring scale. Clinical and dosimetric variables were investigated to determine their correlation with grade ^{3}2 late urinary toxicity. The clinical variables considered for analysis were: age, history of diabetes mellitus, transurethral resection (TUR), adenomectomy or urinary catheterization prior to radiation therapy (RT), inclusion of pelvic nodes or seminal vesicles in radiation fields, administration and length of hormonal therapy and presence of acute GU symptoms during RT. The dosimetric variables considered were: mean ICRU dose, bladder volume, the maximal dose and mean dose to the bladder volume (Dmax and Dmean), NTCP and the volumes (percentage and absolute) of bladder receiving more than 30Gy, 40Gy, 50Gy, 60Gy, 72Gy, 75Gy, 78 Gy and 80Gy. A secondary study was made to investigate the same correlations with grade ^{3}2 hematuria.

Results: 25 of the 213 patients (12%) experienced grade ^{3}2 late urinary toxicity and only 2 patients (1%) had grade 3 complications (ICRU radiation doses 73.3 Gy and 78.5 Gy). No patients developed grade 4 or 5 late toxicities. Of the 25 patients with grade ^{3}2 urinary toxicity, hematuria was the main symptom in 21 (10%) with only 2 patients (1%) experiencing grade 3 hematuria. On univariate analysis, all the dosimetric parameters failed to show a significant correlation with bladder toxicity. Only the history of TUR (p=0.008) was significantly correlated with grade ^{3}2 urinary morbidity. TUR performed prior to RT was also the only significant factor associated with a higher risk of hematuria (p=0.002).

Conclusions: Tolerance of bladder at the prostate radiation dose level of 72 - 84 Gy with 3D-CRT remains acceptable with no grade 4-5 late complications. The present study indicates the absence of dose and dose-volume effect on the risk of GU toxicity at this dose level and suggests that minor surgical manipulations (as TUR of the bladder) are relevant factors contributing to late bladder toxicity.

1040 poster

MALE SEX HORMONES AND GONADOTROPINS AFTER RADIOTHERAPY FOR RECTAL CANCER

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Purpose/Objectif: Radiotherapy is part of the multi-modality treatment of rectal cancer. It is known that scattered radiation to the testes during pelvic radiotherapy can affect testicular function, but there are few reports on hormonal changes after radiotherapy for

rectal cancer.

Materials/Methods: We investigated male sex hormones in a study of late side effects after radiotherapy for rectal cancer. All patients who had received adjuvant radiotherapy (46-50 Gy) for stage II-III rectal cancer were identified from the Norwegian Rectal Cancer Registry. Patients treated with surgery alone, were randomly selected from the same register to serve as controls. All patients were free of recurrence and had been treated during the years 1993-2002. Serum levels of FSH, LH, testosterone and SHBG were analysed using the same laboratory.

Results: In May 2006 the results from 194 male patients were available. Eighty-five had been treated with pre- or postoperative radiotherapy (RT+) and 109 controls with surgery only (RT-). The median age was 62 (RT+) and 65 years (RT-) (p=0.02) and the median follow-up time since surgery was 70 months.

Median FSH was three times higher in the radiotherapy-group than in the control-group (18.8 v 6.4 IU/l, p<0.001). Eighty-one percent of the irradiated patients had FSH levels above the reference range (>12 IU/l), compared to 22% of the non-irradiated patients (p= 0.001). Median LH was 1.5 times higher in the irradiated group (7.5 v 4.8 IE/l, p<0.001). All results remained significant when adjusted for age. The mean testosterone-level was 11.2 nmol/l (RT+) and 13.4 (RT-), the difference remained significant in age-adjusted analyses (p=0.001). Twenty-seven percent of the irradiated patients had testosterone-levels below the reference range (<8 nmol/l), compared to 9% of the non-irradiated patients (p= 0.002). These data are preliminary, final data from approx. 230 patients will be presented at the meeting.

Conclusions: The elevated levels of gonadotropins indicate that radiotherapy for rectal cancer causes testicular dysfunction. A significant portion of the irradiated men also had hypogonadal testosterone levels.

1041 poster

STUDY ON RISK FACTORS OF RADIATION INDUCED LIVER DISEASE AFTER THREE DIMENSIONAL CONFORMAL RADIOTHERAPY FOR PRIMARY LIVER CARCINOMA

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Purpose/Objectif: To identify the risk factors of radiation induced liver disease (RILD) after three dimensional radiotherapy (3DCRT) for primary liver carcinoma (PLC).

Materials/Methods: Between September 1996 and November 2004, 101 PLC patients were treated with conventional fractionated 3DCRT in Shandong Cancer Hospital. Among the 101 patients, only 88 cases, who had full dada, were enrolled the research. All patients were technical unresectable or medical inoperable. 80 patients were male and 8 female. Median age was 57 years, ranging from 27 years to 77 years old. Hepatitis B virus (HBV) showed positive in 63 cases, negative in 25 cases. According to Child-Pugh classification for cirrhosis of liver, 73 patients were in class A, 14 patients in class B, and 1patients in class C. There were 15 patients with portal vein thrombosis and 10 with hepatic portal lymph node metastasis. CT scans showed ascitic fluid in 20 patients. 24 patients had alpha-fetoprotein (AFP) level >400 ng/ml. 72 patients presented a single hepatic tumor, and 16 had multiple lesions. Tumors located in right lobe in 70 patients, in left lobe 12 patients, and in both of them 6 ones. Tumor size ranged from 1.5cm to 17cm with a median of 6.5cm. The planning target volumes (PTV) ranged from 69.4ml to 3168.2ml with a median of 378ml. 5-7 coplanar or noncoplanar fields were used to optimize 3DCRT plans. The PTV margin doses ranged from 30Gy to 63Gy with a median of 45Gy in 1.8Gy-2.0Gy per fraction, while the mean doses of normal liver tissue ranged from 10Gy to 41.3Gy with a median dose of 22Gy. All treatment was delivered by a linear accelerator with 6 or 15 MV photons. 3DCRT was given 5 days a week. 70 patients combined with trans-arterial chemoembolization (TACE) pre- and/or post-3DCRT. Evaluation of tumor response was based on serial CT scans. All patients had CT scans before initiation of 3DCRT and 4-6 weeks after completion of radiation therapy and then at 1-3-month intervals. The relation between RILD and the possible factors, such as gender, age, HBV status, portal vein thrombosis, hepatic portal lymph node metastasis, ascitic fluid , Child Pugh grade of liver cirrhosis , AFP, number of tumors, tumor location, tumor size, PTV, TACE , mean dose of normal liver, dose volume histogram (DVH), and tumor response were analyzed.

Results: An objective response was observed in 61of 88 patients, giving a response rate of 69.3%. 16 patients (18. 2 %) developed RILD. In the univariate analysis of RILD-relation factors, age, portal vein thrombosis , HBV status , ascitic fluid , Child Pugh grade of liver cirrhosis, tumor size, and PTV had significant impact on RILD (p = 0. 025 , 0. 026 , 0. 034, 0. 044, 0. 003 , 0.003, 0.048, respectively) . However, multivariate binary logistic regression analysis showed that only the Child Pugh grade of liver cirrhosis and HBV status were independent factors (p = 0. 025 and 0.041, respectively) . Considering the effect of liver cirrhosis grade, 73 patients with Child Pugh grade A were analyzed and found that except for the above risk factors, V5 (percentage of normal liver volume with radiation dose > 5 Gy), and PTV margin dose were significantly correlated with RILD (p = 0.010 and 0.028, respectively). V10 (percentage of normal liver volume with radiation dose >10 Gy) also had close relationship with RILD (p=0.051).

Conclusions: To lower the incidence of RILD, not only the dosimetry factors but also the clinical factors such as age, portal vein thrombosis , HBV status , ascitic fluid and Child Pugh grade of liver cirrhosis, especially the Child Pugh grade of liver cirrhosis , should be considered comprehensively, while prescribing 3DCRT for PLC.

1042 poster

THE EVALUATION OF SYLBUM MARIANUM AS A PROPHYLACTIC AGENT FOR RADIATION-INDUCED SKIN TOXICITY FOR WOMEN UNDERGOING BREAST IRRADIATION

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Purpose/Objectif: Skin reactions associated with radiation therapy may cause significant discomfort, pain and interfere with the patients´ quality of life. This toxicity could lead to a temporary interruption of the treatment and consequently to a decrease of its efficacy. Although radiation skin toxicity is a prominent clinical problem there are no well established prophylactic skin treatment measures to prevent it.

Materials/Methods: Patients eligible for this prospective study had to be diagnosed with breast cancer with a planned course of radiation to the breast or the chest wall with a minimum dose of 50 Gy. At registration, patients were instructed to begin applying an emulsion with Sylbum Marianum (Radiocrem® emulsion corporal) twice a day. The product was not to be applied within 2 hours of their daily radiation session and no other prophylactic products were allowed in the radiation field while the patients were under study. However, if Grade 3 or 4 toxicity occurred additional treatment was permitted and at the physicians´ discretion. The primary end point was the evaluation of Sylbum Marianum as a prophylactic agent to decrease the radiation-induced toxicity for women undergoing breast irradiation.The secondary end points were the evaluation of pruritus, skin pigmentation and subjective comfort. Skin toxicity was scored by the radiation oncologist in charge of the patient according to the

Radiation Therapy Oncology Group (RTOG) acute toxicity scale. Pruritus, skin pigmentation and subjective comfort were evaluated by the patient according to an Analogical Visual Scale (AVS) graded from 0 to 10. The toxicities were registered in the pre-treatment visit, once per week during the treatment period and a month after the conclusion of it.

Results: From July 2004 to June 2005, 98 patients were enrolled; 84 underwent breast-conserving surgery and 14 underwent radical mastectomy. The median dose in the targeted volume was 57.6 Gy (45-70 Gy) with a standard fractionation (1.8-2 Gy).

The patients were treated as follows:

Energy	N patients	%
Cobalt 60	49	50%
6 MV Photons	46	47%
6 MeV Electrons	3	3%

Table 1: Skin toxicity during radiation treatment.

Toxicity	G0	G1	G2	G3
Week 0	100%			
Week 1	100%			
Week 2	88%	9%	1%	
Week 3	63.5%	24.7%	11.8%	
Week 4	33%	35%	28.5%	3.5%
Week 5	21.7%	39.7%	30%	8.6%
Week 6	12%	24%	50%	14%
1 month	54%	28%	12%	6%

The mean Analogical Visual Scale scores for pruritus, skin pigmentation and subjective comfort were 3. The treatment had to be interrupted in 7 patients and in 33 patients additional treatment (hialuronic acid, topical steroids, ...) were applied.

Conclusions: Skin reactions associated with radiation therapy is a prominent clinical problem in patients with breast cancer. The prophylactic administration of Silybum Marianum has been associated with a decrease skin toxicity during radiation treatment

1043 poster

THE VOLUME EFFECTS OF SMALL-BOWEL TOXICITY DURING RADICAL PELVIC IRRADIATION IN PATIENTS WITH CERVICAL CANCER: A PROSPECTIVE STUDY WITH COMPUTED TOMOGRAPHY-BASED DOSIMETRY

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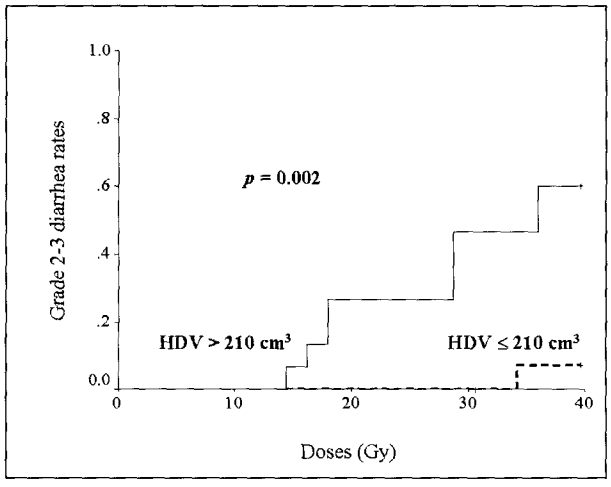
Purpose/Objectif: To evaluate the small-bowel volume effect of diarrhea during radical pelvic irradiation in patients with cervical cancer.

Materials/Methods: From March 2004 through February 2006, 30 patients undergoing 4-field whole pelvic irradiation were analyzed. After computed tomography (CT) simulation, the small-bowel volume and dosimetry were calculated using the ADAC planning system. We recorded 10% to 100% dose volumes at 10% intervals. The volumes for full-dose (FDV) and half-dose volume (HDV) were 100% and 50%, respectively. Initially, external pelvic irradiation (39.6-45 Gy/ 22-25 fractions) was delivered to all patients. We recorded the onset and grade of diarrhea during pelvic irradiation.

Results: In univariate analyses, the effect of overall diarrhea existed at HDV (p=0.001) but not FDV (p=0.436). HDV (p=0.002) and FDV (p=0.030) involved Grade 2 or greater diarrhea. In multivariate analyses, there was an interaction between high HDV > 210 cm^3 and age > 58 (p<0.001) for development of overall diarrhea. Analyses of subgroups revealed that HDV > 210 cm^3 (p=0.020) was the only independent factor of overall diarrhea in patients with age > 58. In addition, age > 58 (p=0.020) was the only independent factor of overall diarrhea in patients with HDV > 210 cm^3. Multivariate analysis of Grade 2 or greater diarrhea also revealed that HDV > 210 cm^3 (p=0.018) was the only independent factor.

Conclusions: HDV instead of FDV can be used as index of overall and Grade 2 or greater diarrhea during radical pelvic irradiation in patients with cervical cancer.



Posters Palliation/Supportive Care

1044 poster

A PILOT PHASE II STUDY OF CONCURRENT CAPESITABINE (XELODATM) AND EXTERNAL BEAM RADIOTHERAPY FOR BONE METASTASES OF BREAST CANCER ORIGIN

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Purpose/Objectif: A recent RTOG analysis demonstrated a highly significant dose response relationship for palliation of pain from bone metastases with radiotherapy (RT). Based on these data, we embarked on a prospective pilot clinical trial in which the biological effective dose was increased using capecitabine as a radiosensitizer. The main theoretical advantages of this approach over escalation of the physical dose are shorter overall treatment time in a palliative setting and a potentially enhanced therapeutic index. Capecitabine was chosen as a radiosensitizer due to its mild toxicity profile, selective accumulation within tumor cells and independent anti-neoplastic activity. The aim of the current study was to evaluate the feasibility of concurrent capecitabine and external beam RT in patients (pts) with bone metastases of breast cancer and to collect preliminary

data on the efficacy of this regimen.
Materials/Methods: Pts eligible for this study had breast cancer and one to three sites of bone metastases. RT was given in 10 fractions of 3 Gy each , up to a total dose of 30 Gy, over two weeks. Capecitabine, 1400 mg/m^2 orally, divided into two daily doses, was given on the days of RT. Pts were asked to rate their pain intensity using an 11 categorical point scale (0=lack of pain, 10=worst pain imaginable). Use of analgesics was recorded as drug frequency and severity, before the initiation of therapy and after its completion. Response was evaluated at 1, 2, 4, 8 and 12 weeks after completion of RT. Complete response (CR) was defined as a pain score of 0. Partial response (PR) was defined as a reduction of pain score ≥ 2 or a ≥ 50 % reduction of the pre-treatment pain score and no increase in the use of analgesics.
Results: Twenty one pts received the study regimen. Chemoradiation was well tolerated. No grade ≥ 3 side effects were recorded. Hematological toxicity was mild. The most common non-hematological toxicities were nausea (43%), fatigue (29%) and diarrhea (24%). Hand and foot syndrome was noted in two pts (10%). Nineteen pts were evaluable for response. The CR rates at 1, 2, 4, 8 and 12 weeks were 21, 53, 53, 53 and 53%, respectively; the corresponding PR rates were 21, 21, 21, 26 and 26% respectively. The overall response rate at 12 weeks was 79%.
Conclusions: Concurrent capecitabine and external beam RT for bone metastases of breast cancer is safe and tolerable. While the overall response rate achieved using this regimen is comparable to those reported for RT alone, the 53% CR rate noted in our study is unusually high. Further evaluation of this approach seems warranted.

1045 poster

ALTERNATIVE GERIATRIC TOOLS FOR PATIENT?S ASSESSMENT OF FUNCTIONAL STATUS PREDICT SURVIVAL OF NON-ELDERS BRAIN METASTASIS PATIENTS

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Purpose/Objectif: To evaluate alternative performance status tools in predicting outcome in brain metastases patients referred for external radiotherapy.
Materials/Methods: Data from 62 patients were analyzed. Radiotherapy treatment consisted of standard palliative RT of 30 Gy in ten fractions of whole brain. No controls after RT were mandatory in our unit, according to the patient's geographical origin and clinical status. In addition to Karnofsky Performance Status (KPS) and neurological evaluation, their physical activity was assessed by means of the activity of daily living (ADL) and instrumental ADL (IADL) scales. A neurocognitive evaluation was assessed with the Pfeiffer Short Portable Mental Status Questionnaire (SPMSQ) and with the Mini-Mental Status Exam (MMSE) if the first test no showed impairment. Pfeiffer SPMSQ and the MMSE, administered with the Lobo's Spanish translate version are screening tools for dementia. The Barthel Index assess ability to conduct ADL thus evaluates ten basic functional capabilities. Lawton and Brody's Scale is a self-reported assessment about abilities to interact with the community. It measures 8 IADL, more complex than the self-care activities. The end-point was overall survival, measured from date for radiotherapy evaluation to death. At time of analysis all patients were death and the date was know.
Results: High rates of cognitive impairment were found by both neurocognitive tools (Pfeiffer: 80.6% of patients; MMSE: 51%). Also dependence was highly prevalent, either measured by the ADL (50%) or by the IADL (42.6%). Median overall survival was 76 days. Prognostic variables on univariate analysis were: gender, tumoral primary site and primary tumor control and extracranial metastatic disease. Neurocognitive and functional variables (ADL and IADL) were, also, found associated with prognosis, except for Pfeiffer and neurological score. On multivariate analysis only retained significance: gender, and independency according to ADL.
Conclusions: Geriatric tools can have significant prognostic value for survival on a oncologic setting assessing non-elders patients.

1046 poster

CLINICAL AND RADIOLOGICAL EVALUATION OF PATIENTS WITH BONE METASTASES FROM SOLID TUMORS: IS THERE A CORRELATION BETWEEN CLINICAL STATUS AND TYPE OF BONE METASTASES?

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Purpose/Objectif: To investigate whether there is an association between the clinical status of patients with metastatic bone disease and the type of bone metastases.
Materials/Methods: 80 patients with skeletal metastases, referred for radiotherapy, underwent both clinical and radiological assessments. The clinical status of each patient was assessed on the first day of radiotherapy by using a bone pain scale graded from 0 to 10 (10 = worst possible pain, 0 = no pain), performance status evaluation (Karnofsky performance status index, 0-100), and a quality of life questionnaire (EORTC-QOL-physical functioning). The analgesic requirement was also recorded. Bone lesions were evaluated with computed tomography (CT), and separated into 3 groups: lytic, sclerotic or mixed, in cases where none of the patterns predominated. The density of each bone metastasis was measured in Hounsfield units (HU).
Results: The patients with osteolytic lesions had the highest mean pain score with 8.1±2.2 points, the least mean scores for quality of life and performance status with 31.4±14.6 and 58.6±9.7 points respectively, the highest opioid consumption (100%), and the least mean bone density (116.3±40.4 HU). On the contrary, the group with sclerotic metastases had the least mean pain score with 4.6±1.3 points, the highest mean scores for quality of life and performance status (61.1±15.5 and 66.6±10 points respectively), the least opioid requirement (55.5%), and the highest mean bone density (444±86.6 HU). The group with mixed lesions had intermediate assessment values. The differences between the three groups were statistically significant for all the parameters evaluated, apart from performance status between mixed and sclerotic groups. The correlation coefficients were statistically significant between all the parameters investigated. Bone density had a strong negative correlation with pain and a strong positive correlation with quality of life.
Conclusions: Our results show a clear correlation between the type of bone metastases and the clinical status of patients. Patients with excessive bone resorption suffer the most, and should be given priority in treatment. CT proved to be a practical and efficient method not only to investigate and classify metastatic bone lesions, but also to measure bone density.

1047 poster

COMPLIMENTARY THERAPY USE AND KNOWLEDGE IN PATIENTS AND ONCOLOGISTS

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Purpose/Objectif: Cancer patients often seek complimentary therapies in addition to those prescribed by a medical practitioner. These can interact with their oncology treatment. No survey has yet

been undertaken to evaluate use or knowledge of complimentary therapies by patients undergoing chemotherapy in the . Determine the frequency of use and nature of complimentary therapies in an unselected group of chemotherapy patients. Evaluate the number of patients at risk from drug interactions. Determine the need for further patient information and medical training on complimentary therapies.
Materials/Methods: A questionnaire was designed and approved by local ethics and research and development committees. This was given to all patients attending clinics for chemotherapy over 3 weeks. The questionnaire was anonymous but included data on age, sex, site of primary cancer, stage of disease and knowledge of complimentary therapies.
Results: Number of replies=67. Male=17, female=50. Primary sites were lung (13), breast (13), sarcoma/melanoma (6), colorectal (11), pancreas/upper GI (7), gynaecological (17). 5 patients were undergoing adjuvant treatment and 62 had advanced disease. Only 5/67 said they had been given information on alternative treatments, whereas 43 said they would like such information. Patient understanding of complimentary therapies ranged widely from herbal remedies to physical therapies and even surgery.16/67 patients were taking complimentary therapies at the time of the survey, 2 of whom faced potential drug interactions. These had not been recorded or recognised by the treating physicians.
Conclusions: Responders to the survey were more likely to be female, have advanced disease, or a cancer for which there are limited treatment options. A significant proportion of patients would like more information on alternative treatments, although it is rarely given. Oncologists may need further education to inform patients and prevent harmful drug interactions.

1048 poster

EUROPEAN FRENCH-SPEAKING STUDY FROM THE GEMO* GROUP ON BONE METASTASES MANAGEMENT: A SPECIAL FOCUS ON EXTERNAL BEAM RADIOTHERAPY PRACTICE SURVEY

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Purpose/Objectif: A lot of surveys of bone metastases management are published in the literature coming from different countries. Also, management practices have changed over the past 2 decades, as a consequence of several important clinical trials. To date, never survey practice study has not been performed including the different physicians involved in the bone metastases management. The aim of the present study was to perform a bone metastases survey practice and the present data to report results focusing on the external beam radiotherapy in order to assess in 2005 the European French-speaking state of the art and to establish in a second time by specialities involved recommendations and guidelines.
Materials/Methods: A large questionnaire about bone metastases based on clinical cases and supplemented with general questions including diagnostic and follow-up strategies, medicine therapies, external and metabolic radiotherapy strategies, surgical treatments, biological markers, supportive care approaches, was sent to 4706 practitioners French-speaking all around in Belgium, France, Luxemburg and Switzerland by TNS Healthcare society. The questionnaire has been elaborated by different recognized experts in the field of bone metastases among European French-speaking.
Results: In total, 644 matched questionnaires were analyzed. Twenty-eight percent was concerned by the radiotherapy approach and judged as able to respond to the part dedicated to external beam radiotherapy. A large part of these practitioners used a total dose irradiation of 30 Gy delivered by 10 fractions (69%). A large majority used 2 opposed fields (Ant-Post) in 78.3 % prescribed at mid length (26.6 %) or non equally ponderated (48.7 %). 71.3 % irradiated also up and down the concerned vertebra with a dosimetry planning treatment in 85 % and using high energy megavoltage produced by a linear accelerator in 42 %. Moreover, 54 % practitioners used short course radiotherapy in routinely practice in relation of the life expectancy of their patients less than 3 months (73 %) or an advanced disease (47%).
Conclusions: From a technical and clinical point of view, standards or widely accepted attitudes progressively emerge for treatment options. Nevertheless, there is still a need for standardization of target volumes and ICRU point of prescription.

1049 poster

FEASIBILITY OF PELVIS RE-IRRADIATION USING INTENSITY-MODULATED RADIOTHERAPY (IMRT)

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Purpose/Objectif: Patients with second pelvic primary or local pelvic recurrence have an unfavorable prognosis. However; a new problem is presented in patients who have received previous irradiation to the pelvis. In these patients, tumor is very often not easily resectable and conventional radiation techniques carry the risk of prohibitive normal tissue complications .The aim of this retrospective study is to evaluate the possibility to treat with relatively high radiation doses in patients with a previously irradiated pelvis.
Materials/Methods: Nine patients were included; five male and four female, median ages was 71. Pelvic pain was the presenting symptom in six; (Three with colo-rectal failure, two with endometrial recurrence and urothelial recurrence in one) and three presented with primary rectal cancer. All were previously treated with pelvic radiation ;(Prostate seed implant in four, vaginal brachytherapy in three and true pelvis external irradiation in two).IMRT was planned for delivery of 50.4 Gy to (PTV1), gross tumor volume plus 1 cm margin and 45 Gy to (PTV 2), pelvic lymph nodes, simultaneously in 25 fractions. Concurrent chemotherapy were given to all patients (oral 5FU"XELODA" in four and weekly cisplatin in five). Daily treatment time was monitored as the patient enters the treatment room. Acute rectal and hematological toxicities were evaluated weekly during radiation using the modified RTOG morbidity criteria.
Results: All patients completed the planned treatment schedule. Average PTV1, PTV 2 volumes were 286.7, 1166.8 cc3 respectively .Median bladder dose was 30.4 Gy. Average daily treatment time was 32 minutes. Seven patients experienced grade 1 hematologic toxicity. Antidiarrhea medication was required for 6 patients. No grade 3 or higher acute rectal toxicities were observed. After chemoradiation, patients with rectal primary underwent anterior resection and six with pelvic pain before treatment had good symptomatic response. At median follow-up of 12 months, seven patients had complete radiological response and stable disease in two.
Conclusions
The described combined treatment is feasible and well tolerated. The possibility to treat with relatively high radiation doses in this ongoing study, may improve patients' outcome

1050 poster

GLUTAMINE AND OESOPHAGIC ACUTE TOXICITY IN THE RADIO-CHEMOTHERAPEUTIC TREATMENT OF LUNG CANCER

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Introduction: Oesophagic acute toxicity is one of the limiting factors of the radiochemotherapy efficacy in patients affected of locally advanced lung cancer. Glutamine is an amino acid that could diminish this toxicity.

Objective: To analyse the acute toxicity in patients affected of lung cancer receiving radiochemotherapy and Glutamine.

Materials/Methods: Seventy-five patients [68 (90,66%) men and 7 (9,34%) women], candidates to radiochemotherapy treatment, were included between September 2004 and April 2006. A total of 59 (78,66%) patients were affected of NSCLC (1,69% IIA, 15,25% IIB, 22,03% IIIA, 59,34% IIIB and 1,69% IV) and 16 (21,34%) of limited SCLC . All they received Glutamine, 10 grams po every eight hours from a week before beginning the radiotherapy up to two weeks later. The mean age was 63,11 ± 22,38. Chemotherapy was previously administered in 26 (34,66%) cases and concomitantly in 49 (65,34%) cases. The mean dose was of 59,02 ± 17,5 Gy, administered by mean of 3D-CRT and three-dimensional dosimetry. The mean length of oesophagus included in the treatment volume was 11,65 ± 5,66 cm.

Results: It was analyzed the onset, grade of oesophagitis and analgesia required according to administered dose. Neither side effects nor toxicity were registered related with Glutamine. Only in a patient was discontinued by an intercurrent process.

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Conclusions: In spite of the limited size of the sample, it seem that the employment of Glutamine causes a delay in the appearance of oesophagitis and diminishes their intensity in patients that receive mediastinal radiotherapy.

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Dose	0 - 20 Gy	> 20 - 40 Gy	> 40 - 60 Gy	> 60 Gy
Oesophagitis (grade, nº of patients)	Grade II (1) *Total: 1 (2,43%)*	Grade I (9) Grade I-II (6) Grade II (5) Grade II-III (2) *Total: 22 (53,65%)*	Grade I (4) Grade I-II (5) Grade II (6) *Total: 15 (36,58%)*	Grade I-II (1) Grade II-III (1) Grade III (1) *Total:3 (7,34%)*
Analgesia (kind, nº of medicines)	Opioids (2) *Total: 2 (4,54%)*	NSAID (15) Corticosteroids (1) Opioids (11) *Total: 27 (61,36%)*	NSAID (5) Corticosteroids (2) Opioids (4) *Total: 11 (25%)*	NSAID (2) Corticosteroids (1) Opioids (1) *Total: 4 (9,1%)*

1051 poster

HYPOFRACTIONATED RADIOTHERAPY IN "POOR PROGNOSIS" PATIENTS WITH GLIOBLASTOMA MULTIFORME: AN INTERIM ANALYSIS OF A RANDOMIZED TRIAL

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Purpose/Objectif: Data from literature show that in glioblastoma multiforme (GBM) patients (pts) "poor prognosis" hypofractionated or accelerated radiotherapy may represent the standard of care. However the standard regimen of palliative radiotherapy has not been defined. Aims of the study is to evaluate, firstly in terms of overall survival (OS), and secondly quality of life (QOL), the efficacy of two different radiation regimens at the half-fase of the accrual.

Materials/Methods: At our Institution, from January 2002 we have enrolled 69 pts affected by histologically confirmed GBM "poor prognosis" (5^{th} - 6^{th} class according to Curran RPA). The patients were randomized between two arms: 30Gy/6fr every other day (arm A) vs 42Gy/14fr every day (arm B). (34 female, 35 male) aged from 47 to 84 years (median age 66 years). The QOL of each patient was evaluated by Karnofsky Performance Status (KPS), Barthel Index, Basic Activities of Daily Living (BADL), Instrumental Activities of Daily Living (IADL) and Mini-Mental-State Examination (MMSE) scales; this evaluation was performed before, at the end of radiotherapy and each follow-up. According to the statistical analysis we estimated a total of 140 pts to be enrolled in the study. Patient characteristics are as follows: gender M/F 35/34; median age 66 years (range 47-84); type of surgery: gross total resection = 27, subtotal resection = 18, stereotactic biopsy = 24). Ninety percent of pts had a KPS ≤ 70% (median KPS 50%).

Results: At the time of the interim analysis 34 pts were enrolled in arm A and 35 in arm B. The QOL evaluation was done in 65% OS calculated by Kaplan-Meyer method and compared by c2 test was:

Months	A (%)	B (%)
6	66.7 ± 8.2	78.8 ± 7.1
12	30.3 ± 8.0	29.6 ± 8.6

No statistically significant difference in terms of OS between the two radiotherapy regimens was demonstrated (p=0.354), nevertheless exists a gap in the period corresponding to mean survival. No acute toxicity was registered in all pts.

Conclusions: The two radiotherapy regimens seem to be feasible and enough effective as palliative treatment for this setting of pts but no difference in terms of OS has been found. The study is on going in order to reach the number of pts established by statistical analysis. We also must underline the diffuculty of performing the cognitive tests in a group of pts with poor clinical condition and fast pathological progression.

1052 poster

INCIDENCE AND MANAGEMENT OF INFUSION PAIN IN PATIENTS TREATED WITH OXALIPLATIN

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Purpose/Objectif: The combination of oxaliplatin and 5 FU (FOLFOX) has become a standard treatment in the management of colorectal cancer (CRC). Oxaliplatin has also been combined with oral capecitabine (XELOX) with similar efficacy but with a different toxicity profile. Infusion pain has rarely been described with oxaliplatin but is thought to be due to acute neurotoxicity. We sought to evaluate the incidence of infusion pain, whether it is related to a specific combination schedule, and what measures can be taken to prevent it.

Materials/Methods: 29 patients with metastatic CRC were treated on 2-weekly schedules of either FOLFOX (85mg/m^2 oxaliplatin and 400mg/m^2 bolus 5 FU on D1 with an infusion of 5FU of 2400mg/m^2 over 2 days given via a central venous access device), or XELOX (oxaliplatin 85mg/m^2 on D1 with 800mg/m^2 capecitabine bid on D

1-10). Oxaliplatin was infused over 2 hours in 250 mls 5% Dextrose. Toxicities (NCI-CTC v2) were recorded throughout and at the end of their treatment. Incidence and severity of pain during the oxaliplatin infusion was recorded. This was correlated with neurological, skin and other toxicities. Management strategies were employed to reduce the severity of the pain and their success recorded.

Results: Of the 27 evaluable patients to date, 9 were treated with FOLFOX and 18 with XELOX. Infusion pain was not seen in any of the FOLFOX patients but was observed in 11/18 (61%) of those treated with XELOX. In 3 of these patients the pain persisted for over 24 hours and interfered with use of that arm. Pain was maximal at cycle 2 after which modifications were made. In all patients with infusion pain heat bags were initially used. In addition 2/11 patients required prolongation in infusion time from 2 to 3 hours, 7 had an increased volume of dextrose given with the oxaliplatin, and 2 patients required dose reductions. In only 1 patient was dose intensity affected by infusion pain. There was no correlation of infusion pain with neuropathy, skin toxicity, performance status, age nor any other toxicity. All other toxicities were G2 or less.

Conclusions: Infusion pain was frequently observed in patients receiving XELOX but not in those treated with FOLFOX. The lack of infusion pain in the FOLFOX patients could reflect the use of long venous catheters required for 5FU administration preventing local toxicity of oxaliplatin, or a specific interaction between capecitabine and oxaliplatin. The frequency of infusion pain in the XELOX treated patients was higher than that expected from published studies. This may be due to differences in drug scheduling. Although distressing to the patient, symptoms were controlled with modifications of oxaliplatin delivery without compromising drug intensity.

1053 poster

INFLUENCES OF TWO DISTINCT RADIOTHERAPY FRACTIATION AND PROGNOSTIC FACTORS IN THE SURVIVAL IN PATIENTS WITH BRAIN METASTASES

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Purpose/Objectif: The objective of this study is to investigate impact of two distinct radiotherapy fractionations and prognostic factors on the survival in patients with brain metastasis retrospectively.

Materials/Methods: Eighty patients who presented to our clinics with brain metastasis between dates March 2002 and November 2004 were randomized to be treated with either 3000 cGy/10 fractions (Group 1) or 2000cGy/5 fractions (Group 2), regardless of whether the metastases operated or not. Primary end-point of the study was the impact of these two radiotherapy (RT) schedules on survival. Secondary end-points were influences of several prognostic factors like age, performance status, primary tumor, state of primary tumor, number of metastatic lesions in the brain, presence of other metastases and whether the brain metastases were operated or not, on survival.

Results: Eighty patients who developed brain metastases were enrolled into the study. Sixty two patients (77,5%) were male, and 18 patients (22,5%) were female. Median age was 59 (20-80) years. The most frequent primary sites encountered in the study were lung cancer (56 cases), breast cancer (7 cases) and cases with unknown primary (5 cases). Thirty nine patients had only brain metastases while 41 patients had other metastases besides brain metastases. Bone was the most frequent secondary metastatic site (41,46%). Metastatic lesion was solitary in half of the patients. In general, the primary foci were under control in 50% of cases. Nine patients (11,25%) underwent surgical intervention to the metastatic lesion in the brain. Patient characteristics are summarized in Table 1. Median survival for the both group was 90 days (95% CI; 41-148). Median survivals were 80 days (95% CI; 0-180) and 80 days (95% CI; 34-145) for group 1 and 2, respectively. No statistically significant difference was notable between two treatment schemes in terms of overall survival (p:0,734). It was concluded that younger patients, those with primary tumor under control, those with breast cancer and unknown primary, and those with good pretreatment performance status had statistically significant advantage of survival compared to the others. Those having solitary metastatic focus in the brain (p=0.208) and those with other organ metastasis besides brain (p=0.227) have statistically insignificant survival advantage. Likewise, operation to the metastases in the brain has not altered the prognosis in the present study (p=0.231).

Conclusions: In this study, no statistically significant difference of overall survival was notable between two distinct radiotherapy schedules. For this reason, it is concluded that patients with favorable prognostic factors should be managed with conventional treatment options that do not disturb general condition, and do increase quality of life; and hypofractionated treatment schedules that decrease the treatment burden should be performed to the patients with shorter life expectancies and to those having poor prognostic factors.

Table 1. Patient Characteristics

Characteristics	Group 1 (n)	Group 2 (n)	Total n (%)
Sex			
Female	30	32	62 (77.5)
Male	10	8	18 (22.5)
Age		Median 59 (20-80)	
<60 years	20	22	42 (52.5)
>60 years	20	18	38 (47.5)
Primary tumor			
Lung	27	29	56 (70)
Breast	3	4	7 (8.75)
Unknown primary	4	1	5 (6.25)
Other	6	6	12 (15)
Site of metastasis			
Only brain	16	23	39 (48.75)
Brain + other(s)	24	17	41 (51.25)
Number of metastatic foci in the brain			
Solitary	19	21	40 (50)
Multiple	21	19	40 (50)
state of primary tumor			
Under control	16	19	35 (43.75)
Uncontrolled	20	20	40 (50)
Unknown	4	1	5 (6.25)
Metastasectomy			
Yes	5	4	9 (11.25)
No	35	36	71 (88.75)

1054 poster

INFORMATION NEEDS OF EARLY-STAGE PROSTATE CANCER PATIENTS: A COMPARISON OF SEVEN EUROPEAN COUNTRIES AND CANADA.

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Purpose/Objectif: To determine if a core of information can be defined to address common information needs of patients with early-stage prostate cancer.

Materials/Methods: A survey of recently treated patients was conducted in Canada, Italy, Germany, Poland, The Netherlands, and Turkey. A rigorous translation and piloting process ensured that culture and language were appropriate. Eligibility criteria were: diagnosed with early-stage prostate cancer, treated within the previous 3-24 months, and could read language of survey. Participants were recruited either as (a) consecutively eligible patients in a followup clinic, or (b) all eligible patients from a database. Each participant used a 4-point Likert scale (essential, important, no opinion, avoid) to rate how important it was to answer each of 92 questions for early-stage prostate cancer patients between diagnosis and treatment decision.
Results: The number of participants in each country were: Canada 130, Italy 47, Germany 48, Poland 55, the Netherlands 103, and Turkey 66 (response rates range from 60%-94%). Within each country, there was wide variability in responses. Every question was rated essential by some of its participants while most questions were also rated avoid by others: Canada (total: 77 questions avoided by some), Italy (77), Germany (61), Poland (71), Netherlands (79), and Turkey (85). However, the mean number of questions rated essential per participant separated the countries into two groups: the higher-information countries (HIC) were Canada (mean: 49 questions), Germany (52), and Netherlands (51), and the lower-information countries (LIC) were Italy (36), Poland (34) and Turkey (31). Countries in the two groups also differed in the percentage of participants who wanted to avoid at least one question, with the HIC having fewer participants who wanted to avoid something: Canada 44%, Germany 38%, and Netherlands 44% compared to the LIC: Italy 81%, Poland 52% and Turkey 61%. Despite the variability, 16 questions were rated essential by at least 50% of participants in each country of both groups. An additional 29 questions were rated essential by more than 50% of participants in each of the HIC; 2 additional question were rated essential by more than 50% of each of the LIC.
Conclusions: A set of 16 questions can be used to create core information that will be considered essential to the majority of patients in each participating country. From there, individualization will be required both by country--with southern and eastern European countries generally wanting less information--and by individuals within each country, in order to address individual patients' information needs. Results from England and Spain will also be included in the presentation.

1055 poster

RANDOMIZED TRIAL FOR BONE METASTASES. A SIX ALTERNED DAYS COURSE RADIATION THERAPY VS MORE STANDARD TREATMENT

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Purpose/Objectif: We examined whether radiotherapy of painful bone metastases can be altered using the same biologically effective dose (BED) without imparing effectivity.
Materials/Methods: 90 patientes with painful bone metastases having no prior surgical intervention or radiotherapy and had a mediam follow-up of 12 months, were analyzed. 2 groups were homogeneous. The primary tumor was located in the breast in 34.4%, in the lung in 30%, and in the prostata in 15.6%. The most frecuent sites of metastases were : axial skeleton (68.9%); extremity (26.7%); and skull (4.4%). 45 patients received a total dose of 27 Gy in 6 alterned days in 2 weeks (dose/day 4.5 Gy), and 45 patients received 30 Gy in 2 weeks, 10 days (daily dose 3Gy) with the same BED ($39Gy_{10}$).
Results: There were no signigicant differences in frecuency, time duration of pain relief, improvement (parcial or complete) of funtionality, recalcification, frecuency of retreatment. There was a light trend favoring 30 Gy in frecuency of improvement of funtionality and survival (1.23 times mayor). There were significant differences favoring 30 Gy in frecuency of pathologic fractures (3.75 times minor)
Conclusions: Higher dose, fractionated treatments produced a greater frecuency and duration of response with an improved net pain relief. The schedule in alterned days lets increased the number of pateintes treated per machine unit, reduces hospital stay and the cost of transport, and improved cuality of life.

1056 poster

REFERRALS FOR SPINAL CORD COMPRESSION STILL ALWAYS ON A FRIDAY

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Purpose/Objectif: Spinal cord compression (SCC) represents a medical emergency, because delayed treatment increases the risk of progression and irreversible deficits, such as motor and sensory dysfunction and loss of sphincter control. Radiotherapy should therefore be initiated as soon as possible. In former research -performed because there was a general feeling that there was a delay in referral for this medical emergency- we showed that there were significantly more referrals on Friday compared to the other days of the week. These results were discussed with the referring physicians and published. We now investigated whether this influenced the referral pattern.
Materials/Methods: The time pattern of referral was analysed for all patients that had been treated for SCC after publication of our former results.
Results: From January 1998 to December 2004, 541 patients were referred for SCC. 36 of those patients had been irradiated more than once for SCC. There were still significantly more referrals on Friday, 26.0 %, compared to 11.6 % on Monday, 15.2 % on Tuesday, 18.1 % on Wednesday, 21.9 % on Thursday and only 4.3 % on Saturday and 2.9 % on Sunday. The variation per hospital was considerable.
Conclusions: Although former results were discussed with the referring physicians and even published to encourage speed of diagnosis and referral, the referral pattern for SCC did change only moderately.

1057 poster

SERIOUS OCULAR COMPLICATIONS OF ZOLEDRONATE

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Purpose/Objectif: Zoledronate is a third-generation bisphosphonate agent that has recently gained popular use among oncologists because it is many times more potent than pamidronate. It has recently become standard treatment for patients with metastatic breast cancer, lung cancer, myeloma and hormone-resistan prostate cancer. Little known is the fact that Zoledronate can cause side effects that can permanently affect a patient's vision. We present two cases seen at our institution and a literature review of the topic in order to bring these problems to the attention of treating clinicians.
Materials/Methods: The ocular side effects of zoledronate in two patients are described. Literature review is presented. Effective treatment for this condition is described and a prophylactic regimen for futrure use of zoledronate is given.

Results: Two cases of severe ocular side effects were seen. These patients were being treated for localised prostate cancer in the context of a randomised trial for localised prostate cancer. 72 -96 hours after the administration of zoledronate, these patients developed signs and sypmtoms consistent with bilateral uveitis and scleritis. Synaechiae with cell and flare reaction were seen in the eyes, indicative of an ongoing serious immunological reaction that was likely to progress to permanent damage of the eyes if left untreated.
These patients were given a regimen of antihistamines and topical and systemic steroids that successfully resolved the ocular reactions. In addition to this, an ongoing prophylactic regimen of antihistamines and steroids were given at the time of rechallenge to zoledronate. Using these treatments, the patients were able to continue to receive zoledronate on a monthly basis. This is in contrast guidelines in the published literature which necessitate the cessation of bisphophonate use
Conclusions: Clinicians should be alert to side-effects that threaten vision when administering zoledronate to their patients. Patients need to be promptly examined and treated with an intensive regimen of steroids and antihistamines when these effects occur. It is possible to continue bisphosphonate use after the development of these side effects.

1058 poster

SINGLE-FRACTION 8GY RADIOTHERAPY FOR BONE METASTASES OF LUNG CANCER

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Purpose/Objectif: In the recent trials it was concluded that radiotherapy is clearly effective in reducing pain from painful bone metastases and it is seemed that there no evidence in efficacy between different fractionation schedules. We carried out the prospective study aimed to evaluate 8 Gy single-dose radiotherapy in painful bone metastases in pts with lung ca assessing pain relief and treatment related complications.
Materials/Methods: There were 84 pts included in the study over the period January 2002 to April 2003, including criteria: histologically proven lung malignancy, one or more bone metastases demonstrated by radiography and/or skeletal scintigraphy, no prior irradiation of the metastatic area, without pathological fractures except spine and estimated life expectancy of >6 weeks. 78 pts were evaluable for study assessment. Median age was 61,5 yrs, M/F=94%:6%. Site of bone meta: spine 31%, pelvis and femur 36%, humerus 18%, and other sites 15%. Histologically the majority of pts had NSCLC (48,7%) and among them 76,3% with GIII differentiation. 70% pts were noticed not to have dissemination outside the skeletal system. All pts received megavoltage X-ray irradiation through one direct field or two parallel opposed fields and TD 8Gy/1fr. Antiemetics were not prescribed. Evaluation was performed at the first month each week after irradiation and monthly thereafter using pre and post treatment WHO performance status rating, pain scale and analgesic requirement scale. Also we used nausea/vomiting and tiredness scale on the first follow-up visits and opiate analgesia had to be continued.
Results: One month after RT response was noticed in 88,4% pts, CR in 38,3%. 8 pts did not responded, opiate analgesia had to be continued. The majority of pts had improvement in the first week 58%, CR in 7,5%. In pts with spinal compression neurological symptoms was disappeared in 75% during the four weeks after RT. There was not significant difference between groups according to histological subtype. Overall survival from the time the pts received RT was 3,6 mths. 60% pts experienced no anorexia, nausea and vomiting and just 15% had vomiting to a varying degree. Some degree of tiredness was reported by the 70% pts. Due to short time of life after RT no late adverse effects was diagnosed.
Conclusions: 8 Gy given in a single-dose in pts with lung cancer and metastatic bone disease is effective management in pain relief with acceptable acute side complications.

1059 poster

TARGET SELECTION IN MULTIPLE SPINAL METASTASES

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Purpose/Objectif: Prevention of spinal-cord compression is one of the aims of radiation therapy (RT) for spinal metastases. To find lesions with high risk of symptomatic spinal-cord compression, we examined features of spinal metastases caused symptomatic spinal-cord compression.
Materials/Methods: Fifty three patients were treated with RT for cervical and/or thoracic spinal metastases in 2004-2005. Among these patients, 49 patients (56 lesions) were evaluable by magnetic resonance imaging, and reviewed in this study (lesions of cervical spine with and without extension to upper thoracic spine, 8; lesions of thoracic spine, 48). Twenty-one patients (43%) had symptoms of spinal-cord compression at presentation.
Results: Incidence of symptomatic spinal-cord compression of thoracic lesions and cervical (with and without extension to upper thoracic spine) lesions at presentation were 42% and 13%, respectively (p=0.017). Ninety percent of lesions with symptomatic spinal-cord compression had involvement of lamina of the vertebra. Fifty-six percent of lesions with involvement of lamina caused symptomatic spinal-cord compression and 10% of lesions without involvement of lamina caused symptomatic spinal-cord compression (p=0.006).
Conclusions: Timing of RT tended to be delayed in lesions of thoracic spine compared to lesions of cervical spine. It was likely that involvement of the lamina is a risk factor for symptomatic spinal-cord compression. Spinal metastases with involvement of lamina of the vertebra may be targets of RT whether they are painful or not.

1060 poster

WHOLE BRAIN RADIOTHERAPY (WBRT) FOR RTOG RPA 3 PROGNOSTIC CLASS PATIENTS WITH BRAIN METASTASES: PRELIMINARY RESULTS OF A PROSPECTIVE TRIAL.

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Purpose/Objectif: The real benefit of whole brain radiotherapy (WBRT) for RTOG RPA 3 prognostic class patients with brain metastases is unknown. There are patients in KPS<70 with dismal median survival of approximately 2 months. Although in retrospective studies WBRT is considered as effective in relieving symptoms, its real benefit independent of steroids usage remains unknown for this group of patients. These patients are usually not subjects of clinical trials. A prospective clinical trial with an aim of determining a palliative benefit of WBRT for such patients is conducted. Preliminary results of this study are presented.
Materials/Methods: Forty four patients with brain metastases in RTOG RPA 3 prognostic class were included in the study up to now. Primary sites were as follows: 26 - lung, 8 - breast, 8 - unknown primary, 2 - colorectal. All patients received WBRT (20 Gy/5 fractions)

and were asked to complete an identical questionnaire on symptoms before and one month after radiotherapy. Patient's symptom checklist consisted of 17 symptoms scored from 0 to 3. Higher score meant higher intensity of symptoms. Doctors evaluated general (KPS) and neurological (EORTC scale) condition and steroids usage, prior and one month after radiotherapy. Total scores from questionnaires were considered and changes in score after treatment were assessed. Comparison of doctor's and patient's opinion upon improvement was done.
Results: Thirty six patients had a follow-up > 1 month and were evaluated. Fourteen (39%) out of 36 analyzed patients filled both questionnaires. Among 21 non-responders to second questionnaire, there were 15 who died before evaluation period. Mean scores of patients symptom checklist were 17.0 (SD=7.49) and 22.4 (SD=7.05), before and one month after radiotherapy, respectively (p=0.02). Only 2 patients reported improvement of symptoms after radiotherapy, 12 patients declared worsening of symptoms. Of 14 patients who returned questionnaires, there were 12 evaluated by radiotherapist. There was discordance between doctors and patients evaluation of radiotherapy effect. According to doctor's statements concerning performance status and neurological condition, deterioration was noticed in 4 and 3 cases, respectively. Other (respectively, 8 and 9) patients were evaluated as with stable or improved functions. Ten out of 14 patients tapered doses of steroids one month after WBRT. Results based on larger group will be presented at the meeting.
Conclusions: Our preliminary results suggest that WBRT in RTOG RPA 3 prognostic class patients with brain metastases does not yield real benefit. If our preliminary results were confirmed, supportive care or shorter radiation schedules would be proposed to these patients.

Posters Patient Positioning

1061 poster

A SIMPLE METHODE TO REDUCE ORGAN MOTION IN PROSTATE CANCER - USE BY QUANTIFICATION OF INTERFRACTION MOTION OF THE GLAND

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Purpose/Objectif: Several procedures - often resource intensive, investigate that aim to compensate organ motion during high dose irradiation of prostate cancer (TD > 75 Gy). The purpose of this study was to examine a simply method to receive an better effect of immobilization by interfractional organ motion of prostate gland.
Materials/Methods: In 2 consecutive IMRT-series, respectively 15 patients with prostate cancer (volume of prostate: 33 - 160 cm^3), we performed serious weekly CT-investigations of pelvis (thickness 2 mm). In series II antiflatulence diet prior to treatment and daily medication of a deflatulence (simethicon 240 mg) prescribed. Identical positioning of each slice of the current and the previous CT-scans was achieved. The "Varis-Vision" planning modul allow the matching of comparable CT-scans choosing of four several points of the skeleton. Hereby in all directions the 3-dimensional deviation of CTV "prostate" was detectable in every of the 7 CT-series.
Results: The mean values of deviations of CTV prostate in series I/II were 0.39 ± 0.32 cm vs. 0.27 ± 0.19 cm in anterior-posterior direction (max. deviation 1.34 vs. 1.08 cm), in lateral (RL) direction 0.11 ± 0.1 cm vs. 0,09 ± 0,05 cm (max. deviation: 0,88 vs. 0.25 cm) respectively in cranio-caudal direction 0.16 ± 0.17 cm vs. 0.11 ± 0.09 (max.deviation: 0.88 vs. 0,67 cm).
Conclusions: Our findings suggest, that prostate organ motion occurs predominantly in the anterior - posterior direction. Therefore the influence of the empty rectum is recognizable. By using in simply method of medical deflatulation we were able to reduce interfraction motion of prostate more than 30 % in the second series.

1062 poster

BENEFITS OF 6-DOFS COUCH IN AUTOMATIC PATIENT POSITION CORRECTION: A RETROSPECTIVE ANALYSIS IN EXTRA-CRANIAL RADIOTHERAPY ON A 90?PATIENT POPULATION

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4 - European Institute of Oncology, Radiotherapy Division, Milan, Italy

Purpose/Objectif: To investigate the clinical impact of 6 dofs (degrees of freedom) versus a traditional 3 or 4 dofs treatment couch for high precision radiotherapy treatments.
Materials/Methods: In this study, 285 therapy fractions coming from a 90 patient population undergoing stereotactic extracranial radiotherapy and conformal pelvic irradiation were analyzed. Patients were fitted with a set of 5-8 infra-red reflective markers for optoelectronic localization. The three-dimensional coordinates of fiducials were acquired during the treatment and were retrospectively analyzed to evaluate the best method for correcting patient misalignments (considering 3dofs, 4dofs and 6dofs, respectively). A point-based registration procedure was applied in order to compute the trasformation for the minimization of the displacements between the current and the reference configuration of the external control points. After the implementation of each correction, the new position of the isocenter point was reconstructed by means of a dedicated target registration algorithm. The Euclidean distance between the corrected and the planned location of isocenter was calculated and compared to the initial mismatching.

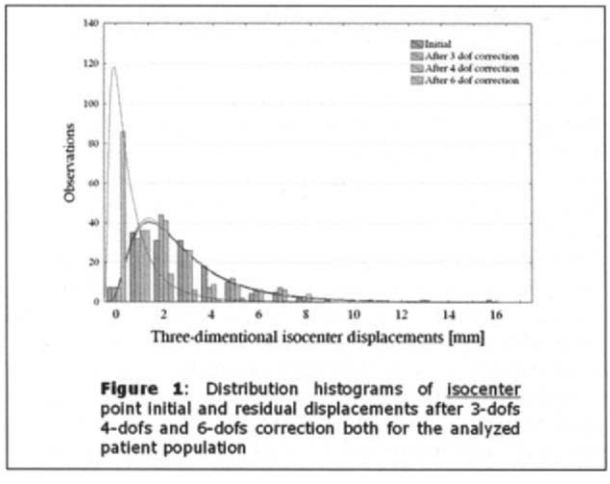

Figure 1: Distribution histograms of isocenter point initial and residual displacements after 3-dofs 4-dofs and 6-dofs correction both for the analyzed patient population

Results: Initial and after correction median±quartile displacements affecting external control points (averaged on the entire patient population) were 4.13±3.25 mm (initial), 2.91±1.31 mm (3 dofs), 2.78±1.30 mm (4 dofs) and 2.38±1.98 mm (6 dofs). The importance of a six parameters adjustment was particularly evident when evaluating the results relative to the isocenter position before and after the re-alignment (see figure 1). In this context, the Euclidean distance between the planned and the current isocenter turned to 0.87±1.24 mm (median±quartile values) after the rototraslation in opposition to the initial displacement of 3.60±3.50 mm. No statistical improvements were found after 3 and 4 dofs correction (2.95±3.27 mm and 2.82±3.10, respectively).The maximum range of rotational errors were found about cranio-caudal axis within ±6°. Translational misalignments were up to 17 mm along the antero-posterior direction.
Conclusions: Results of this study significantly support the 6 dofs

correction potentialities, as a way to increase the possibility of a fully automatic in-room adjustment of patient position, without requiring additional manual intervention. This result is in line with the current approach to the problem of patient positioning proposed by the major manufacturers of conventional radiotherapy systems, which are moving to the idea of realizing computerized treatment tables with full translational and rotational degrees of freedom.

1063 poster

CHESTWALL AND BREAST IMMOBILIZATION FOR 3DCRT AND IMRT

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Purpose/Objectif: Purpose of the study is the investigation of the feasibility of using individual thermoplastic mask fixation of the thoracal region for adjuvant 3D conformal and intensity modulated radiotherapy of breast cancer patient.
Materials/Methods: 18 patients after surgery (7 postmastectomy, 11 breast conserving surgery) underwent postoperative 3DCRT 25x2 Gy /5 weeks in supine position on AIO Solution™ (ORFIT) in three groups: group A without mask; group B with diagonal mask (contralateral breast-abdomen); group C transversal mask fixation. Portal images were obtained weekly using Electronic Portal Imaging Device. The set up accuracy was defined comparing the portal image to the DRR derived from the planning system (XIO-CMS). The breathing movement was evaluated by measurement of the central lung distance (CLD) and the area of the Margin(field)-Costo-Phrenical Triangle (MCPT) durind the delivery of radiation in expiration and in inspiration. Adverse reactions were assessed and graded weekly over the baseline using CTCAE v. 3.0.
Results: In the group A 10-20 mm correction of the position was neccessary in 3/6 cases in the group B in 1/6 cases and no correction was requested greater than 5 mm in the group C. The average difference in inspiration and expiration of the CLD and MCPT were in group A 1.66 mm and 209.22 mm^2; in group B 0.94 mm and 80.36 mm^2; in group C 0.67 mm and 74.2 mm^2 respectively. We have not observed acute skin reaction in 3 cases and there were no grade 4 skin toxicity. Grade 3 radiodermatitis occured in 2/6, grade 2 in 1/6, grade 1 in 2/6 cases if the radiated area was covered by mask material and 1/12 grade 3, 2/12 grade 2 and 7/12 grade 1 if not. (group A+B).
Conclusions: The transversal thermoplastic mask fixation reduces the breathing motion remarkably during the treatment delivery and assures high repositioning accuracy, but in the same time slight increase of the acute skin reaction was detected. Therefore the two or better four points transversal mask fixation can be recommended for irradiation of the chestwall, where the bolus effect is advantageous, for 3D partial breast RT and IMRT. For standard CRT the diagonal mask could be a solution to avoid the skin toxicity, but it needs further optimisation to achive the same degree of breathing motion reduction and repositioning accuracy.

1064 poster

EFFICACY OF IMMOBILIZATION DEVICES FOR SETUP VARIATIONS IN RADIATION TREATMENT OF BREAST CANCER

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Purpose/Objectif: Retrospective analysis of setup error in patient positioning with two immobilization devices from two institutions for tangential field treatment of breast cancer.
Materials/Methods: Sixty patients from two institutions with identical treatment techniques in three arms were analyzed: 1) Alpha-cradle (AC) in institution A; 2) Med-Tec board in institution B and 3) AC in institution B. Med-Tec breast board device is adoptable to varying degree of patient's anatomy to provide reproducible setup. The analysis compared simulation films of the medial and lateral tangential fields to subsequent portal films. A total of 492 portal films were analyzed. A visible anatomic structure, such as the nipple, was marked as reference point for each patient. From each portal film, superior, inferior, apex and central lung distance (CLD) were measured and compared to the same parameters from simulation films to provide an indication of the setup variability.
Results: Figure 1 shows the average differences between the simulation and the portal films among 3 arms. These average differences were all less than 4 mm, and were mainly in apex and superior direction. Standard deviations are shown with error bars to assess the variability between simulation and portal films. These standard deviations were less than 8 mm, and were larger superiorly and inferiorly. There were no clinically significant differences between the two immobilization devices or between the two institutions.
Conclusions: This study shows that current immobilization devices are effective for breast cancer treatment with acceptable daily setup variation. There were no clinically significant differences between the two immobilization devices between the two institutions. Breast setup can be adequately achieved as long as immobilization device is tailored for comfort for individual patient.

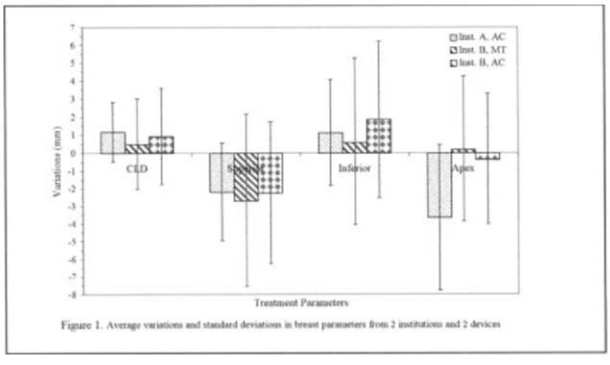

Figure 1. Average variations and standard deviations in breast parameters from 2 institutions and 2 devices

1065 poster

INTERIM REPORT ON CLINICAL TESTING OF A COMPREHENSIVE SOLUTION FOR PATIENT POSITIONING AND IMMOBILISATION FOR HIGH TECH RT

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Purpose/Objectif: Purpose is to report on the first results of the multicentric investigation on the clinical applicability and on the patient (pts) comfort of the innovative Accurate Integrated Organ-specific (AIO) pts immobilisation solution, both for imaging for treatment planning and for treatment delivery.
Materials/Methods: AIO solution™ v. 0.1 (ORFIT), composed of a base plate which can be secured to any CT and treatment table, of region specific positioning cushions and of multi-point thermoplastic masks, is currently under evaluation in 5 RT centres world wide. To date 4970 pts completed the 3DCRT/IMRT positioned by AIO. We have analysed the structured report of physicists, therapists and physicians on different aspects of the AIO approach. 214 pts have filled in the questionnaires (13 items graded from 0 to 4 and the final evaluation on the system from 1 to 6) on the convenience of the anatomical structures, muscle relaxation, feeling concerning the positioning and mask fixation in different localisation (102 breast, 6 head, 4 neuraxis, 22 head and neck, 32 lung, 38 pelvic in supine and

32 pelvic in prone using the belly board of the AIO) Two independent observers performed the comparison of 742 portal images to the BEV-DRR.

Results: The positioning error rate in x, y, z direction for the entire group was 3.2 mm (±4.3mm) (4.8mm (range 5-18,8mm) of pelvic, 3.9mm (3,35-16,9mm) of breast, 3.4mm (1,35-12,8mm) of lung, 1,0mm (0,36-3,2mm) of brain and 1.2mm (0,42-6,28mm) of head and neck RT. In the report of the technicians and physicians the advantageous features have dominated (high intra and interfraction stability, organ protection /small bowel, contralateral breast/ and easy handling.) Pts satisfaction index on the comfort of the positioning devices and on the mask fixation was high in 92% of the entire group.

Conclusions: The AIO solution proved to be an acceptable and safe method to achieve high inter- and intra-fraction positioning accuracy for 3DCRT, IMRT and radio-surgery. The easy to handle the positioning and individual immobilization devices could be confirmed. The systematic review of staff members and pts evaluation on the AIO solution leads to further optimization in pts positioning and immobilization for advanced RT resulting in AIO v.0.2.

1066 poster

INTRODUCTION OF LARGE SURFACE MASK (LSM) AND 3D CONFORMAL RADIATION TECHNIQUE (CRT) IN THE TREATMENT OF THE NEUROAXIS (NA)

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Purpose/Objectif: The irradiation of the neuroaxis requires special technique in order to achieve precise patient (pts) immobilisation, correct field matching, homogenous dose distribution and protection of the surrounding tissues. Our goal was to perform a phase I clinical testing of the NA irradiation with introduction of individual vacuum cushion- thermoplastic mask combination and LSM immobilisation for 3D CRT.

Materials/Methods: We analysed the dose distribution and treatment delivery of 5 pts (1 child, 4 adults) with individual immobilisation (vacum mattress, LSM /AIO Solution™ ORFIT/) 2 pts in prone and 3 in supine position. Pts were treated with 3D CRT (XIO(CMS) planning system). The 2 opponal, lateral, MLC-collimated, rotated 6MV fotonfields were used for the brain. The spinal cord of the adults was treated with 2 (the child's with 1) wedged, direct 6MV fotonfields. All field matchings were moved weekly. The total NA dose was 25.2-36 Gy, the boost dose was 17.6-33.4 Gy with 1,8-1,6 Gy/fr. The tumours histology were ependymoma, dysgerminoma and 3 medulloblastomas.

Results: For the whole group 95-97% of the PTV was within the 95% isodose. 4-10% of the PTV received less than 95% of the prescribed dose, and 3-10% of the PTV recieved higher than 105% of the reference dose. In 4 cases we could achieve the PTV dosehomogenity according to the ICRU recommendation (95-105%).

The doses of the organs at risk:	D_{Mean} (Gy)	% of D_{Mean}
Left lens	1.44-4.97	5.1-14.8
Right lense	1.37-4.84	4.9-14.5
Left lung	0.8-2.49	3.0-6.9
Right lung	1.92-3.54	7.1-10.0
Heart	6.59-16.3	24.4-46.4
Left kidney	0.51-1.77	1.9-5.0
Right kidney	0.36-1.93	1.4-5.5
Bowels, stomach	5.04-7.71	14.0-21.4
Liver	2.72-6.54	10.8-18.6

We did not detect significant difference of the doses homogenity and the toxicity of the protected organs between the prone and the supine position.

Conclusions: The supine position proved to be superior because of pts comfort, intra-, and interfraction position stability and reproducibility. Therefore we prefer the supine position, but using a LSM is always necessary. Our data suggest that this immobilisation and planning technique could be used in a larger scale in the practise of the NA irradiation.

1067 poster

POSITIONING OF PROSTATE PATIENTS BY IGRT USING THE BAT-US SYSTEM

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Purpose/Objectif: BAT (B-Mode Acquisition and Targeting System) is a mobile ultrasound based patient positioning system with a position sensing arm, an ultrasound probe and a computer. Patients can be positioned by Image Guided Radio Therapy (IGRT), after outlined structures of the treatment planning procedure are superimposed by the ultrasound image. Relative to the calculated isocenter displacements in all directions are indicated. After the repositioning process of the patient lying on the patients couch, data can be saved to the computer in order to evaluate the alignments. This leads to a new possibility of patient alignment to the following application of dose.

Materials/Methods: Between 01/2005 and 11/2005 48 patients were re-aligned using the BAT system before each fraction. 45 patients were conformal treated up to 74 Gy (single fraction 2 Gy up to 70 Gy, boost: 2 x 2 Gy). Within this group 4 patients refused continuing the BAT alignment because of adversarial anatomy. At the beginning, once a week orthogonal x-rays documented the positioning progress. 3 patients, who were positioned on vacuum mattress, underwent Intensity Modulated Radio Therapy (IMRT) up to 76 Gy. The age of the collective was in average 71 years, with a range from 56 up to 85 years. The initial PSA of 16.97 ng/ml (0.5 up to 99 ng/ml) was as well listed as the Gleason score (average: 7, range 2 up to 9). The average outlined target volume was 225 cm^3 ranging from 90 up to 388 cm^3.

Results: The average alignments after BAT were left/right: 3.21/3.19 mm, anterior/posterior: 6.07/7.71 mm, inferior/superior 3.14/5.67 mm). The maximum deviation in comparison to the average was approximately 8 times higher for left/right, 5 times higher to anterior/posterior and inferior/superior.

Overall 48 BAT patients leaded to 1586 alignments, where more than 96% of left/right and superior/inferior alignments were within 0-15 mm. More than 95% of left/right and inferior were calculated between 0 and 10 mm, as well as 85% of inferior displacements were between 0 and 10 mm. Because most of the deviations were observed in posterior direction, alignments have to be done in superior direction.

Conclusions: BAT can easily become routine (additional positioning time ~ 5 minutes/patient), with the major advantage that set up errors can be minimized. As in conventional laser alignments problems may occur when organs are filled differently by day to day treatment. In the future dose escalation by increasing tumour control probability, as well as minimizing margins can be discussed.

This evaluation was supported by the Austrian National Bank, Project Nr: 11449

Posters Predictive Assays

1068 poster

AGE-BASED PROGNOSTIC FACTORS FOR 1347 BREAST CANCER PATIENTS TREATED WITH BREAST CONSERVATION SURGERY AND ADJUVANT RADIOTHERAPY

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3 - M.D.Anderson Cancer Center, *Dept. of Biostatistics and Applied Mathematics, Houston, USA*

Purpose/Objectif: Compare risk groups for local failure (LF) and disease free survival (DFS) for different age cohorts after breast-conservation surgery + radiotherapy (RT) ± adjuvant systemic hormone- and/or chemotherapy (HT, CT).

Materials/Methods: Between 1984 and 1997, 1485 patients were treated in our institution with breast conservative therapy for a pT1-2 pN0-1-2 breast cancer. Complete data were available for 1347 patients. After tumorectomy, N pos patients had HT and/or CT. All patients underwent whole breast RT and an additional boost. For the LF and DFS endpoints, recursive-partitioning analysis (RPA) was used to estimate prognostic cut points in three age ranges for the following variables: T-stage, grade, number of positive axillary nodes, ratio (%) of the number of pos axillary nodes to the number of excised nodes (n-ratio), tumor location (loc), ER- and PR-status, menopausal status (meno), HT, CT, and presence of surgical marker clips (clips). The hazard ratio relative to the median patient (RHR) was estimated for each prognostic group.

Results:

A) Age < 45 yrs. (n=220):

For LF, n-ratio was the most important prognostic parameter, followed by PR.

For DFS, again n-ratio was the most significant factor, followed by T-stage and loc.

B) Age 45 - 65 (n=752):

For LF, administered HT was the most important prognostic parameter, followed by T-stage.

For DFS, n-ratio was the most significant factor, followed by T-stage, PR and loc.

C) Age > 65 (n=375):

For LF, administered HT was the one and only significant factor. For DFS, HT was followed by n-ratio.

Conclusions: The prognostic factors for LF and DFS differ from one another and differ for age-cohorts. N-ratio appears to be the most consistent adverse prognostic factor for both endpoints in both subgroups. Surprisingly, tumor location is relevant in patients up to 65 years, for whom the medial tumors have the worst prognosis. In elderly patients HT impacts LF and DSF significantly. The usual measure of risk, number of positive nodes, was insignificant whenever n-ratio was included in the fit.

1069 poster

ASSESSMENT OF THE INDIVIDUAL RISK OF BRAIN TUMOR RELAPSE WITH A DECISION SUPPORT SYSTEM BASED ON BAYESIAN INFERRING

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Purpose/Objectif: This paper describes a study designed to determine the usefulness of Bayesian inferring in an assessment of the individual risk of cancer relapse or progression after treatment. Such an assessment would allow for individualized treatment approach as opposed to current approach based on analyses of large patient groups of relapse risk created according to the classical statistics.

Materials/Methods: Data of 142 patients diagnosed with brain tumor treated with radiotherapy from year 2000 to 2005 were analyzed. Based on data collected by author and literature search 96 attributes related to the cancer type, patient and treatment mode were chosen. Continuous attributes were discretized. Each attribute was presented in binary form (1 or 0), depending on its presence or not. These data consisted of a training set for naive Bayesian classifier learning. The classifier calculated an individual conditional probability of being assigned to one of two classes: relapse/progression within three months from completing radiation treatment or no relapse/progression after three months. Results of classification were compared with actual treatment results to verify the accuracy of the classifier. That enabled to calculate classification accuracy expressed as percentage. Accuracy of attribute selection was determined by leave-one-out method. Quality of the classifier was determined by cross validation method. Classifier was also tested in the clinical setting. Data of 20 patients who have completed treatment and remained under follow up consisted the test set. Treatment results at the classification were unknown. After three months actual treatment outcome was compared with classification result.

Results: High classification accuracy was achieved, with 82% accuracy both for training as well as test sets.

Conclusions: Bayesian classifier is a useful tool for the assessment of an individual risk of relapse or progression in patients diagnosed with brain tumor undergoing radiation therapy postoperatively. High classification accuracy was achieved. These results warrant further studies on clinical application of Bayesian classifier in decision support systems, based on principles of artificial intelligence methods.

1070 poster

ASSOCIATION BETWEEN CD28 GENE POLYMORPHISM AND CERVICAL CANCER

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Purpose/Objectif: The CD28 gene encodes the main T cell costimulatory molecule. Dysreguated CD28 expression has been reported in several neoplastic diseases among them in cervical cancer. We estimed the association between CD28 gene polymorphism and cervical cancer.

Materials/Methods: A hunderd patients with cervical cancer and 144 healthy subjects were examined.

Results: The genotype, allele and phenotype frequencies did not differ significantly between cervical cancer patients and controls. The genotype CC in patient group and control group were 4% and 2.7%; genotype CT- 18% and 25%, and genotype TT- 78% and 72.2% respectively. The allele C in patient group was 13%, in controls was 15.2%; allele T were 87% and 84.7% respectively.

Conclusions: The present study was unable to reveal any association between CD28 gene polymorphism and cervical cancer.

1071 poster

HEMOGLOBIN PRETREATMENT VALUE - A TRUE INDEPENDENT PROGNOSTIC FACTOR FOR CERVICAL CANCER, RETROSPECTIVE SURVIVAL ANALYSIS OF 20 YEARS DATA

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Purpose/Objectif: Tumor hypoxia is a powerful and independent prognostic marker in cervical cancer. In spite of that hemoglobin (Hb) level is only one of the factors influencing tumor oxygenation, it has been shown to have as well a prognostic and predictive value for cases treated by radiotherapy. Moreover the relationship between Hb values and tumor oxygenation has been established in detail. Both low and high values contribute to a reduced oxygenation. The optimal oxygenation is confined to values between 12 and 14 g/dl. We tried to analyze if this phenomenon translates into a prognostic significance of pre-treatment Hb values in spite of that only the values developing during therapy have been shown to be of any significance.
Materials/Methods: A single institution retrospective analysis of a group of cervical cancer patients treated between 1970 and 1990 was performed. 2272 hospital records were reviewed and 1762 were found eligible for survival analysis. All stages of the disease were homogenously represented. All patients have been treated by either brachyradiotherapy or external beam radiotherapy or both. Both therapies developed substantially within the screened period. 445 pts. (25,3%) have undergone surgery. The following parameters were analyzed: 1/ Independence of pretreatment Hb values and FIGO stage, surgery, kind of radiation therapy or age (Cox regression analysis). 2/ The dependence of survival data upon Hb value as a categorical or continuous value (Cox regression analysis). 3/ The proportionality of the risk curves related to Hb value categories (Weibull analysis).
Results: There was no covariation between Hb values and FIGO stage, surgery, kind of radiotherapy or age. The median survival has not been achieved. The mean survival estimates in Kaplan-Meier increased up to an Hb value between 13,8 and 15,0 g/dl, for higher values decreased. (Max. 417 months for 11,4 - 12,6 g/dl, min. 66 months for 5,4 - 6,6 g/dl, medians achieved up to 9,05 g/dl only) There was a significant increase of the age corrected risk (shortened survival) for Hb values below 7,72 and 9,92 g/dl and significant decrease of the risk for Hb values above 9,84 and 12,22 g/dl for categorical and continuous Hb values respectively. There was a tendency to an increased risk for Hb values above 15,0 g/dl in both analyses, however it did not achieve significance. The time - risk curves for categorical Hb values were proportional for all values.
Conclusions: The Hb pretreatment value has shown a prognostic value for survival. There is a clearly increased risk for low values. A tendency to an increased risk for high values, however not significant (perhaps due to a disproportionally low number of cases with high values) may reflect an impaired tumor oxygenation. The proportional risk characteristics for all Hb values (categorical) confirm the independence of pretreatment Hb as a prognosticator. The results presented may contribute to the controversial strategy of pretreatment Hb correction.

1072 poster

IDENTIFYING PATIENTS AT RISK OF SEVERE RADIOTHERAPY TOXICITY ? EVALUATION OF A POTENTIAL BIOMARKER OF NORMAL TISSUE RADIOSENSITIVITY

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Purpose/Objectif: 5-10% of patients treated with radiotherapy for cancer will suffer from unexpectedly severe radiation-induced side effects. If it were possible to identify individuals with increased susceptibility to normal tissue radiation damage prior to commencing radiotherapy the prescribed dose might be modified, or alternative therapeutic strategies could be pursued. A major goal of translational research in radiation oncology is the development of a quick, easy and reliable predictive assay of normal tissue radiosensitivity. To date no such assay has been identified as suitable for routine use in the clinic. There is evidence that levels of phosphorylated histone H2AX (γH2AX) at sites of DNA damage following irradiation correlates with radiosensitivity in cultured cell lines. The aim of this study was to determine whether it is possible to quantify γH2AX induced by in vitro irradiation of human peripheral blood lymphocytes, and then to assess whether the technique used is sufficiently robust to warrant further investigation as a potential predictive assay of normal tissue radiosensitivity.
Materials/Methods: Lymphocytes were isolated from whole blood, irradiated in vitro, fixed and then stained for γH2AX using an indirect immunofluorescence technique. The fluorescent signal obtained was quantified by microscopy (counting foci) or flow cytometry. Repeat samples from 8 volunteers were used to assess reproducibility and intra- and inter-individual variation in assay results.
Results: Quantification of γH2AX by flow cytometry was more reliable than by microscopy. Even so, repeat assays using flow cytometry in 8 volunteers have shown considerable intra-individual variation in results which exceeds inter-individual variation for all potential assay end points examined. Whilst transportation of blood samples from the clinic to the laboratory does not affect assay results, storage of blood samples under different conditions upon arrival in the laboroatory prior to analysis does have a significant effect.
Conclusions: Whilst it is possible to quantify H2AX in isolated human peripheral blood lymphocytes, there is poor reproducibility of assay results in a single individual which may limit its potential as a clinically useful test. Rigouous quality control in relation to blood handling and storage is required.A pilot study assessing its clinical usefulness in identifying radiosensitive patients is on-going.

1073 poster

PROGNOSTIC SIGNIFICANCE OF HPV 16/18 INFECTION, PROLIFERATION RATE AND P53 STATUS IN RADIOTHERAPY OF CERVICAL CANCER PATIENTS

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Purpose/Objectif: The aim of this study was to assess the influence of HPV 16/18 infection, proliferation rate (Ki-67) and p53 status on radiotherapy (RT) outcome in the group of 70 patients with squamous cell carcinoma (SCC) of cervix treated with RT alone.
Materials/Methods: There were 16 tumours with FIGO stage IIA, 23 with IIIB and with 18 IIIB. All biological parameters were assessed on formalin fixed, paraffin-embedded tumour samples. HPV 16/18 infection was detected by in situ hybrydization. The percentage of infected tumour cells (%HPV) and type of HPV signal were analysed. Diffused (DS) - representing episomal HPV DNA, and punctate (PS) - representing integrated HPV DNA signals were distinguished. Ki67 and p53 proteins were assessed by immunohistochemistry.
Results: In the examined group the percentage of HPV positive tumours was 91.4, with mean value of %HPV 38.9 ± 2.9 (SE). The mean values of Ki-67 LI and p53 LI were 50.8%± 1.3 (SE) and 12.0%± 1.6, respectively. There was significant difference in Ki67 LI between pre- and postmenopausal women (p=0.019), and between tumour grade 1+2 and 3 in Ki67 LI (p=0.048) and p53 LI (p=0.003). In univariate analysis there was significant difference in the probability of disease free survival (DFS) between postmenopausal patients having tumours with DS and PS in %HPV>46.0 (8 patients without cancer progression) and patients with at least one of negative factors: %HPV£ 46.0, premenopausal status or PS only (61 patients, Kaplan-

Meier DFS 51.7%), (p=0.049). Pre-menopausal women with faster tumour cell proliferation (Ki67 LI>45.0% -optimal cut off point) had significantly higher (p=0.05) 2-year DFS than those with lower proliferation. Such relation was not found for women after menopause. However, Cox multivariate analysis showed that only HPV DS and PS detected in more than 46.0% of tumour cells and postmenopausal status are independent positive prognostic factors for women with cervical cancer.

Conclusions: Our data may indicate that all postmenopausal cervical cancer patients having tumours with diffuse and punctate HPV signals in more than half of the analysed cells, may survive without incidence of cancer longer than other women for whom clinicians should consider more aggressive treatment.

1074 poster

STEFIN A (SA): ANALYSIS OF ITS PROGNOSTIC VALUE IN OPERABLE HEAD AND NECK (H&N) CANCER

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Purpose/Objectif: SA is endogenous inhibitor of cysteine cathepsins, which are involved in proteolysis during invasion and metastasizing of tumor cells. The aim of the study was to evaluate prognostic value of SA in operable squamous cell carcinoma of the H&N.

Materials/Methods: SA concentrations were measured in cytosols prepared from primary tumor obtained during curative surgery from 182 pts. Female/male ratio was 14/168 and median age was 58 yrs (range 36-80). Primary tumor origin was oral cavity 29, oropharynx 44, hypopharynx 24, larynx 85. Tumor characteristics were as follows: pT3+4 113, pN+ 105, pTNM IV 106, extracapsular extension 63. Postoperatively, 166 pts were irradiated to 50-70 Gy (median 56). For quantitative analysis of SA in tumor cytosols, a commercially available enzyme-linked immunosorbent assays (KRKA d.d., Novo mesto,) was used. SA concentrations were determined consecutively in 3 groups of pts: in 1995 41 pts, 1998 49 pts, 2005 92 pts.

Results: All but two survivors were followed for ^{3}7 yrs (range 2.4-12.8, median 8.5). Disease recurred locally/regionally in 29 pts and at distant sites in 19 pts; 44 pts died of disease progression. 5-yr failure-free survival (FFS, first failure at any site) was 71.4% (95% CI, 64.5-78.4). In all 3 groups, non-laryngeal primary, pN+, pTNM-stage IV, extracapsular tumor spread and lower SA concentration were predictive for worse FFS (log-rank test, P<0.05). The optimal cut-off concentration of SA that gave best discrimination between survival rates of SA-low and SA-high pts was similar in all 3 study groups: 29th, 30th and 28th percentile, respectively. To avoid bias arising from time difference between biochemical analyses, SA concentrations (Xi) from 3 datasets were pooled together after standardization using group specific mean (Xm) and standard deviation (SD) values according to the formula: (Xi-Xm)/SD. In Cox multivariate regression analysis, standardized SA was the strongest independent predictor for FFS, irrespective of being introduced as binary variable (dichotomized according to optimal cut-off value: P<0.001, RR 0.35, 95% CI 0.19-0.61; or according to median value: P=0.007, RR 0.43, 95% CI 0.23-0.79), or as continuous variable (P=0.007).

Conclusions: The prognostic impact of SA was suggested in all three independent groups of pts. The consistency of this result was demonstrated in pooled analysis confirming strong and independent prognostic value of cytosolic SA in operable carcinoma of the H&N.

1075 poster

TUMOR-INFILTRATING CYTOTOXIC T CELLS AS WELL AS B CELLS PREDICT OUTCOME IN SQUAMOUS CELL CARCINOMA OF THE OROPHARYNX

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Purpose/Objectif: To assess the prognostic value of tumor infiltrating lymphocytes (TIL) and clinical factors in squamous cell carcinoma of the oropharynx after radical surgery and postoperative radiotherapy (RT).

Materials/Methods: Between 1985 and 1995, a total of 82 patients with 84 tumors were entered onto the study. Forty-two primary tumors (50 %) involved the tonsils, 23 (27 %) the soft palate, and 19 (23 %) the base of the tongue. The pT- and pN-categories (UICC 1997) were: T1 (24), T2 (36), T3 (18), T4 (6), N0 (31), N1 (12), N2 (38), NX (8). Postoperative RT to the primary and regional lymphatics was given with 60 Gy in 6 weeks and single daily fractions of 2 Gy. Prognostic impact of tumor infiltrating lymphocytes (TIL) was assessed using tissue microarrys constructed from resection specimen of the primary tumor. The following antibodies were selected: CD3, CD4, CD8, granzyme B and FoxP3 (all for T cells with different function) and CD 20, CD79 (for B cells). Prognostic effect of TIL subsets was evaluated by the logrank test comparing locoregional control rated and survival rates for groups with high and low numbers using median values as cutoff. Median follow-up was 43 months (range, 14-132 months).

Results: Overall survival-, disease-free survival-, and locoregional tumor control rates were 59 %, 70 % and 76 % at 5 years. Median numbers of TIL per 100 tumor cells were 10.3 for CD3 (range, 2-34), 6.6 for CD4 (range, 0-31), 5.7 for CD8 (range, 0-27), 4.2 for FoxP3 (range, 4-14), 0.5 for granzyme B (range, 0-41%), 7 for CD68 (range, 1-26), 1 for CD20 (range, 0-13) and 0 for CD79 (range, 0-9). Locoregional control was significantly influenced by the following subgroups of TILs: CD8 (81% for TIL > median vs 64% for TIL < median, p=0.05), CD 20 and CD79 (89% for TIL > median vs 57% for TIL < median, p=0.03). Impact on disease-free survival was noted for CD 8 (p=0.08) and CD20/CD79 (p=0.03). Additional significant prognostic factors for disease-free survival were: tumor site (tonsils: 83 % vs soft palate: 66 % vs base of tongue: 49 %, p=0.02), duration of RT (£ 47 days: 83 % vs > 47 days: 55 %, p=0.03). A significant prognostic impact on locoregional control was noted for the duration of RT (p=0.01), tumor site (p=0.02).

Conclusions: resence of high numbers of cytotoxic TIL (CD8) as well as (unexpectedly) B-cells (CD20/CD79) were associated with improved outcome in this group of patients with squamous cell carcinoma of the oropharynx after radical surgery and postoperative radiotherapy. Knowledge of local immune responses is important for the development of immunotherapeutic strategies.

Posters Prostate Cancer

1076 poster

A PROSPECTIVE OBSERVATIONAL STUDY OF 3D CONFORMAL RADIOTHERAPY FOR CLINICALLY LOCALIZED PROSTATE CANCER

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Purpose/Objectif: A prospective observational study was conducted in order to evaluate the rate of acute and late toxicity and biochemical failure of patients (pts) treated with conformal radiotherapy for clinically localized prostate cancer.

Materials/Methods: From January 2002 to November 2005, 102 pts with T1-2N0M0 prostate cancer were treated to a dose of 74-76 Gy with 3-field conformal radiotherapy. Patient characteristics were

as follows: median age 72 years (range 54-82 years); stage T1 in 24 (23.5%) pts, T2a in 38 (37.3%), T2b in 19 (18.6%), T2c in 21 (20.6%); Gleason score 2-6 in 70 (68.6%), Gleason score 7 in 22 (21.6%) and 8-10 in 10 (9.8%). The median baseline PSA level was 10 ng/ml (range 0,9-208 ng/ml); median pre-radiation PSA was 1.03 ng/ml (range, 0.02-26.0 ng/ml); 74 (72.5%) pts received HT consisting of luteinizing hormone-releasing hormone agonist (LHRH analog) and/or an antiandrogen. Hormone therapy (HT) was administered for a median of 5 months (range, 2-26 months). RT was delivered with 18 MV photons to the prostate and seminal vesicles (SV) in 51 (50%) pts (50Gy on prostate and SV plus a 24-26 Gy boost on prostate) and to prostate alone in 51 (50%) to a total dose of 74 Gy, in 2 Gy daily fractions, in 96 pts (94%), and 76 Gy in 6 (6%); we excluded SV from the CTV calculating the risk of involvement for each patient (> or < 15%). Biochemical failure was defined according to ASTRO consensus criteria, clinical failures were determined by rectal examination, transrectal ultrasound, radiographic or radionuclide scan studies.

Results: Median follow-up was 13 months (range 6-49 months). Eight pts (7.8%) had biochemical failure, the baseline PSA value in these pts was >10 ng/ml (median 16 ng/ml, range 11-208 ng/ml). The median time to biochemical failure was 20 months (range, 4-34 months). No distant metastases were detected at this time. Three pts died of other causes, 2 of other malignancies, 1 of chronic obstructive pulmonary disease; none of them developed local or distant failure. Acute and late toxicity were graded according to RTOG scale. Acute toxicity was: RTOG grade II gastrointestinal (GI) in 22 (21.6%) pts, grade II genitourinary (GU) in 28 (27.5%); no patient experienced grade III or higher morbidity. Only one patient (1%) developed grade III late GU morbidity (uretral stricture requiring dilatation). Erectile function was assessed in all pts before and after RT; 2 (2%) pts were impotent before treatment, 5 (5%) became impotent after the starting of HT and remained so after RT.

Conclusions: 3D-conformal radiotherapy to doses of 74-76 Gy is feasible, associated with minimal acute and late toxicity. Comparing this results with previous data referring to pts treated up to 70 Gy we can asses that the risk of grade 2 or higher GI and GU morbidity is not increased with higher dose values. Higher doses, administered through special techniques as IMRT, will be evaluated in pts with locally advanced disease.

1077 poster

ACCELERATED HYPOFRACTIONATED RADIATION THERAPY WITH NEOADJUVANT AND CONCOMITANT HORMONE THERAPY FOR INTERMEDIATE RISK PROSTATE CANCER

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Purpose/Objectif: The alpha/beta ratio for prostate cancer has been estimated to be about 1.5 Gy, possibly lower than the normal surrounding tissue. This signifies that prostatic tumours react as late-responding tissues with a higher sensitivity to larger fractions. Therefore, an accelerated hypofractionated regimen can lead to a therapeutic gain while decreasing short term side effects; without necessarily compromising long term side effects or quality of life.

Materials/Methods: Forty-two patients with intermediate-risk prostate cancer, as defined by the RTOG 9910 protocol were recruited for this study (T1b to T4 disease with gleason scores of 2 to 6 and pretreatment prostatic specific antigen [PSA] levels between 10 and 100 ug/L; or T1b to T4 disease with gleason score of 7 and PSA below 20 ug/L; or T1b-T1c disease, gleason score of 8 or above and PSA below 20 ug/L). Patients had a calculated risk of pelvic lymph node disease of less than 15%, as well as negative pelvic CT and bone scan. Hormone therapy consisted of one intramuscular injection of leuprolide acetate (lupron depot 30 mg, 4 months preparation) and one month of oral non-steroidal anti-androgen medication (bicalutamide 50mg po qd) starting on the day of the injection. Conformal radiation treatment was started 8 weeks after the leuprolide injection and was administered using at least 4 fields, with beams of 18MV or more. Patients received 57 Gy in 19 fractions. Treatment failure was noted if there was clinical evidence of local or distant recurrence, if hormone therapy was started or if there was a biochemical failure. Biochemical failure was redefined at time of analysis to be a PSA value equivalent or greater than the nadir after treatment plus 2 ug/L.

Results: Follow-up time ranged from 18 to 50 months (median 40 months). Data was available on 39 patients for acute toxicity and 38 patients for chronic toxicity and PSA monitoring. Radiation therapy was well tolerated and no treatment interruptions occurred. The majority (56%) had grade 0 or 1 acute genito-urinary (GU) toxicity, while 36% had grade 2 and 8% had grade 3 acute GU toxicity. There was no significant acute gastro-intestinal (GI) toxicity, with only grade 1 or 2 side effects observed. Chronic grade 1, 2 and 3 GU toxicity was seen in 8%, 5% and 5% respectively. Only chronic grade 1 GI toxicity was observed (18%). Eighty-two percent (82%) of patients had no long term side effects from the treatment. At time of analysis, 79% showed no sign of treatment failure.

Conclusions: Accelerated hypofractionated radiation with neoadjuvant and concomitant androgen blockade is well tolerated with no significant short or long term morbidity after a median follow-up time of 40 months. Control rate seems good, however longer follow-up is needed to see if this is maintained and if the treatment will impact survival. Sponsored in part by Abbott Laboratories.

1078 poster

ACUTE TOXICITY OF HIGH DOSE HYPOFRACTIONATED 3D CONFORMAL RADIOTHERAPY IN LOCALISED PROSTATE CANCER

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Purpose/Objectif: To evaluate the acute toxicity of 3D conformal techniques with high dose hypofractionated radiotherapy (HYPORT).

Materials/Methods: Men with localised T1c-T3a adenocarcinoma of the prostate, were eligible for this study. The prescribed dose was 67.6 Gy for the Low Risk Group, and 70.2 Gy for the Intermediate and High Risk Groups. Treatment was administered during 5.2 to 5.4 weeks, 5 days a week, 2.6 Gy per fraction (equivalent to 79-82 Gy in 2 Gy fractions, assuming an $\alpha/\beta = 1.5$). Patients that needed prophylactic irradiation of the pelvic/sacral lymph node areas and/or seminal vesicles were excluded. To prevent for inter-observer variability, the same physician (V.M.) did the treatment planning (XiO 4.1.1,CMS) and as well as the follow-up of all patients. Androgen deprivation was delivered to patients with intermediate and high-risk prostate cancer. The primairy endpoint is acute toxicity using the RTOG/EORTC scales with slight modifications. Recording of the toxicity was carried out every week during the radiotherapy, 1 month after the end of irradiation. Final scores represent the maximum toxicity during the radiotherapy treatment.

Results: From September 2004, 100 consecutive patients with localised prostate cancer were enrolled. Overall, acute toxicity was low, grade 1 and 2. Only 1 patient experienced urinary G3 toxicity. We

found significant differences between the maximal urinary and rectal toxicity during radiotherapy (p< 0.001). Both urinary and rectal toxicity decreased significantly in the period until one month after the end of radiotherapy, 11% (p<0.001) and 2% (p=0.002) respectively. At this time point, there was no longer any difference between urinary and rectal toxicity. Treatment time was reduced by 3 weeks with respect to conventional fractionated radiotherapy.

Conclusions: The delivery of a high total dose using hypofractionated 3D conformal radiotherapy was well tolerated. Our results are similar with regard to acute toxicity than published using 3DCRT or IMRT in a high dose hypofractionation schedule (1-3). If, as expected, a longer follow-up confirms low late toxicity and equal or higher cure rates, HYPORT will be an alternative and more convenient technique for delivering high doses to localised prostate cancer. The treatment period has been reduced by nearly 3 weeks, which is more convenient for the patient. Furthermore, it has logistic and economic advantages for the most prevalent cancer in men in developed countries.

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1079 poster

CLINICAL RESULTS OF IMAT IN ADENOCARCINOMA PROSTATE CANCER

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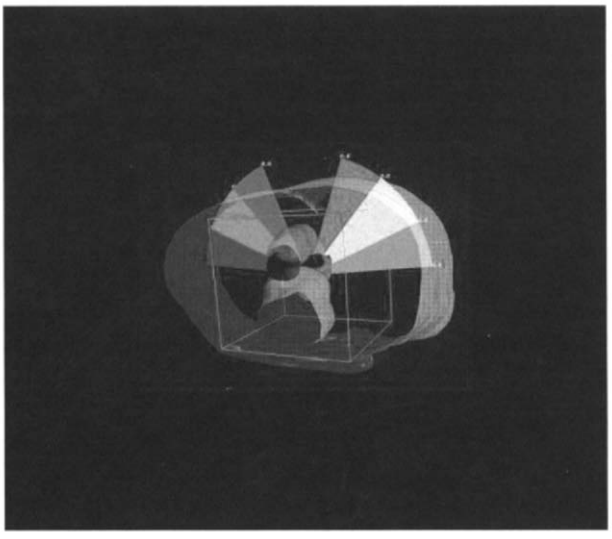
Purpose/Objectif: Since 1998 a new dynamical technique with intensity modulated arc therapy (IMAT) started for prostate cancer in our RT dept. Treatments were delivered using a dynamic MLC (leaves of 5 mm). Dose escalation study is performed. Biochemical outcomes and G1 urinary and rectal acute and late toxicity according to dose are reported, according to RTOG morbidity grading scale.

Materials/Methods: From 1998 to 2002, 79 consecutive T1-T3 N0 M0 non operated prostate cancer pts are studied. The mean age was 71 years (range 59-82), mean Gleason score 7, mean initial PSA 12,1. Minimum follow up accepted was 23 months, total dose varies from 69 up to 82.8 Gy. IMAT has been performed with two coplanar lateral intensity modulated arcs wide of 70° (20° to 90° and 270° to 340°). Pts have been treated in prone position with vacuum cushions. ERGO 3Dline TPS was employed to prepare forward plans for 6 MV photon beams. Arc intensity modulation has been manually carried out. CTV includes prostate or prostate and seminal vesicles; PTV has been achieved with additional margin of 10 mm in all directions except for the posterior where 5 mm margin was added. Analysis is performed on three groups of pts: with dose less or equal to 72 Gy, from 72.1 to 75.6 Gy and from 75.6 up to 82,8 Gy. Three risk groups have been classified: favourable, intermediate and unfavourable; defined parameters are PSA, GS and Stage.

Results: 18 pts (9 treated with 72 Gy and 9 pts treated from 72.1 up to 75.6 Gy) developed acute G1 rectal and urinary toxicity, no pts experienced acute G2/3. 5 pts developed late G1 rectal toxicity and 10 pts late G1 urinary toxicity. 4 pts treated from 75,6 up to 82,8 Gy developed late G1 rectal toxicity; no pts with late urinary toxicity and 3 pts experienced late G1 rectal and bladder toxicity. The 5-year actuarial PSA relapse-free survival rates for 3 risk groups patients are for the first 50 pts (up to 75,6 Gy) are 85%, 60% and 50% respectively; in group treated with higher doses (up to 82,8 Gy) are 88%, 84% and 79% respectively.

Conclusions: IMAT offers a very good uniform dose distribution for target volume and a IMRT comparable sparing of rectum and urinary bladder. The improvement in treatment techniques (Arc intensity modulation optimisation) allowed to improve the target and OAR DVH, in consequence should improve the dose, the cure rate and minimized the toxicity. These physical evidences are confirmed by our clinical results, in the set of patients treated with higher dose.



1080 poster

CLINICALLY SIGNIFICANT INTRAFRACTION PROSTATE MOTION DURING RADIOTHERAPY TRACKING OF IMPLANTED TRANSPONDERS

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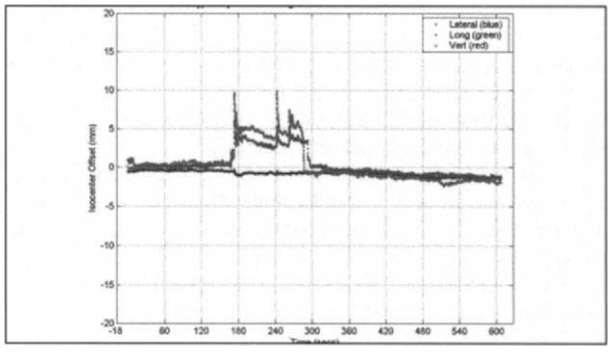
Purpose/Objectif: Advances in precision for treatment delivery mandate equal advances in accuracy, to ensure that fields consistently encompass the target volume. Much has been reported regarding the interfraction motion of the prostate, however, less is known about the intrafraction movement of the gland. Using implanted Beacon® transponder devices (Calypso Medical, Seattle, WA,) and electromagnetic tracking, we report the magnitude and incidence of significant intrafraction motion.

Materials/Methods: Institutional and FDA approvals were obtained for a clinical study at 5 centers, on 35 men treated with 38-45 (median 39) daily fractions for prostate cancer. Prostate motion was continuously tracked in the lateral, longitudinal, and vertical axes (measured in mm from the approved set up position) during radiation delivery from "beam on" until the completion of each fraction.

Results: Tracking data from entire fractions were available for analysis from 1157 fractions (20-40 fractions per patient). Treatment duration ranged from 540-660 seconds. An example of tracking for a single fraction is shown in Fig. 1. Prostate motion of ≥ 5mm was documented in 34/35 patients (97%). In 29 patients (83%), prostate motion was >30 seconds duration corresponding to 15% of treatment fractions. Motion of >3mm lasting >30 seconds was seen in all patients, representing 41% of all fractions. Significant individual variation was evident, ranging from 3.4% to 85.3% of fractions for specific patients. Intervention (i.e., delayed initiation, beam interruption, or patient repositioning) was performed in more than 10% of fractions as a result of documented intrafraction motion.

Conclusions: Electromagnetic detection of Beacon® transponders

is an effective means of tracking the prostate during radiotherapy. Clinically significant intrafraction motion is present during radiotherapy, ranging from 15%-41% of fractions for this study population. There is significant variation between individuals that cannot yet be predicted without continuous tracking. Based on the frequency and magnitude of documented motion and the experiences from this clinical study, interventions may be made that allow realignment to isocenter while operating within the basic treatment time allotted. As centers gain experience and confidence in these new technology interventional strategies are expected to evolve.



1081 poster

COIL MARKER STABILITY IN PROSTATE LOCALIZATION

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Purpose/Objectif: Fiducial markers within the prostate gland are often used for image-guided radiotherapy (IGRT) of prostate cancer. Many institutions implant radiopaque "seed" markers within the gland for this purpose; however, such seed markers can migrate an average of 1.2 mm over the course of therapy.[1] We investigated the positioning reproducibility of serrated gold coils (Visicoil™) implanted within the prostate glands of patients undergoing definitive external beam radiotherapy for prostate cancer.

Materials/Methods: Radiopaque Visicoils™ of diameter 0.75 mm and median length 3 cm (range 2-4 cm) were implanted, one into each lobe of the prostate glands of 18 patients. A transperineal approach with ultrasound guidance was used. The coils were visualized on treatment planning CT scan performed before therapy (SIM) and again after 25 fractions of treatment (5 weeks, 5WK). The magnitude and direction of changes in relative coil positions from the original CT scan were determined. For localization purposes five points were specified along the length of each coil. For each patient the SIM and 5WK scans were fused using a computer algorithm that mapped these specified points from the SIM scan onto the 5WK scan. Changes in the coil position, relative to the central axis of the fusion data set, and also relative to the other coil, were analyzed.

Results: Data from 18 patients were studied, of whom ten were receiving androgen ablation therapy. Comparison of the top and bottom points of each coil demonstrated some degree of movement or position uncertainty, with an average of 1.6 mm (+/- 0.8 mm) position uncertainty of the top of the coil relative to its bottom point. However, the average absolute shift across the entire length of coil between SIM and 5WK scans was only 0.8 mm (+/- 0.3 mm), relative to coil center. Average residual errors (standard deviations) following adjustment of patient position were only 0.5 mm LR, 0.6 mm AP, and 0.4 mm IS. Differences between patients undergoing hormonal therapy and those not receiving hormones were not statistically significant.

Conclusions: The observed stability of the Visicoil™ was excellent, with average residual errors (standard deviations) of 0.4 - 0.6 mm across the coils. Possible volume changes due to androgen ablation treatment did not significantly affect Visicoil™ fiducial accuracy. The resultant safety margins (2 SDs) to account for residual position uncertainty would be 0.8 - 1.2 mm, values which may be better than the margins needed to account for residual position uncertainty seen with "seed" markers.[2]

References

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1082 poster

COMPARISON OF DOSE-RESPONSE RELATIONS OF ANAL SPHINCTER AND ANAL CANAL REGARDING THE RADIATION EFFECTS OF FAECAL LEAKAGE AND BLOOD OR PHLEGM IN STOOLS FROM PROSTATE CANCER RADIOTHERAPY

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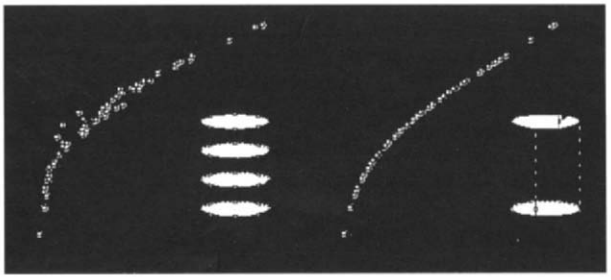
Purpose/Objectif: In the optimization of prostate cancer radiotherapy, it is important to estimate the parameters that describe the dose-response relations of anal sphincter and anal canal regarding the clinical endpoints of faecal leakage and blood or phlegm in stools. Furthermore, the association of the irradiated regions of anal sphincter and anal canal with the clinical follow-up results for these two endpoints needs to be examined.

Materials/Methods: In this study, 65 patients who received radiation therapy for clinically localized prostate adenocarcinoma are analyzed. The clinical treatment outcome and the 3D dose distribution delivered to anal sphincter and anal canal were available for each patient. A questionnaire was used to assess the clinical bowel and urinary symptoms. The best parameter estimates of the relative seriality model were calculated performing a maximum likelihood fitting. Furthermore, similar parameter sets were calculated for the radiobiological models of LKB and Parallel. The estimated model parameters were validated clinically by predicting the treatment complication probabilities in a subset of the patient population.

Results: For anal spincter, the estimated values of the parameters for the two clinical endpoints are D50=70.2 Gy, γ=1.22, s=0.35 for faecal leakage and D50=74.0 Gy, γ= 0.75, s 0 for blood or phlegm in stools. Another set of parameters was also calculated for the anal canal region. The standard deviations of the parameters were also calculated together with the confidence intervals of the dose-response curves. The analysis proved that by using the relative seriality model, the observed pattern of the treatment outcome could suitably be reproduced for this patient material. A small difference was observed in the clinical outcome prediction regarding analsphincter against anal canal for the two examined clinical endpoints.

Conclusions: For anal sphincter and anal canal, a strong volume dependence (low relative seriality) was found for the endpoint of blood or phlegm in stools whereas faecal leakage is characterized by a medium relative seriality. The risk of faecal leakage or blood or phlegm in stools for patients irradiated for prostate cancer may be significantly reduced by diminishing the biologically effective uni-

form dose (BEUD) or equivalent uniform dose (EUD) to anal sphincter and anal canal below 40-45 Gy.



1083 poster

COMPARISON OF MULTI-MODALITY PROSTATE CANCER IMAGING WITH MRI/MRS AND ULTRASOUND TISSUE-TYPING (UTT) TO WHOLEMOUNT PATHOLOGY: A PRELIMINARY STUDY

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Purpose/Objectif: Two functional imaging techniques, magnetic resonance imaging/magnetic resonance spectroscopy (MRI/MRS) and ultrasound tissue-typing (UTT), have shown the potential to differentiate cancerous regions in the prostate. The purpose of this work is to evaluate if their combination could further improve accuracy for identifying tumor-bearing regions within the prostate.

Materials/Methods: In our preliminary study fifteen prostate cancer patients were studied with *in vivo* MRI/MRS and UTT prior to their prostatectomies. The MRI/^{1}H-MRS study was carried out using a Phillips 1.5T Gyroscan imager (Phillips Medical Systems, The Netherlands). High resolution MRI and 3D-localized high spatial resolution ^{1}H-MRS was acquired using four external synergistic probes for MRI and an endorectal coil for ^{1}H-MRS. Transverse spin-echo T_1-weighted MR images and thin-section transverse and coronal T_2-weighted fast spin-echo images were obtained. The UTT data was obtained with a conventional ultrasound machine (B & K Medical System, Hawk, 7.5 MHz probe). 3-D ultrasound radio-frequency (rf) data of the prostate were acquired in a sequence of parallel axial scans which were 2 mm apart. The reliability, reproducibility, and accuracy of the imaging methodologies were tested against histopathologic studies done on the patients' prostatectomy specimens.

Results: For the MRI/MRS study, the characteristic signals of citrate, choline, and creatine were integrated into the ^{1}H-MRS data and the log-transform of the ratio [Choline + Creatine]/Citrate calculated for each spectrum. Values ≥3.0 (indicative of malignancy) were marked on a grid and overlaid on corresponding MR images. For the UTT imaging, the ultrasound rf data were analyzed with 2-D spectrum technique to identify cancerous tissues. The resulting depictions of cancerous tissue and gland borders as well as anatomical markers were rendered into 3-D volumes in UTT, MRI/MRS and whole-mount sets for spatial correlation. Our preliminary results indicate 1) larger tumors demonstrated the best correlation between sets; 2) smaller tumors, especially outside the peripheral zone, were more likely to be missed by both UTT and MRI/MRS images; and 3) some cancerous areas detected in one image set were not shown in the other image set, suggesting the combination of the two image modalities could derive improve accuracy in the detection of cancerous regions in the prostate.

Conclusions: MRI/MRS provides anatomical and metabolic information of the prostate. UTT imaging provides physical properties of the prostate. Our preliminary study demonstrated that these functional imaging techniques can be combined to improve the detection of cancer-bearing regions inside the prostate gland. Multi-modality functional imaging offers a promising new approach for non-invasive prostate cancer detection and image-guided prostate cancer radiotherapy.

1084 poster

CONFORMAL RADIOTHERAPY FOR PROSTATE CANCER - A PHASE I- II PROSPECTIVE STUDY.

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Purpose/Objectif: To evaluate feasibility and toxicity (tx) of conformal radiotherapy (3DCRT) in prostate cancer (PC) as newly implemented technique in our center.

Materials/Methods: From January to November 2005, 21 consecutive patients with intermediate or high risk PC were treated on a prospective basis with 3DCRT to a target dose of 76 Gy. The clinical target volume (CVT) consisted of the prostate (P) and the seminal vesicles (SV) with the external & internal iliac lymph nodes only if their estimated risk of involvement based on Roach's formula N+ = 2/3 PSA + (GS- 6)x 10 exceeded 15 %. The CTV- planning target volume (PTV) margin was 1 cm all around except 0.5 cm toward the rectum. PTV1 including P+SV+/-N was irradiated to 46Gy/23fr with a "box" technique, than 6 fields were used for a PTV2 = P + same margins for additional 30 Gy/15fr. For T3b the entire length of the SV was kept in the PTV up to 54 Gy, whereas their base remained in the PTV2 for 76 Gy. Dose constraints were: for P- Dmin= 72 Gy, V85= 74 Gy (mandatory); for bladder- D max≤ 100%, V50 ≤ 85.5% and for rectum Dmax ≤ 95% & R25 ≤ 90%. If the latest ones were not fulfilled, the total dose was lowered to 74 Gy. Opposite fields were checked by portal imaging before treatment, and weekly thereafter, accepting deviation of less then 5 mm. All patients received 2 months of neoadjuvant complete androgen blockade (CAB), followed by CAB concomitantly with 3DCRT for intermediate risk, respectively adjuvantly for high risk- scheduled for 2 years for LHRH or indefinitely if orchidectomy. RTOG/EORTC criteria were used for scoring acute and late tx..

Results: With a median follow- up of 1year (6 to 18 months) we noticed 38 % G1, 38 % G2 and 24 % G3 acute urinary (U) tx., 53% G1, 33 G2 and 9.5 G3 digestive (D) tx., respectively 23% G1, 38 % G2 late U tx , 33% G1 and 5 % G2 late D tx. There were noG3-4 late U or D tx and 38% of patients preserved their erectile function.

Conclusions: 3DCRT to 76 Gy is feasible and safe if certain dose constraints to rectum and bladder are carrefully respected. This schedule became our "standard" RT for intermediate and high risk PC.

1085 poster

DAILY ULTRASOUND PROSTATE LOCALIZATION USING SONARRAY SYSTEM: RESULTS OF A PROSPECTIVE STUDY

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Purpose/Objectif: The aim of this study is to assess the feasibility of a daily target volume repositioning using ultrasound imaging (Sonarray/Z-Med) before IMRT for prostate cancer.
Materials/Methods: From April 2003 until September 2004, 37 consecutive patients received IMRT for prostate cancer. Patients were setup in supine position with knee support and were aligned on the isocenter skin marks. Computer-assisted transabdominal ultrasonography which allowed real-time prostate localization was then performed. Couch displacement moved patients to the treatment position according to the results of Sonarray imaging before treatment. Setup accuracy was assessed using portal images for the first 20 patients. Toxicity was registered using the Common Toxicity Criteria scale version 3.
Results: Among the 37 patients, Sonarray system provided high image quality in 35 patients. The mean movement of the prostate and standard deviation observed by ultrasound acquisition (combined to portal imaging) were 0.4+/-4 mm,-2.1+/- 4.5 mm and 0.5+/-5 mm in lateral, SI and AP directions respectively. The sole ultrasound procedure was able to detect both setup error and prostate motion and the mean shifts and standard deviation of the isocenter displacements in lateral, SI and AP directions were 0.2 +/- 4.4 mm, -2.9 +/- 4.7 mm and 4.1 +/- 6 mm respectively. While the dose delivered to the prostate was increased to 78 Gy, no grade 3 or 4 acute toxicity was observed.
Conclusions: Sonarray ultrasound is a non-invasive system allowing real-time prostate localization. It could authorize reduction of margins applied around the target volume from 10 mm to 5 mm.

1086 poster

DEVELOPMENT AND APPLICATION OF A SPECIFIED PELVIS PHANTOM FOR TESTING THE IMPLEMENTATION OF MRI / MRS INTO THE IMRT TREATMENT PLANNING PROCESS IN CASE OF PROSTATE CANCER

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3 - Schleifring und Apparatebau GmbH, *Fürstenfeldbruck, Germany*

Purpose/Objectif: Until today in case of prostate cancer, the treatment planning is based on CT data. However, with the introduction of the intensity-modulated radiotherapy it is desired to include further information about exact tumor extend. Therefore, morphologic and metabolic information about the prostate gland as provided by MR imaging and MR spectroscopy are required for improved dose escalation and exact target volume definition. Modern clinical high field MR scanners operating at field strength of 3 Tesla provide further improvement of spatial and spectral resolution of MRSI data.
Purpose of this study was to implement a specific pelvis/prostate phantom for the preclinical assessment of potential integration of MRI / MRS data into IMRT treatment planning process. Spatial precision and distortions in the MRI / MRS setup are compared with CT images of the phantom.
Materials/Methods: A human pelvis phantom mimicking the anatomical *in vivo* structure, metabolite concentrations, and relaxation times of healthy and malignant prostate tissue, has been developed. The phantom includes the prostate with a small tumor, a surrounding fat layer, and the rectum as intake for the endorectal coil and for testing different rectal fillings. Additionally, an artery is implemented for the simulation of flow artifacts. The phantom provides an accurate determination of image distortions caused by the inhomogeneity of the magnetic field and the nonlinearity of the gradients of whole body MR unit. The resolution boards in the three spatial dimensions enable to estimate the image resolution. All MR experiments were performed on a 3T MAGNETOM Trio system (Siemens Medical Solutions, Germany) with a combined spine and phased array coil. MRI / MRS sequences were applied according to clinical standards with diagnostic resolutions and in a reasonable total measurement time. The distances given by the CAD design were measured in the transverse, coronal, and sagital T_2-weighted MR images and compared with the CT data. An image registration between planning CT and treatment MRSI was performed and used for the treatment planning process.
Results: The distances in the images corresponded to the CAD data with an acceptable accuracy of less than 2 mm. The deviations between the construction dimensions and the image distances accomplish the specifications and are small compared to the geometric margins for the target volumes caused by prostate gland motions. The included resolution phantoms are well defined in the images. Local susceptibility variations caused by the air in the "rectum" have considered for image artifacts. The typical prostate spectra with signals of citrate, choline and creatine were measured throughout the whole "prostate". The included "tumor" was clearly visible in all T_2-weighted images and in the CSI spectra. Because of the abandonment of an endorectal coil, the "prostate" was not deformed. Therefore, a rigid image registration algorithm could be used.
Conclusions: The presented pelvis phantom is able to simulate the morphologic and metabolic conditions *in vivo* and can be used for the preclinical quality assurance and evaluation of MRI / MRS into the IMRT treatment planning process.

1087 poster

DO PROSTATE DISPLACEMENTS BETWEEN 1.5 AND 4.4 MM NEED CORRECTION? A RANDOMIZED STUDY

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Purpose/Objectif: To assess the effect of correcting for daily prostate displacements between 1.5 and 4.4 mm during whole-pelvis IMRT.
Materials/Methods: 18 patients with 3 intraprostatic fiducials underwent daily on-line verification according to an in-house protocol. A lateral port film was taken after patient set up. If prostate displacement along the Z (AP) and/or Y (SI) axes was between 1.5 and 4.4 mm compared to the planning position, the decision whether to correct or not was based on a random list. If the displacement along either the Z- or Y-axis exceeded 4.4 mm, it was corrected and the session considered not eligible for randomization. Also, if both Z/Y measurements were within 1.5 mm, no action was taken and the session not randomized. Randomization was stratified by patient and resulted into two groups of sessions: corrected (C) and not corrected (NC). After correction/no correction, another lateral port film was taken just before treatment and a third one at completion of treatment. Mean time interval (SD) between the `initial` and `before` treatment films was 9 minutes (4 min) while it was 22 minutes (6 min) between the start and the end of treatment. The purpose of the study is to compare systematic (S) and random errors between the two groups at the three film time points, `initial`, `before` and `after`. Errors were defined as per Van Herk and computed using a mixed model, that takes into account within-patient correlation. The difference in the magnitude of errors between the 2 arms was evaluated using an F test.
Results: Of 18 patients, 3 were excluded; 2 because of only one eligible session and 1 because of noncompliance. 239/545 (43.8%) of sessions had prostate displacements between 1.5 and 4.4 mm, and were randomized: 117 (49%) to NC and 122 (51%) to C.
The systematic errors (mm) by randomization are reported in the

table. Correction of errors translated into a significantly smaller pre-treatment S for both axes. At the end of treatment, the benefit for C over NC remained highly statistically significant along the Z axis and was borderline significant along the Y axis. Regarding the random error, we observed »15-20% average reduction for C as compared to NC for both Z- and Y-axes when assessed over the entire time period, though the difference was not statistically significant.
If the overall treatment course consisted of only the sessions with an error between 1.5 and 4.4 mm, correcting for prostate displacement would translate into a margin reduction of 2-3 mm for C over NC.
Conclusions: The results support taking action to correct prostate displacements between 1.5 and 4.4 mm after set-up to minimize the systematic error. The benefit also holds true after prolonged treatment sessions especially along the Z-axis.

1088 poster

DOSE ESCALATION FOR LOCALLY ADVANCED PROSTATE CANCER FROM 74GY TO 78GY

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Purpose/Objectif: To assess & compare 3D conformal radiotherapy (3DCRT) and intensity modulated radiotherapy (IMRT) techniques for escalating the dose in locally advanced prostate cancer from 74 to 78Gy
Materials/Methods: 10 patients with localized prostate carcinoma, who were simulated and planned according to a defined protocol with bladder and bowel preparation, were randomly selected to represent the treated population. The reference plan for the purpose of this study is the centers standard technique, over the last 4 years, to deliver the 74 Gy in 37 fractions i.e. 5 field 3DCRT.
The study techniques to deliver 78 Gy in 39 fractions are

5 field 3DCRT
6 field 3DCRT
6 field inverse planned IMRT

Contouring, target dose constraints and goals were the same for all techniques. Dose volume constraints and dose maximum constraints were defined for organs at risk (OAR) i.e. rectum and bladder, ano-rectal junction, urethra and femoral heads.
The major endpoint was to compare rectal sparing of the 78 Gy techniques relative to the standard 74 Gy technique for the equivalent CTV and PTV dosimetric coverage. The minor endpoints were to evaluate doses to the other OAR for all techniques.
Results: All of the 78 Gy plans were able to achieve equivalent target dosimetric coverage as compared to the previous standard 74 Gy plan while achieving OAR dose constraints. A comparison of the 78 Gy plans showed that the IMRT plan delivered lower values for the more important higher rectal dose constraints i.e. V>50Gy (percentage rectal volume receiving greater than 50Gy) to V>75Gy. However, it produced slightly higher V>20Gy to V>40Gy values than the 3DCRT techniques due to dose dumping. Of the 78 Gy 3DCRT techniques the 6 field plan did better than the 5 field plan for all defined rectal dose volume values. Similar results were seen with the 78Gy techniques with the bladder wall constraints i.e. the IMRT technique producing lower values for the higher dose constraints but higher values for the lower dose constraints. The 78 Gy IMRT technique produced lower dose volume values for the remaining OAR i.e. ano-rectal junction, urethra and femoral heads. Of the 3DCRT techniques the 6 field plan produced better OAR sparing, including bladder than the 5 field technique.
Conclusions: All of the 78 Gy plans were able to achieve equivalent dosimetric coverage while meeting OAR constraints as compared to the previous standard 74 Gy plan. Of the 78 Gy plans the IMRT technique produced the greatest rectal and OAR sparing. The 6 field 78 Gy 3DCRT spared the OAR to a greater degree compared to the 5 field.

1089 poster

DOSE-ESCALATED IMRT OF PROSTATE CANCER - SIDE EFFECTS AND LOCAL TUMOR CONTROL

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Purpose/Objectif: During the past 4 years the implementation of IMRT ("sliding window") into our clinical practice permitted, especially for prostate cancer, a dose-escalated radiation therapy (< 76Gy TD to the whole organ). Simultaneously a satisfying protection of adjacent organs at risk (OAR) like urinary bladder and rectal wall can be achieved. Within 1 to 60 months of follow-up (median: 23,5 months) we registered acute as well as long-term side effects prospectively.
Materials/Methods: Starting in January 2000, an overall amount of 191 Patients with clinically localized prostate cancer received an individualized primary radiation therapy of the prostate gland and in 11 cases (6%) also an additional treatment of the loco-regional lymphatic drainage. The applicated total dose (TD) for the whole prostate gland ranged from 66,6Gy (in case of a previously performed TURP) up to a maximum of 78,8Gy. The gross tumor volume (GTV) as visible with MRI, Ultrasound or PET/CT is commonly saturated to a TD of about 80,0Gy, presuming that no TURP or other manipulation has been performed leaving the risk of massively increased side effects. Furthermore the PSA score was monitored up to 5 years after radiation therapy, starting at the time of diagnosis. The appearance of therapy-induces side effects (diarrhea, dysuria, nycturia, incontinence) and potential loss of weight during and after radiation therapy were analysed using the NCI Common Toxicity Criteria.
Results: Under radiation therapy we registered mostly grade I and in fewer cases grade II urinary discomfort/disfunction (NCI/CTC); 31,8% and 14,1% respectively. So far only two patients (1,0%) suffered from acute grade III urinary dysfunction during RT, both of them were free of complaints 3 months after RT. In 5 patients we observed persistent grade I urinary dysfunction lasting more than 3 months after RT, and another 18 months later in only two of those patients the complaints persisted. Acute grade I and II rectal toxicity was seen in 11 (5,8%) and 3 (1,6%) patients, respectively. Persistent radiation-induced rectal toxicities (such as diarrhea, rectal bleeding, proctitis or rectal pain) were not ovserved. In approximately 30% or our patients with successively decreasing PSA levels during RT an increasing PSA level several months after RT could be observed. While this PSA "bounce" was in turn followed by decreasing PSA levels, in 10% of those cases the ASTRO definition of a biochemical recurrence was fulfilled with three consecutive rises of the PSA level. Several patients have not jet or just recently finished radiation therapy and are to be included into the study afterwards.
Conclusions: IMRT allows irradiation of the prostate gland with a TD way above 72 Gy, which is necessary to achieve satisfying tumor control rates; and at the same time the adherence to normal tissue tolerances and existing dose constraints for organs at risk is assured. Both the observed remote proportion of severe side effects as well as the verifiable treatment success (PSA-Monitoring) argues for this method.

1090 poster

DOSIMETRIC EVALUATION AND ORGAN SPARING USING SLIDING WINDOW IMRT TECHNIQUE FOR LOCALIZED HIGH RISK PROSTATE CANCER

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Purpose/Objectif: IMRT is superior to 3-D CRT in reducing the major limiting toxicities of dose-escalated prostate radiotherapy. IMRT simultaneous integrated boost strategy (SIB) irradiates the prostate via hypofractionation while irradiating pelvic nodes with the conventional fractionation; carries the risk of increased toxicities. A sequential two-phase IMRT planning, initial and boost irradiation, requires two different dosimetric plans and potentially two different treatment setups, which increasing the chance for errors and the cost of patient care. The aim of the study to describe a novel and straightforward single phase (IMRT) technique simultaneously deliver high radiation dose to the prostate and lower dose to the pelvic nodes with conventional fractionation.
Materials/Methods: Data of 5 patients with high risk prostate cancer were used as example cases. A single phase IMRT was planned for delivery of 79.2 Gy to PTV1 (prostate and seminal vesicle plus 1.5 cm margin) and 45 Gy to the pelvic lymph nodes (PTV2) at 1.8 Gy per fraction simultaneously. A sequential two-phase IMRT plan, initial pelvic nodes then boost, was retrospectively generated for each patient. Dose -volume histograms for PTV1, PTV2, bowel, bladder and rectum were compared. Acute toxicities were evaluated weekly during treatment using the Radiation Therapy Oncology Group morbidity grading scales.
Results: All plans were generated using commercial inverse planning software (Pinnacle[3] version 6.2b). The mean V90, V95 and V100 (percent PTV volumes receiving 90, 95 and 100% of the prescribed dose) were 100, 100 and 95%, respectively in both techniques. The mean bowel, bladder and rectum doses were equivalent; however the single phase IMRT reduced the volume of bowel receiving 40.5 Gy by 30%. Overall, four patients experienced no acute gastrointestinal (GI) toxicity. Antidiarrhea medication was required for 1 patient. No cases of late radiation enteritis were observed.
Conclusions: Single phase (IMRT) strategy resulted in further reduction in the volume of bowel receiving high radiation doses. Patients' setup and reproducibility were accurate and treatment time was short which added great convenience for the patients. These dosimetric findings correlated with low rates of acute GI morbidity.

1091 poster

ENHANCED QUALITY OF HDR- INTERSTITIAL PROSTATE IMPLANTS DUE TO ONLINE-PLANNING PROCEDURE

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Purpose/Objectif: Several well-known approaches for treatment planning of prostate cancer do exist. We describe our clinical experiences of introducing and routinely performing the online-planning technique in temporary high dose rate (HDR) brachytherapy for prostate cancer.
Materials/Methods: After the needle implant (without pre-planning) the transversal ultrasound (TRUS) images are acquired in 5mm steps with the VariSeed™ software. The Dicom images are transferred to the BrachyVision™ system and the planning process starts. The online-planning procedure allows the use of real-time acquired TRUS images and to adopt the actual geometry of both the implantation needles and the prostate in a 3D-treatment planning process (3D dose calculation, 2D axial images without gaps). We present the first dosimetric results for a consecutive cohort of 55 out of 750 implants within the first 2.5 years of online-planning. Two target volumes were defined: the entire prostate gland (CTV2 with a fraction dose of 8-9 Gy) and a peripheral zone of the prostate (CTV1 with a fraction dose of 15 Gy).
Results: The technique was accepted by the team in a short time due to its obvious advantages: better sparing of the organs at risk and optimised dose conformity in the target volumes. Furthermore the online-planning with duration of 30 to 40 minutes is less time consuming compared to the preplanning method with typically 90 minutes time consumption. The learning curve showed time consumption of nearly 180 minutes at the beginning and 30 - 40 minutes at getting routine. The preliminary evaluation of 37 implants resulted in the following values: D90(prostate gland) = 6.5 Gy, D90(periphery of the prostate) = 13.6 Gy, D5(urethra)=10.2 Gy, D1(rectum)= 8.7 Gy.
Conclusions: Online-planning procedure improves the quality of temporary HDR interstitial implants for intermediate and high risk prostate cancer and results in lower time consumption of the treatment. Future work will include the evaluation of the dosimetric data of all patients as well of clinical outcome.

1092 poster

FUNCTIONAL MRI TO INVESTIGATE CHANGES IN OXYGENATION AND VASCULARITY OF THE PROSTATE GLAND CAUSED BY ANDROGEN DEPRIVATION

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Purpose/Objectif: To investigate the changes in oxygenation and vascularity of the prostate gland caused by androgen deprivation using BOLD (blood oxygen level dependent) MRI and DCE-MRI (dynamic contrast enhanced MRI).
Background: Hypoxia is a known cause of radioresistance and is a poor prognostic indicator in prostate cancer. Androgen deprivation has a potent effect on prostate vasculature, potentially inducing tumour hypoxia. It is therefore possible that neo-adjuvant androgen deprivation leads to a reduction in clonogen number at the expense of an increase in tumour cell radioresistance.
Materials/Methods: Patients that were due to be treated with neo-adjuvant androgen deprivation prior to radical radiotherapy for prostate cancer underwent 5 MRI investigations; 2 prior to the commencement of androgen suppression to define the baseline values and check for reproducibility, 1 after a month of hormone treatment and two scans after 3 months of therapy. BOLD-MRI consisted of a series of gradient echo sequences at increasing echo times from which quantitative parametric R_2* maps were calculated. Quantitative DCE-MRI following an infusion of Gd-DTPA with T1 weighted sequences was used to determine micro-vessel permeability surface area product (K^{trans}).
Results: Analysis of 13 patients showed that after 3 months of androgen deprivation there was a marked increase in R_2*, from 15.1 to 21.5 s^{-1} ($p < 0.0001$), and a marked decrease in K^{trans}, from 0.61 to 0.27 min-1 ($p = 0.0003$) compared with baseline.
Conclusions: Increasing R_2* may indicate an increase in blood deoxyhaemoglobin concentration (or possibly may reflect the development of prostate gland fibrosis) and independent verification of intraprostatic pO_2 levels is required to clarify the cause of such

an increase. The reduction of K^{trans} is compatible with a decrease in blood flow and vascular permeability caused by the apoptosis of vascular endothelial cells initiated by androgen deprivation. These results have implications for the development of future prostate radiotherapy schedules and the design of forthcoming clinical trials with regard to the timing of androgen deprivation.

1093 poster

IDENTIFICATION OF MEN WITH A GENETIC PREDISPOSITION TO PROSTATE CANCER: TARGETED SCREENING IN BRCA1 AND BRCA2 MUTATION CARRIERS AND CONTROLS: THE IMPACT STUDY

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Purpose/Objectif: This international collaboration aims to conduct the largest screening study of men with a known genetic predisposition to prostate cancer. Prostate cancer may be an indolent disease and screening the general population is controversial with no established reduction in mortality. Mutations in BRCA genes may increase the relative risk of prostate cancer by up to 23-fold. We aim to establish whether male BRCA1 and 2 mutation carriers indeed have a higher prostate cancer incidence, are at risk of aggressive prostate cancer and if a targeted screening programme is feasible in this population. We will also undertake proteomic profiling of urine and serum in these men.

Materials/Methods: 850 tested BRCA1/2 mutation carriers and 850 tested non-carriers will be recruited over 5 years in 39 European centres. Annual serum PSA and free: total PSA will be taken. If PSA is less than 3, the test will be repeated the following year. If the PSA is greater than 3, prostate biopsy will be offered. In the event of a cancer diagnosis, treatment will be according to local centre guidelines. Serum, plasma and urine samples will also be taken to investigate proteomic profiles of these fluids in an attempt to identify more specific markers for prostate cancer. PSA and free: total PSA will undergo external quality control measures to document the accuracy of results.

Results: Recruitment started in November 2005; 24 men have been enrolled, 10 BRCA2 carriers, 8 BRCA1 carriers and 6 controls. One BRCA1 carrier has a PSA of 3.8 and is currently awaiting a biopsy. All other men have a PSA less than 3. The one man with a PSA greater than 3 also has a free: total PSA of 11%. In total, 3 BRCA1 carriers have a free: total PSA less than 15%, all other men have levels above this value.

Conclusions: 100 men will be recruited by the end of 2006. Baseline PSAs, prevalence of undiagnosed prostate cancer, and the age of onset in male BRCA1and 2 mutation carriers will be compared with the control group. Analysis of proteomic profiles will be established between BRCA1 and BRCA2 carriers, controls negative for these mutations and carriers and non-carriers with a diagnosis of prostate cancer. We would like to present our preliminary results.

1094 poster

IMAGE GUIDED PROSTATE FOSSA RADIOTHERAPY AFTER BIOCHEMICAL FAILURE FROM RADICAL PROSTATECTOMY

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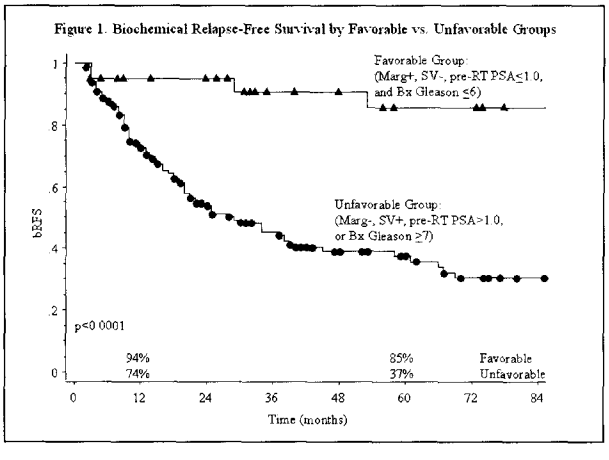
Purpose/Objectif: To report the biochemical relapse-free survival (bRFS) rates after definitive image guided external beam radiotherapy (IGRT) delivered to the prostate fossa in men experiencing biochemical failure (bF) after radical prostatectomy for localized prostate cancer.

Materials/Methods: A total of 200 cases were identified between 1987 and 2005 with localized prostate cancer previously treated with radical prostatectomy and subsequent biochemical failure treated with radiotherapy. Patients who had a minimum of 6 months or 2 PSAs after the end of radiation were included in this study. IGRT was delivered in 26% of patients. The location of the prostate fossa was verified and adjusted daily with the BAT™ transabdominal ultrasound system. Seventy-four percent of the cases were treated by a 4-field box technique (STD) without image guidance. None received adjuvant AD (AdjAD). The pathologic parameters from the prostatectomy were as follows: surgical Gleason score sGS >7 in 75% (86% IGRT vs. 72% STD, p=NS), extra capsular extension (ECE) in 60% (54% IGRT vs. 63% STD, p=NS), surgical margin involvement (SM) in 60% (39% IGRT vs. 66% STD, p= 0.0006), seminal vesicle extension (SV) in 21% (18% IGRT vs. 22% STD, p=NS). The median PSA level at the time of salvage therapy was 0.6 ng/mL (range: 0.1 to 25.9). The median PSA follow-up time after RT was 44 months (range: 2-226). The median radiation dose to the prostate fossa was 70Gy for both IGRT and STD. Kaplan-Meier and Cox proportional hazards methods were used to analyze the data. bF was determined by persistent rise after radiotherapy. Toxicities were measured using RTOG scores.

Results: For the entire cohort the 5-year bRFS was 46%. The 2-year bRFS rate for IGRT was 56.8% and for STD was 64.6% (p=NS). On multivariate analysis, SM neg vs pos (p=0.0010, RR=2.5), SV neg vs pos (p=0.0016, RR=0.4), preRT PSA <1.0 vs >1.0 (p=0.0082, RR=0.5), biopsy Gleason score-bGS <6 vs >7(p=0.0094, RR=0.5) and total dose (continuous - p=0.0007, RR=1.0) were the significant predictors of bRFS; while ECE and RT technique were not. The rates of late toxicity (any grade, RTOG criteria) were 9% for gastrointestinal (GI) and 18% for genitourinary. The rates of grade >2 toxicity were 2% for GI and 7% for GU. There was no grade >3 GI toxicities, but 1% had grade 3 GU toxicity. Patients treated with IGRT had less toxicity (any grade) than STD; 8% vs. 9% for GI and 10% vs. 22% for GU (p=NS). Two risk groups were identified: Favorable (SM+, SV-, and preRT PSA < 1, and bGS < 6) and Unfavorable (SM- or SV+ or preRT PSA > 1 or bGS > 7). The 5-year bRFS rates for patients with favorable vs. unfavorable risk were 85% and 37%, respectively (p<0.0001, Fig 1).

Conclusions: Salvage prostate fossa radiotherapy after biochemical failure from radical prostatectomy is effective in achieving durable response in selected patients with favorable risk factors (positive surgical margins, negative seminal vesicles, preRT PSA < 1, bGS < 7). There is no significant difference in bRFS between IGRT and STD. With image guidance, lower GI and GU side effects can be expected than standard technique when delivering higher doses of radiation to the prostate bed to improve outcomes.



1095 poster

INTENSITY-MODULATED RADIOTHERAPY (IMRT) AS PRIMARY THERAPY FOR PROSTATE CANCER: THE EXPERIENCE OF THE GHENT UNIVERSITY HOSPITAL (GUH).

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Purpose/Objectif: To report on biochemical relapse free survival (bRFS) and late gastro-intestinal (GI) and genito-urinary (GU) toxicity after IMRT for prostate cancer.

Materials/Methods: 133 patients were treated with IMRT as primary therapy for prostate cancer T1-4 N0 M0 at GUH. Table 1 shows their characteristics. The clinical target volume (CTV) was the prostate +/- seminal vesicles (1). The planning target volume (PTV) was created with a 7 mm isotropic margin around the CTV (2). First, patients were treated to a maximum rectum dose of 72 Gy (R72, n=51). Then, patients were treated to a maximum rectum dose of 74 Gy (R74; n=82). Median CTV dose was 76 and 78 Gy for R72 and R74 respectively. The median PTV dose was 75 Gy and 77 Gy respectively, given in 36 or 37 fractions. Patients were divided into three risk groups to determine the use of androgen deprivation (AD). Thirty-four patients refused AD.

1.low risk: PSA <10 and Gleason <6 and T</=T1c: no AD.

2.intermediate risk: PSA 10-19.9 or Gleason 6 or 7(3+4) or T2: AD for 6 months.

3.high risk: PSA >/=20 or Gleason ≥ 7(4+3) or T3-4: AD for 3 years.

Biochemical relapse was defined according to the ASTRO criteria (3).

To record late GI and GU toxicity, patients were seen every 3 months for the first year, every 6 months until year 5 and annually thereafter. GI and GU late toxicity was scored using the RTOG criteria (4), supplemented by an in-house developed toxicity scale (2). Overall GI and GU scores were calculated for each follow-up visit as the worst GI or GU score during that visit. For every patient, a pre-treatment registration of rectal and urinary morbidity was present.

Results: The median follow-up was 42 months. The overall 5-year bRFS was 82% (Figure 1). A statistically significant difference (p=0.01) in 3-year bRFS was found between R72 and R74 (80% vs. 92% respectively). For patients in the low, intermediate and high-risk group, five years bRFS was 100%, 86% and 67% respectively (p<0.01).

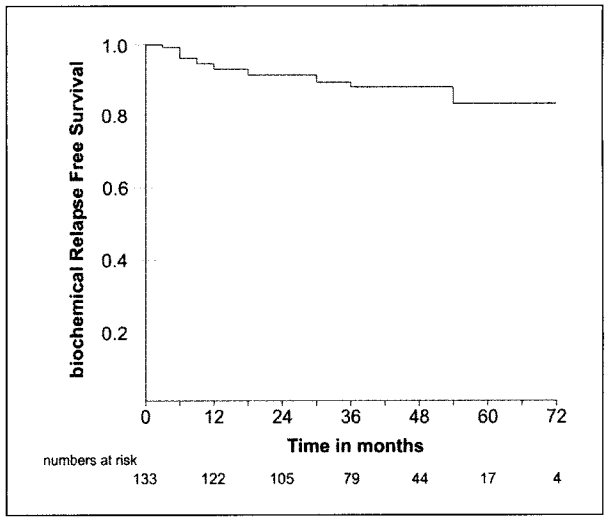
There was no grade 4 late toxicity. One patient had grade 3 anal red blood loss (ARBL). The only grade 3 GU late effects were nocturia (n=3) and incontinence (n=3). Grade 2 GI and GU late toxicity was scored in 17% and 19% respectively. Most frequent grade 2 late GI-toxicities were ARBL (8%), abdominal cramps (6%), incontinence (5%) and diarrhoea (5%). Most frequent grade 2 late GU-toxicities were nocturia (20%), hematuria (18%), and increased frequency (9%). Except for hematuria, grade 2 side effects disappeared after 6 months (median). Hematuria always disappeared after increased water intake.

Conclusions: IMRT as primary therapy for localized or locally advanced prostate cancer offers very good bRFS. Late toxicity is low.

References:

1. Diaz: Int J Radiat Oncol Biol Phys1994; 30:323-29.
2. De Meerleer: Int J Radiat Oncol Biol Phys 2004; 60: 777-87.
3. ASTRO Consensus Panel. Int J Radiat Oncol Biol Phys 1997; 37: 1035-41.
4. Cox: Int J Radiat Oncol Biol Phys 1994; 30: 323-29.

Characteristic	All (n=133)	74R72 (n=51)	76R74 (n=82)	p-value
Age (years)				
median (range)	69 (50-79)	69 (51-78)	69 (50-79)	ns
Follow-up (months)				
median (range)	42 (3-60)	54 (6-60)	36 (3-60)	
PSA level (ng/ml)				
<10	63 (47)	23 (45)	40 (49)	ns
10-19.9	46 (35)	16 (31)	30 (37)	
>20	24 (18)	12 (24)	12 (15)	
median (range)	10.9 (0-150)	11.4 (0.1-150)	10.2 (0-90)	
Gleason score				
2-5	58 (44)	22 (43)	36 (44)	ns
6	35 (26)	12 (24)	23 (28)	
7(3+4)	27 (20)	9 (18)	18 (22)	
7(4+3) - 10	13 (10)	8 (16)	5 (6)	
Tumor stage				
T1	47 (35)	17 (33)	30 (37)	ns
T2	64 (48)	24 (47)	40 (49)	
T3	18 (14)	7 (14)	11 (14)	
T4	4 (3)	3 (6)	1 (1)	
Node stage				
cN0	112 (84)	38 (75)	74 (90)	p=0.03
pN0	21 (16)	13 (25)	8 (10)	
Androgen deprivation				
yes	80 (59)	24 (47)	54 (67)	p=0.04
no	55 (41)	27 (53)	28 (33)	
Risk group				
Low	20 (15)	11 (22)	9 (11)	p=0.01
Intermediate	71 (53)	19 (37)	52 (62)	
High	42 (32)	21 (41)	21 (27)	



1096 poster

INTER-OBSERVER VARIABILITY IN CONTOURING CTV AFTER RADICAL PROSTATECTOMY: THE AIROPROS01-04 MULTI-CENTRIC STUDY

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Purpose/Objectif: Accurate contouring of the clinical target volume(CTV) is a fundamental prerequisite for successful conformal radiotherapy after radical prostatectomy(RP). This study investigates variability in contouring CTV after RP.

Materials/Methods: Eighteen radiation oncologists (One observer for each Institution) participated in a dummy-run within the Italian AIROPROS01-04 trial evaluating post-operative CTV in prostate cancer. Three patients were considered for this study. The patients underwent CT with half-full bladder condition. Physicians were asked to draw three different CTVs on CT slices (5mm step) on Plato 2.5.2 (Nucletron) 3D Treatment Planning System (TPS). CTV1 was defined as the surgical prostate bed without seminal vesicles, CTV2 as surgical prostate bed with seminal vesicles and CTV3 as pelvis. The contouring uncertainty were analyzed in different ways. Firstly

the CTVs volumes were calculated ant the differences between the inserted contours were estimated. Beside the differences in cranial and caudal CTV border definition and the distances between the mean inserted contours (named mean contour distances or MCDs) were measured from BEV analysis.

Results: Results showed a large inter-observer variability.The volumes varaibility for each patient is shown in the table below.

	CTV	Vol min(cc)	Vol max(cc)	Pt
1	CTV1	7.0	161.3	75
2	CTV1	5.1	214.0	68
3	CTV1	17.5	223.2	38
1	CTV2	16.1	233.5	82
2	CTV2	18.9	287.8	71
3	CTV2	33.6	320.1	45
1	CTV3	283.9	1006.6	74
2	CTV3	188.8	1335.9	64
3	CTV3	346.9	1595.7	43

When considering cranial and caudal border definition, the maximum difference from the most probable caudal limit was 25mm for CTV1 and CTV2 (mean 14mm) and 55mm for CTV3 (mean 40mm). For the cranial target definition, the maximum difference was 40mm for CTV1 and CTV2 (mean 12mm and 9mm respectively) and 50mm for CTV3 (mean 27mm). Large differences were founded also for MCDs. For CTV1 the largest value was 16mm (SD=7mm) in left/right direction and 29mm (SD=6mm) in anterior/posterior direction. For CTV2 the largest value was 20mm (SD=6mm) in left/right direction and 29mm(SD=7mm) in anterior/posterior direction. For CTV3 we founded 45mm (SD=11mm) and 53mm (SD=13mm) for left/right and anterior/posterior direction respectively.

Conclusions: Our investigation showed an important inter-observer difference in definition of CTV1, CTV2 and CTV3. The impact of contouring uncertainty in postoperative setting is very significant and need furthers studies to achieve a consensus on delineation of these volumes.

1097 poster

INTERSTITIAL HIGH DOSE RATE (HDR) BRACHYTHERAPY + IMRT VS. HDR MONOTHERAPY FOR EARLY STAGE PROSTATE CANCER

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2 - University of Miami, Radiation Oncology, Miami, USA

Purpose/Objectif: Transrectal Ultrasound (TRUS) guided interstitial implant for prostate cancer using High Dose Rate (HDR) + External Beam Radiation Therapy (EBRT) technique has been reported with results comparing favorably to surgery, Low Dose Rate (LDR) brachytherapy +/- EBRT, EBRT, and Intensity Modulated Radiation Therapy (IMRT). The role of supplemental EBRT in brachytherapy is controversial. We compare our results of HDR + IMRT vs. HDR monotherapy.

Materials/Methods: Between 1997 and 2006, 290 patients with T1 and T2 localized prostate underwent TRUS guided interstitial implant. There were no Gleason Score or PSA exclusions. After discussion of treatment options, 109 patients elected HDR Implant + IMRT and 181 patients underwent HDR monotherapy. No patient received Hormonal Blockade. Median Gleason Score was 7 (range : 4 to 10). Median PSA was 9.8 (0.60 to 39.8). IMRT treatment volume included the prostate + seminal vesicles + 2 cm margin. Implant treatment volumes ranged from 42 cm^3 to 196 cm^3. In patients who received IMRT + HDR, 4500 cGy in 25 fractions was given via IMRT and 1650 cGy to 2000 cGy in 3 fractions via HDR. Our protocol for HDR alone, has called for two HDR Implants. The treatment volume received 2,250 cGy in 3 fractions prescribed to the 100% Isodose line, given over 24 hours. A 2nd implant was performed 4 weeks later, delivering a further 2,250 cGy in 3 fractions, bringing the final dose to the prostate to 4,500 cGy in 6 fractions. Urethral dose points (12-16) were followed, and limited to < 105% of the prescription dose.

Results: There was no significant difference between the treatment groups with respect to T-Stage, Gleason Score, and PSA. With a median follow-up of 70 months (range : 6 months to 120 months), the overall PSA disease free survival was 89.3% (259/290). In patients undergoing IMRT + HDR Implant, PSA disease free survival was 89.0% (97/109) vs. 89.5% (162/181) for patients undergoing HDR alone (p=0.6). The 5 year actuarial survival was 86% for the group receiving IMRT + HDR vs. 89% with HDR monotherapy (log rank = 0.5). Urethral stricture requiring dilatation has developed in 3.8% (11/290) of patients. Urinary stress incontinence has occurred in 2.8% (8/290). RTOG late bladder toxicities were : 0% Grade 4, 0% Grade 3, and 2.8% (8/290) Grade 2. RTOG late rectal toxicities were : 0.3% (1/290) Grade 4, 0% Grade 3, 3.8% (11/290) Grade 2, and 4.5% (13/290) Grade 1. RTOG late rectal toxicity was higher in patients undergoing HDR + IMRT with 15.6% (17/109) of patients experiencing Grade 2 and 1 symptoms, vs. 3.9% (7/181) receiving HDR alone (p < 0.01).

Conclusions: We have observed no significant difference in PSA disease free survival in patients undergoing HDR monotherapy vs. HDR + IMRT. Complications were similar, though RTOG Grade 1 and 2 late toxicity was higher in patients receiving HDR + IMRT. HDR monotherapy compares favorably to EBRT, LDR +/- EBRT, and HDR + IMRT, both with regard to PSA disease free survival, and complications. With regard to implant technique, HDR brachytherapy offers other advantages over LDR, such as no radiation exposure to hospital personnel, no seed migration, greater dose flexibility and precision of radiation dose delivery. Larger volumes can be treated with HDR. By omitting EBRT, rectal complications may be reduced.

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INTERSTITIAL HIGH DOSE RATE (HDR) BRACHYTHERAPY FOR EARLY STAGE PROSTATE CANCER

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3 - Joe Arrinton Cancer Center, Radiation Oncology, Lubbock, USA

Purpose/Objectif: Transrectal Ultrasound (TRUS) guided interstitial implant for prostate cancer using Low Dose Rate (LDR) and High Dose Rate (HDR) technique has been reported with results comparing favorably to surgery and External Beam Radiation Therapy (EBRT). Often, HDR and LDR interstitial implant is combined with EBRT. There is little published data on HDR alone. We report our results with HDR alone.

Materials/Methods: Between 1997 and 2006, 181 patients with T1 and T2 localized prostate underwent TRUS guided interstitial implant, under spinal anesthetic or local anesthetic. There were no Gleason Score or PSA exclusions. No patient received EBRT or Hormonal Blockade. Median Gleason Score was 7 (range : 4 to 10). Median PSA was 9.3 (2.7 to 39.8). Treatment volumes ranged from 42 cm^3 to 196 cm^3. Treatment volume included the prostate and seminal vesicles in all cases. Radiation Treatment planning was performed using CT Scanning and the Nucletron Plato Treatment Planning System. HDR treatment was given using the Nucletron afterloading system with Ir-192. Median source activity was 6.7 Curies (range : 4.3 - 9.6). Our protocol for HDR alone, has called for two HDR Implants, spaced 4 weeks apart. The treatment volume received 2,250 cGy in 3 fractions prescribed to the 100% Isodose line, given over 24 hours. A 2nd implant was performed 4 weeks later, delivering a further 2,250 cGy in 3 fractions, bringing the final dose to the prostate to 4,500

cGy in 6 fractions. Urethral dose points (12-16) were followed, and limited to < 105% of the prescription dose.

Results: With a median follow-up of 72 months (range : 6 months to 120 months), PSA disease free survival was 89.5% (162/181). The procedure was well tolerated, with all patients having completed the procedure. Acute and chronic complications were uncommon. Acute urinary retention occurred in 4.4% (8/181) of the patients, requiring temporary insertion of an indwelling foley catheter. Deep venous thrombosis occurred within one month of HDR in 2.2% (4/181) of the patients. Urethral stricture requiring dilatation has developed in 4.9% (9/181) of patients. Urinary stress incontinence has occurred in 3.9% (7/181). RTOG late bladder toxicities were : 0% Grade 4, 0% Grade 3, and 3.9% (7/181) Grade 2. RTOG late rectal toxicities were : 0.5% (1/181) Grade 4, 0% Grade 3, 1.7% (3/181) Grade 2, and 2.2% (4/181) Grade 1. There have been no cases of rectal incontinence to date.

Conclusions: Six year results with HDR implant alone compare favorably to EBRT, LDR +/- EBRT, and HDR + EBRT, both with regard to PSA disease free survival, and complications. HDR offers other advantages over LDR, such as no radiation exposure to hospital personnel, no seed migration, greater dose flexibility and precision of radiation dose delivery. Larger volumes can be treated with HDR. By omitting EBRT, bladder and rectal complications appear to be significantly reduced.

1099 poster

INTERSTITIAL HIGH DOSE RATE (HDR) BRACHYTHERAPY UNDER LOCAL ANESTHESIA FOR EARLY STAGE PROSTATE CANCER

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1 - Joe Arrington Cancer Center, Radiation Oncology, Lubbock, USA

Purpose/Objectif: Transrectal Ultrasound (TRUS) guided interstitial implant for prostate cancer using Low Dose Rate (LDR) and High Dose Rate (HDR) techniques has been reported with results comparing very favorably to external beam radiation therapy. TRUS interstitial implant of the prostate has been traditionally performed under general or spinal anesthetic in an operating room. We report our results with a technique performed under local anesthesia in a Department procedure room.

Materials/Methods

Patients with T1 and T2 localized prostate cancer were judged to be candidates for TRUS guided interstitial implant.

Results

Between 2002 and 2006, 274 TRUS guided prostate implants were performed under local anesthesia. Conscious sedation consisted of intravenous Morphine (12-22 mg) and Versed (6-14 mg), or intravenous Demerol (50-175 mg) and Versed (3-12 mg). Local anesthetic was given with a mixture of 1% Lidocaine, 0.25% Marcaine, 1:100,000 Epinephrine, and 4% Sodium Bicarbonate neutralizing solution (20-120 cc). Local anesthesia was given to a 5 x 5 cm perineal area to a depth of 10 cm under TRUS guidance. The implants were placed under mobile multi-plane prostate template (Radiation Therapy Products Prostate Template) guidance using from 3 to 4 planes, and 12 to 22 needles. Needle spacing was 1.0 cm. The implant procedure included sigmoidoscopy and cystoscopy. Median implant time was 45 minutes (range : 30 to 150 minutes). HDR treatment was given using the Nucletron afterloading system. The implant volume received 2,250 cGy in 3 fractions prescribed to the 100% Isodose line, given over 24 hours. Urethral dose points (12-16) were followed, and limited to < 105% of the prescription dose. The procedure was well tolerated, with all patients having completed the procedure. One patient developed respiratory suppression, and required reversal with Narcan. He recovered uneventfully. Otherwise, there have been no acute complications to date.

Conclusions

TRUS interstitial implant of the prostate under local anesthesia is feasible. Implant time and complications compare favorably to general or spinal anesthetic technique.

1100 poster

LACK OF CORRELATION BETWEEN RECOGNIZED DOSE-VOLUME GUIDELINES AND LATE RECTAL TOXICITY AFTER HYPOFRACTIONATED RADIATION THERAPY FOR PROSTATE CANCER

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Purpose/Objectif: Hypofractionation has become an attractive option in the curative treatment of prostate cancer. A downside to this approach is the potential increase for late rectal toxicity due to the large dose/fraction. Several dosimetric constraints have been set as guideline predictors for late rectal toxicity after curative radiotherapy. We studied the relative value of three recognized dose-volume guidelines in predicting the development of late rectal toxicity in a homogeneous group of prostate cancer patients treated with hypofractionation.

Materials/Methods: 61 patients with low/intermediate prostate cancer were treated with hypofractionated RT alone between October 2002 and April 2004. For each patient, a 3D treatment plan consisting of five 18MV photon fields was used to deliver 66Gy in 22 fractions at the isocenter. PTV consisted of the prostate plus a uniform 7mm margin. Daily ultrasound was used to confirm setup. Patients had the rectum uniformly contoured by the same radiation oncologist. Late rectal toxicity was prospectively graded by the CTC v.3. Late rectal toxicity was correlated to the Canadian PROFIT hypofractionation study, the RTOG protocol 0126, and the MD Anderson dose-volumes guidelines. For the last 2 studies, we converted these guidelines to 3 Gy/fraction using the linear quadratic model with an $\alpha/\beta=3$ for the rectum.

Results: All patients had > 18 months of minimum follow-up (median = 27.2 months). Median age was 72 years. Median initial PSA was 6.7 ng/ml. A total of 26% of the patients had grade 1 late rectal toxicity by CTC v.3 criteria, while 16% had grades 2 or 3. There was no toxicity >grade 3. The DVH analysis revealed that, although many patients exceeded the various dose-volume guidelines, there was no relationship between these violations and rectal toxicity, irrespective of the grade of toxicity (Table).

Conclusions: Despite the use of recognized guidelines in a homogeneously treated group of patients, we were unable to establish a significant correlation between late rectal toxicity and these guidelines. These results suggest that for this group of patients other non-dosimetric factors may account for the late rectal toxicities observed.

	RTOG (V_{46Gy}<50%)		MDAnderson (V_{39Gy}<25%)		PROFIT (V_{37Gy}<50%)	
	Meet criteria(%)	Exceed criteria(%)	Meet criteria(%)	Exceed criteria(%)	Meet criteria(%)	Exceed criteria(%)
Grade 0	50	71	67	59	59	61
Grade 1	30	19	25	24	29	23
Grade2+	20	10	8	16	12	16

1101 poster

LATE RTOG/EORTC, LENT SOMA AND CTCAE GRADED BLADDER TOXICITY IN RELATION TO DOSE DISTRIBUTIONS IN THE BLADDER DURING RADIOTHERAPY FOR PROSTATE CANCER

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Purpose/Objectif: To assess the association between the dose distributions in the bladder and late RTOG/EORTC (RTOG), LENT SOMA (LENT) and CTCAE version 3.0 (CTC) graded bladder toxicity among patients with prostate cancer treated with radiotherapy.
Materials/Methods: In this prospective study, 124 patients that received three-dimensional conformal radiotherapy (3D-CRT) for prostate cancer were included. A total dose of 70 Gy in 2-Gy fractions was applied with conventional fractionation. All patients filled in questionnaires regarding bladder complaints before, during, and after radiotherapy (median follow-up 36 months). DVH-parameters of the filled bladder, defined by the outer contour, were analysed in relation to late bladder grade ≥ 2 toxicity, according to RTOG, LENT, and CTC criteria. ROC analyses were performed to assess the most predictive DVH parameters and logistic regression analyses were used to analyse the association with DVH-parameters and toxicity. Patients with pre-treatment grade ≥ 2 toxicity according to a given grading system were excluded from statistical analyses regarding that particular system.
Results: Pre-treatment grade ≥ 2 toxicity was assigned to 19(15%), 64(52%) and 21(17%) of the patients according to the RTOG, LENT and CTC systems, respectively. With respect to both relative and absolute DVH-parameters, the bladder volume receiving ≥ 40 Gy (V40) was most predictive for late grade ≥ 2 toxicity, irrespective of the grading system used. However, significant associations were only found for the relative V40 with use of the LENT system in univariate analyses (p=0.036). On the basis of the ROC coordinates, V40 was dichotomised by a volume of 40%. Significant associations between this factor and toxicity were only found with use of the LENT system (p=0.004). In a multivariate model including other prognostic and volumetric factors, the dichotomized V40 remained significant (p=0.003). V40, dichotomized by a volume of 110 cm^3, was significantly associated with the LENT system in univariate and multivariate analyses (p=0.002). No significant associations were found with use of the RTOG and CTC systems.
Conclusions: The current analysis showed that the relative V40 of the bladder was the most important prognostic factor with regard to radiation-induced bladder morbidity. Associations were only found between the bladder V40 and the LENT SOMA grading system. The results indicate that dose-volume-effects for the bladder are present but their clinical significance depends on the grading system used.

1102 poster

LATE RTOG/EORTC, LENT SOMA AND CTCAE GRADED RECTAL TOXICITY IN RELATION TO DOSE DISTRIBUTIONS IN THE RECTUM DURING RADIOTHERAPY FOR PROSTATE CANCER

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Purpose/Objectif: To assess the association between the dose distributions in the rectum and late RTOG/EORTC (RTOG), LENT SOMA (LENT) and CTCAE version 3.0 (CTC) graded rectal toxicity among patients with prostate cancer treated with radiotherapy.
Materials/Methods: In this prospective study, 124 patients that received three-dimensional conformal radiotherapy (3D-CRT) for prostate cancer were included. A total dose of 70 Gy in 2-Gy fractions was applied with conventional fractionation. All patients filled in questionnaires regarding rectum complaints before, during, and after radiotherapy (median follow-up 36 months). DVH-parameters of the rectum, defined by the outer contour from the anal verge to the sigmoid flexure, were analysed in relation to late rectum grade ≥ 2 toxicity, according to RTOG, LENT, and CTC criteria. ROC analyses were performed to assess the most predictive DVH parameters and logistic regression analyses were used to analyse the association with DVH-parameters and toxicity.
Results: With respect to both relative and absolute DVH-parameters, the rectal volume receiving ≥ 70 Gy (V70) was most predictive for late grade ≥ 2 toxicity, irrespective of the grading system used. However, significant associations were only found for the relative V70 with use of the LENT system in univariate analyses (p=0.03). On the basis of the ROC co-ordinates, V70 was dichotomised by a volume of 20%. Significant associations between this factor and toxicity were found with use of the LENT (p=0.01) and CTC systems (p=0.02). In a multivariate model including other prognostic and volumetric factors, the dichotomised V70 remained significant with use of the LENT (p=0.04) and CTC systems (p=0.04). V70, dichotomised by an absolute volume of 12 cm^3, was significantly associated with the LENT system in univariate and multivariate analyses (p=0.005). The most optimal threshold for V70 with the CTC system was 28 cm^3. This factor was significantly associated with toxicity in univariate as well as multivariate analyses (p=0.008). No such associations were found with use of the RTOG system.
Conclusions: The current analysis showed that the V70 of the rectum was the most important prognostic factor with regard to radiation-induced rectal morbidity. The strongest association was found between the rectal V70 and the LENT SOMA grading system. The results indicate that dose-volume-effects for the rectum are present but their clinical significance depends on the grading system used.

1103 poster

LATE TOXICITY DATA FOR HYPOFRACTIONATED (55GY IN 20 FRACTIONS) RADICAL EXTERNAL BEAM CONFORMAL RADIOTHERAPY TO THE PROSTATE

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Purpose/Objectif: Recent research has suggested that the α/β ratio for prostate cancer is much lower than previously thought, and therefore more sensitive to fraction size. We have analysed prospectively collected toxicity data to compare with conventional dosing regimes of 65-70 Gy in 1.8-2 Gy fractions.
Materials/Methods: We have analysed toxicity data on all 61 patients treated with radical radiotherapy to the prostate under the care of a single Clinical Oncologist between July 2002 and July 2005. Radiotherapy was delivered to a planning target volume defined by 3D CT (prostate plus or minus seminal vesicles depending on clinical risk with 10mm margin posteriorly, 15mm superior and inferior, and 12mm margin to the anterior and lateral borders) with a 4-field conformal technique to a dose of 55Gy in 20 fractions over 26 days. All data was collected prospectively, urogenital and gastrointestinal (GI) toxicity was documented using the Radiation Therapy Oncology Group toxicity scoring system. Scores were assessed at specific time points after completion of radiotherapy: 6 months-1yr, 1-2yrs, 2-3yrs, and 3-4yrs.
Results: Data was available for 57 of the 61 patients at 6-12months, the incidence of grade 1 bladder toxicity was 7%(4), and grade 1 GI toxicity 30% (17), there was no bladder or GI toxicity grade ^{3} 2. At 1-2yrs there was data for 48/52 patients, bladder toxicity was as follows; grade 1 = 6.3%(3), grade ^{3} 2 = 0, GI toxicity; grade 1 = 16.7%(8), grade 2 = 6.5%(3), grade ^{3} 3 = 0. At 2-3yrs there was data for 22/24 patients, bladder toxicity; grade ^{3} 1 = 0, GI toxicity; grade 1 = 27.3%(6), grade 2 = 4.5%(1), grade ^{3} 3 = 0. There was 3-4yr data for 8/9 of the patients, again bladder toxicity; grade ^{3} 1 = 0, GI toxicity; grade 1= 12.5%(1), grade ^{3} 2 = 0. A retrospective review of the electronic notes revealed confirmed radiation proctitis in 2 of the 4 patients with documented grade 2 GI toxicity.
Conclusions: This analysis suggests that hypofractionated ra-

diotherapy (55 Gy in 20) to the prostate is associated with similar bladder and GI toxicity as conventional radiotherapy regimes. The advantages of hypofractionated regimes include the potential for improved tumour control in view of the low a/b ratio of carcinoma of the prostate. Shorter courses of radiotherapy are beneficial both in terms of resource utilisation and convenience for patients.

1104 poster

LONG-TIME RESULTS WITH A MEDIAN FOLLOW UP OF 80 MONTHS IN 3-D CONFORMAL RADIOTHERAPY OF LOCALIZED PROSTATE CANCER AT MODERATE DOSE: BIOCHEMICAL RESPONSE, DISEASE SPECIFIC SURVIVAL, OVERALL SURVIVAL AND LATE SIDE EFFECTS

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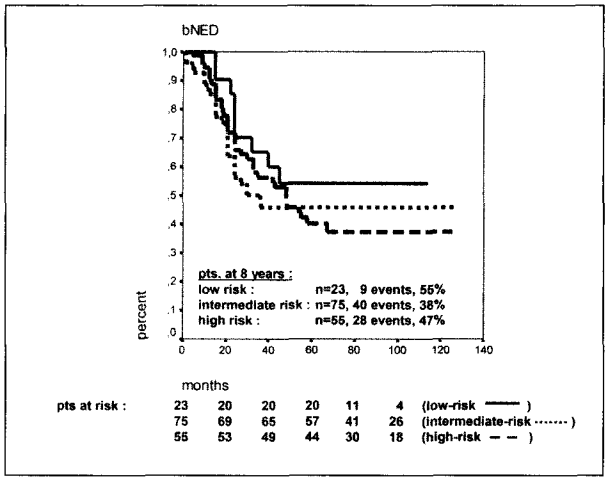
Purpose/Objectif: Biochemical control (bNED), disease specific survival (DSS), overall survival (OS) and late gastrointestinal (GI) and urogenital (UG) side effects (EORTC/RTOG) of patients with a long time follow up were evaluated.

Materials/Methods: Three dimensional conformal radiotherapy up to a total dose of 66 Gy with or without hormonal therapy was performed in 154 localised prostate cancer (T1-3N0M0) patients between 02/1994 and 04/1999. According to T-stage, pre-treatment PSA and grading patients were divided into low-, intermediate- and high-risk gruop. The 5-, 8- and 10 year actuarial rates of bNED (ASTRO definition), DSS and OS and late side effects were calculated.

Results

Median follow up of all patients was 80 months and 95 months of the surviving patients respectively. Additional hormonal therapy was given in 57% of patients with amedian duration of 22 months. Distribution concerning risk gruops (low-; intermediate-; high-) showed 15%, 49% and 36% of patients, respectively. bNED 5-, 8- and 10 year actuarial rates were 46%, 44% and 44%. DSS 5-, 8- and 10-year actuarial rates were 96%, 90% and 82%. OS 5-, 8- and 10-year rates were 81%, 64% and 56%. In comparison to an age matched Austrian male population OS curve of our patients at 10 years was decreased by only 9%. In univariate and multivariate analysis only pre-treatment PSA (<10 vs. >10ng/ml ; p<0,05) and PSA-nadir (<0,5 vs. >0,5 ng/ml ; p<0,0001) affected significantly bNED. Age, risk-group, t-stage, grading and hormonal therapy had no significant influence on bNED, DSS and OS. Late GI and UG > grade 1 actuarial rates at 5 years were 17% and 15%.

Conclusions: 8 year DSS and OS rates for patients treated up to a total dose of 66 Gy show respectable results. Current dose escalation studies with improved bNED rates may be able to further increase long term clinical outcome.



1105 poster

MARGINS FOR PROSTATE TREATMENT USING ONLINE POSITION VERIFICATION, FOCUSSING ON THE MAGNITUDE OF PROSTATE ROTATION

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Background: With the ExacTrac X-ray system of BrainLab, on-line position verification and correction can be performed within the same time slot as an off-line protocol. Using an on-line protocol only small translation errors remain, enabling us to decrease the CTV-PTV margin. However, other factors, such as the geometrical accuracy of the accelerator and prostate rotation, become as significant to the extent of the margins as the small translational errors. Sofar, these factors have not been taken into account in the commonly used margin recipes.

Purpose: To investigate the effects of several components on the CTV-PTV margin, such as the three-dimensional prostate rotation.

Materials/Methods: For this study we used data from a group of 6 prostate cancer patients, each one implanted with four gold seeds. In total 171 fractions were analysed. Once a week, images were acquired both before and after treatment. Prostate rotations were converted into translations at critical contour points. Together with estimations of other inaccuracies (e.g. isocentre accuracy, ExacTrac accuracy) these results are used in an extended margin recipe.

Results: The following results for prostate rotations and the resulting translations were found:

	AP-axis [°]	CC-axis [°]	LR-axis [°]	A-P [mm]	C-C [mm]	L-R [mm]
Mean of means:	-0.1	-0.2	-0.8	-0.3	-0.7	-0.2
Systematic error:	1.2	1.5	2.7	1.5	1.5	0.3
Random error:	1.7	2.0	3.4	1.8	1.8	0.9
Range:	-6.0 - 5.7	-7.3 - 6.5	-9.9 - 8.3	-5.4 - 4.1	-5.7 - 4.2	-3.0 - 2.6

We confirm that the largest rotation is around the LR-axis.

When using our extended margin recipe without rotations, CTV-PTV margins of 4.9 mm (C-C), 3.4 mm (L-R) and 4.8 mm (A-P) are found. However, when taking the rotations into account these values change into 6.5 mm (C-C), 3.6 mm (L-R) and 6.4 mm (A-P).

Conclusions: Rotation of the prostate has a significant effect on the extent of the CTV-PTV margin using an online positioning protocol. In our study we want to lay stress on the fact that, accelarator inaccuracies and delineation uncertaincies must be included in the determination of optimal CTV-PTV margins.

Future research will investigate both the influence of rotations of the prostate and technical inaccuracies in general on the dose distribution.

1106 poster

NADIR PSA AND TIME TO NADIR PSA AFTER RADIOTHERAPY +/- ANDROGEN DEPRIVATION AS A PREDICTOR OF PROSTATE CANCER OUTCOME.

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Purpose/Objectif: To determine whether nadir prostate-specific antigen (nPSA) < 1 ng/ml and the time to nPSA (TnPSA) are associated to biochemical or clinical failure after external beam radiotherapy for localised prostate cancer.

Materials/Methods: From 1979 to 1999, 981 men with T1b-T4 N0M0 stage prostate cancer were treated with radical external beam radiotherapy (EBRT) ± androgen deprivation (AD). Initial PSA values (median PSA:11.3 ng/ml) were available in 811 patients. In 651 of these, there were at least 4 PSA determinations at follow-up to study the biochemical failure (BF) incidence -according to ASTRO definition-. In this group we studied the nPSA and its association with BF and analysed whether a nPSA < 1 ng/ml was an outcome predictor compared to other factors including stage, Gleason, pretreatment PSA level, and RT dose. We have also studied whether there is an association between the time to nPSA and BF.

Results: The median nPSA for BF free patients was 0.20 ng/ml and 0.49 ng/ml for the group with BF ($p< 0.001$). This difference was also observed for patients treated with RT alone (0.6 ng/ml vs 0.92 ng/ml, respectively; $p< 0.001$) or RT + AD (0.24 ng/ml and 0.06 ng/ml, respectively; $p < 0.001$). BF was observed in 178/651 (27%) patients; for patients with nPSA ^{3} 1 ng/ml the risk of BF was greater (44/122; 36%) than for those with nPSA < 1ng/ml (134/529 ;25%) ($p= 0.013$; OR:1.66) independently of treatment modality. Multivariate analysis confirmed that age, stage, Gleason score, pretreatment PSA, dose RT and nPSA < 1 ng/ml were all significantly associated with BF and clinical failure. Multivariate cox regression showed stage and nPSA < 1 ng/ml to be the only parameters associated with cause-specific survival ($p< 0.001$ and $p = 0.001$ respectively). A TnPSA longer than 1 year was associated with less BF (52/284; 18%) than TnPSA £ 1 year (126/367; 34%) ($p < 0.001$;OR:2.15).

Conclusions: A lower nPSA (< 1 ng/ml) and longer TnPSA (> 1 year) were associated with improved outcome. There was a close correlation between nadir PSA ^{3} 1 ng/ml and subsequent development of biochemical and clinical failure.

1107 poster

NON-METASTATIC HORMONE-REFRACTORY PROSTATE CANCER (HRPC): IS THERE ANY PLACE FOR THREE- DIMENSIONAL CONFORMAL RADIOTHERAPY (3D-CRT) IN THE MANAGEMENT?

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Purpose/Objectif

Patients with diagnosis of hormone refractory prostate cancer (HRPC) present very heterogeneous population and therefore, it has been proposed to sub-categorize them into two subgroups depending on presence or absence of distant metastases. While the former subgroup has been typically treated with palliative intention, for the latter apparently there is no standard approach. The role of three-dimensional conformal radiotherapy (3D-CRT) for this subgroup, which confers significant amount of prostate cancer patients, has not been well documented in the literature. Thus, the purpose of this work is to analyze the results of treatment of non-metastatic HRPC with 3D-CRT and to investigate the potential prognostic factors which influenced the results.

Materials/Methods: Of 425 patients with diagnosis of localized and locally advanced prostate cancer who were treated between 1997 and 2004 in our centre, forty-four (n=44) patients were referred as to non-metastatic HRPC. Distant metastases were excluded by negative bone scan, negative chest X-ray and negative pelvic CT for lymph node metastases. The median pre-hormonotherapy PSA (pre-HT PSA) level for this group was 25 ng/ml (range; from 1 to 201) and 5.7 ng/ml (range; 0.06 to 27) at the beginning of radiotherapy (pre-RT PSA). Clinical T stage distribution, defined according to the 2002 AJCC, was as following: T1c = 12, T2 = 23, and T3 = 9 patients, respectively. Of 44 patient's 39 had a Gleason score of 2-7 and 5 had a Gleason score of 8-10. All patients with diagnosis of non-metastatic HRPC were treated with 3D-CRT with the daily fraction dose of 2 Gy to a median total dose of 68 Gy (range; from 60 to 74 Gy). The median duration of androgen ablation therapy before RT was 26 months (range; from 7 to 96). The median time of follow-up after 3D-CRT was 27 months (range; from 13 to 62) and from the beginning of androgen ablation was 53 months (range; from 20 to 158). The following prognostic factors were evaluated in univariate and multivariate analysis: age, pre-HT PSA, pre-RT PSA, Gleason score, total dose, PSA doubling time (PSADT< 6 months vs PSADT > 6 months).

Results: The 5-year actuarial overall survival was 82% and 5-year clinical relapse free-survival rate was 49%. During the follow-up 15 patients developed clinical relapse (locoregional and/or distant and/or biochemical) and two patients died of prostate cancer. The univariate analysis indicated that pre-HT PSA > 20 ng/ml, pre-RT PSA > 4ng/ml, the high-risk group defined according to NCCN criteria (PSA >20 ng/ml and Gleason score >7), and Gleason score > 7 were statistically significant factors for the risk of clinical relapse. Multivariate analysis (Cox proportional hazard models) indicated that only the high-risk group (pre-HT PSA >20 ng/ml + Gleason score > 8) was an independent prognostic factor for relapse after radiotherapy.

Conclusions: Radiotherapy for patients with non-metastatic HRPC is valuable and highly effective method of treatment in terms of relapse-free survival provided it is administered to the subgroup of patients with pre-HT PSA<20 ng/ml and Gleason score < 8. For patients referred as to high risk group according to NCCN criteria 3D-CRT seems to be an ineffective treatment due to observed high incidence of distant failure and should be viewed as costly and sophisticated yet palliative intervention.

1108 poster

PROSPECTIVE STUDY IN PROSTATE CANCER 3D-CONFORMAL RADIOTHERAPY (3D-CRT) USING A NO-ACTION LEVEL (NAL) OFF-LINE CORRECTION PROTOCOL: RESULTS ON SET-UP ACCURACY IN 26 CONSECUTIVE PATIENTS.

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Purpose/Objectif:

Accurate daily patient positioning plays a crucial role in the outcome of 3D-CRT. At the radiotherapy Department of S. Maria della Misericordia Hospital in Udine (Italy), we have designed prospective study to assess set-up errors during 3D-CRT of prostate cancer.

In this setting our study is based on the comparison of the images taken by an electronic portal imaging device (EPID) to the digitally reconstructed radiographs (DRRs) of the planned treatment portals using a No-Action Level (NAL) off-line Correction protocol.

The aims of this study are to verify that the 3D-margins of CTV to PTV adopted by our Department are adequately safe and allow sufficiently small margins to introduce dose-escalation protocols.

Materials/Methods: Between January and April 2006, 26 consecutive patients received 3D-CRT (2Gy/fraction, 68 Gy mean total ICRU dose) for prostate cancer and were assessed for set-up accuracy. A CT-based virtual simulation procedure was carried out and digitally reconstructed radiographs (DRRs) were generated for each treatment field. All pts were treated supine, with an immobilization device for knees and feet without individual cast. Patients were asked to evacuate their rectum (also by means of enema compound), with

empty bladder in the case of radical RT (10 pts) and full bladder for RT after prostatectomy (16 pts). Planning target volume (PTV) was automatically contoured with an isotropic margin of 15 mm cranial-caudal, medial-lateral and anterior posterior around clinical target volume (CTV), which consisted of prostate gland plus seminal vesicles. Treatment portals were conformed by a multi-leaf collimator (MLC) with 7 mm margin around PTV to account for beam penumbra. Irradiation was delivered with 10 MV photons and a box technique, while 2 patients were irradiated with a five-field technique. Treatment fields were checked by comparing DRRs and on-line portal images of each field, obtained with EPID (IView - Elekta) during the first fraction at 0°, 270° and 90°. In the following two consecutive days and then weekly, during the whole radiotherapy cycle, we have checked the portal images obtained at 0° and 270 degree following a NAL off-line correction protocol with an action level for setup error of 5 mm. We have valued our data, using the Van-Herk formula, that allows to identify the margins to assure to cover the target by PTV with a goof level of confidence.
During the study a total of 130 portal images were analysed and 598 measurements were performed.
Results: These measurements showed a systematic error of about 2,5 mm anterior-posterior (A-P), 1,5 mm cranial-caudal (C-C) and 2 mm medial-lateral (M-L) respectively. We observed that the random error was 1,6 mm in A-P, 1 mm in C-C and 1 mm in M-L.
The analysis showed that the means of differences of each EPID measure with respect to DRR did not significantly change with the staff's turnover (Kruskal-Wallis $p = 0.19$, 0.88, and 0.62 for A-P, C-C, and M-L axis respectively), considering two teams of two technologists, each with a different staff composition, having similar individual training and experience, in two separate but homogeneous time intervals.
Conclusions: This study confirms the usefulness of NAL off-line correction protocols in reducing systematic set-up error in prostate cancer 3D-CRT, regardless of radiation technologists' staffs turnover. So we can use, in order to achieve a good accuracy on target, a PTV isotropic margin of 10 mm around the CTV and start a dose escalation protocol for radical radiotherapy.

1109 poster

RADIATION AND LONG-TERM HORMONAL THERAPY FOR PATIENTS WITH PROSTATE CANCER AND PATHOLOGICALLY CONFIRMED LYMPH NODE METASTASES

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Purpose/Objectif: To evaluate biochemical relapse free survival and toxicity of patients with prostate cancer and pathologically positive lymph nodes treated with 3D conformal radiotherapy (3DCRT) and long term hormonal therapy.
Materials/Methods: The study cohort comprised 101 men treated from 1996 to 2004 with external beam radiotherapy and long term hormonal therapy. 7 of these patients were randomized in a multi-centre German phase III trial (AP 03/95: Hormonal treatment alone versus hormonal treatment and external beam radiotherapy in lymph node positive prostate cancer) which was prematurely closed due to poor patient accrual. All patients underwent laparoscopic (n=92) or open (n=9) pelvic lymph node dissection and were entered into the study when at least one lymph node was positive. The mean number of positive lymph nodes was 2.46 (range: 1-22). Radiotherapy started in prone position with a 3-D conformal 3-4 field-technique and 1.8 Gy per fraction up to a dose of 50.4 Gy. The boost to the prostate was applied in supine position up to a median total dose of 72 Gy using a four-field 3DCRT. Orchiectomy, antiandrogens, and LHRH as the only hormonal treatment were applied in 11, 23, and 19 patients. Forty-eight patients had a combination therapy. Survival data were analyzed according to Kaplan-Meier calculations.
Results: The median follow-up was 49 months (51 months for the living patients). The 5-year progression free survival, metastasis free survival, cause specific survival, and overall survival for the entire cohort were 74.0%, 81.4%, 86.0% and 86.0%, respectively. Most patients experienced none or only mild to moderate toxicity (according to CTCAE 3.0). Grade 3 acute GI and GU toxicity occurred in two and one patients, respectively. With regard to late toxicities, one patient experienced rectal bleeding grade-3 and one patient suffered from grade-3 bladder spasm.
Conclusions: The combination of radiotherapy and long-term hormonal treatment provides long-term tumour control in patients with prostate cancer and pathologically confirmed lymph node metastases. The rate of acute and late toxicity is low. Similar to recently published single institution experiences of radical prostatectomy in lymph node positive prostate cancer, combined radiation and hormonal therapy offers the chance to provide long-term tumour control and may even cure a good proportion of these patients, who were often treated with (non-curative) hormonal therapy alone in the past.

1110 poster

RECURRENCES AFTER HIGH DOSE RATE BRACHYTHERAPY (HDR-BT) OF PROSTATE CANCER VISUALISED WITH 11C-ACETATE POSITRON EMISSION TOMOGRAPHY (AC-PET) AND MAGNETIC RESONANCE SPECTROSCOPY IMAGING (MRSI)

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Purpose/Objectif: To analyse the localisation of recurrences in patients (pts) with prostate cancer treated with conformal external beam radiotherapy (EBRT) in combination with HDR-BT in our hospital.
Materials/Methods: Data from 229 pts treated from 1996 to 2003 were analysed. The median follow-up was 42 months (range 12-110. EBRT was given with 2 Gy fractions to 50 Gy. HDR-BT was given in two 10 Gy fractions. Preirradiatory hormonal therapy was given to 184 pts (80%). PSA recurrence was seen in 52 pts and these were selected for further analysis. Bone scans were performed in 45 pts and computer tomography in 24 pts. Ac-PET was performed after 2002 in 22 pts and MRSI in 12 pts.
Results: Biochemical failures were seen in intermediate risk (9 of 66) pts and high risk (43 of 125) pts, not in low risk (0 of 38) pts. In 42 out of 52 pts it was possible to determine anatomical localisation of the recurrence. Skeletal metastases developed in 25 pts. Lymph node metastases were diagnosed in 28 pts, where 10 pts had paraaortal and 5 pts inguinal lymph node involvement. Local recurrences were detected in 17 pts. Of these, 4 pts had local recurrence only. With Ac-PET 9 local, 13 regional and 4 skeletal recurrences were diagnosed. MRSI indicated local recurrence in ten pts. Ac-PET and MRSI detected local recurrences in two pts where the HDR-BT had been inadequate.
Conclusions: Ac-PET and MRSI increased the detection of local recurrences. Skeletal and regional recurrences were nonetheless more frequent than local failures after EBRT with HDR-BT. Ac-PET and MRSI

provided information for future improvement of this treatment. The risk for regional and systemic recurrence in high risk patients should be taken into account.

1111 poster

SALVAGE 3D CONFORMAL RADIOTHERAPY AFTER HIFU (HIGH INTENSITY FOCUSED ULTRASOUNDS) FOR PROSTATE CANCER: TOLERANCE EVALUATION AND EARLY CLINICAL RESULTS

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Purpose/Objectif: To evaluate tolerance and initial clinical results of salvage three-dimensional conformal radiotherapy (3DCRT) performed after a primary HIFU treatment for localized prostate carcinoma.

Materials/Methods: Five patients affected by persistent, biochemically or clinically relapsed of localized prostate adenocarcinoma after primary treatment with HIFU were salvaged by 3DCRT. Salvage irradiation was performed with a 3DCRT approach , consisting of a five-fields isocentric technique, by 10-MV X-rays. MLC was used to customize the field shape to the target volume. All patients were treated in a supine position with a knee-foot immobilization device (Sinmed, NL). The average dose was 74 Gy (range 72-76), in 2 Gy fractions, delivered on a CTV including prostate only with a 10 mm margin (8 mm posteriorly) for PTV expansion. No hormonal treatment was used. Patients charateristics were: mean age: 68 years; clinical stage pre HIFU: T1c=1, T2=3, T3a=1; mean Gleason scores 6 ; mean pre-3DCRT PSA value: 4.8 ng/ml. Mean interval between HIFU and 3DCRT was 12.1 months. Radiation tolerance was evaluated with the RTOG (Radiation Therapy Oncology Group) bladder and bowel toxicity score. Mean follow-up after 3D-CRT was 19.2 months (range: 5-36 months).

Results

RTOG score	G1	G2	G3	G4
Urinary toxicity (patients)	0	4	1	0
Bowel toxicity (patients)	4	1	0	0

At a median follow-up of 19.2 months, no patients had evidence of biochemical or clinical failure. In term of clinical results, mean of nadir of PSA value is 0.15 ng/ml.

Conclusions: At our knowledge and till now, data of feasibility, tolerance and clinical impact of salvage radiotherapy after HIFU failure have not been published. Our preliminary data show that salvage 3DCRT is a safe and feasible treatment, with a low profile morbidity. Early clinical results appear quite promising, even if a longer follow-up is clearly needed.

1112 poster

SHORT-TERM NEOADJUVANT TOTAL ANDROGEN DEPRIVATION AND HDR BRACHYTHERAPY USED AS A BOOST FOR INITIAL AND LOCAL ADVANCED PROSTATE CANCER. IS THE MORBIDITY INCREASED?

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Purpose/Objectif: We verified the influence of short-term neoadjuvant androgen deprivation (sNAAD), less than 6 months, on acute and late intestinal (GI) and urological (GU) morbidity when high dose rate brachytherapy (HDR) was used as boost to conventional external beam radiatiotherapy (EBRT) in prostate cancer.

Materials/Methods: From 03/97 to 06/03 189 patients with biopsy proven adenocarcinoma Gleason scored, 1992 AJCC clinical stage T3a or lesser were treated with a course of EBRT 6MV photons to a median dose of 46Gy to the prostate and seminal vesicles only. For HDR-BT treatments patients were grouped into four groups: low (LR) and high risk (HR) for biochemical failure, with or without sNAAD. The LR group encompassed patients who presented GS < 6, initial PSA < 10ng/ml and T2a or lesser. They received 16 or 20Gy (4 to 5Gy fractions, BID) HDR. The remaining patients were grouped into HR and received 20 or 24Gy (5 to 6Gy fractions, BID). Biological effective doses (BED) for acute and late responding tissue were calculated and matched with late gastro-intestinal (GI) and urological (GU) morbidity.

Results: Median age of patients was 68 years old (range 47 to 83) and median follow-up 46 months (range 24 to 96). One hundred and two (53.9%) patients had NAAD as first approach. Acute GU and GI morbidity G1-2 were seen in 19% (36/189) and 11.1 % (21/189) of patients. Late GI and GU morbidity G1-2 were seen in 12.2 % (23/189) and 8.9 (17/189) of patients. Seven patients (3.7 %) developed G3 GU late morbidity, as urethral strictures (UR). The predictive factors for UR were active length of needles greater than 3.5cm (p=0.0495) and age > 65 years (p=0.0432). There was no influence of sNAAD, with statistical significance, in the incidence of acute or late side effects. On multivariate analysis by Cox regression age older than 65 years was the only predictive factor for the development of UR (p = 0.032).

Conclusions: The use of sNAAD previously to EBRT boosted by HDR seems to have no influence on the incidence of GU and GI morbidity, but instead of it, the increased age seems to correlate with higher incidence of UR.

1113 poster

SIDE-EFFECTS AND EFFICACY OF CONFORMAL RADIATION THERAPY (CRT) IN PATIENTS WITH PROSTATE CANCER.

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Purpose/Objectif: To evaluate late side effects and biochemical recurrence free survival (bNED) in patients with definitive CRT for localized prostate cancer.

Materials/Methods: 385 patients with localized prostate cancer (cT1-T4N0M0) were retrospectively analyzed. Median follow-up was 60 months (12-128 m.). The median dose to the prostate was 70 Gy (59-72 Gy), 78% of the patients received short term neoadjuvant hormonal therapy (median duration: 4.6 months, 1-15 m.). Late side-effects were graded according to a modified RTOG score. Every macroscopic bleeding was scored at least as grade 2 toxicity. BNED was defined according to the ASTRO criteria (3 consecutive rises).

Results: The incidence of grade II and III late side effects at 5 years (Kaplan-Meier) is listed in table 1. No grade IV or V toxicity was observed. Rectal bleeding was mostly minor and intermittent without affecting the patient's daily activities. In multivariate analysis acute grade II/III rectal toxicity was associated with a higher incidence of late grade II/III rectal toxicity (p<0.001). Acute grade II/III urologic toxicity and concomitant peripheral arterial disease were associated with a higher incidence of late grade II/III urologic toxicity (p<0.001 and p=0.006, respectively). Five-year biochemical free survival (bNED) was 69%. In multivariate analysis the following variables were significantly associated with bNED: initial PSA (p<0.001), grading (p=0.005) and T-stage (p=0.020). The 165 (43%) patients in the high risk group (cT3/T4 and/or G3 and/or initial PSA > 20 ng/ml) had a 5-year bNED of 67% vs. 77% in patients with low and intermediate

risk tumours. Biochemical recurrence significantly correlated with local recurrence, distant metastasis and disease specific survival but not with overall survival.

Late side-effect	Incidence of grade II toxicity at 5 years	Incidence of grade III toxicity at 5 years
Defecation frequency	4%	1%
Mucous/pain	8%	0.3%
Rectal bleeding	22%	3%
Pollakisuria	10%	3%
Nycturia	17%	2%
Urodynia	2%	0.3%
Haematuria	5%	0.5%
Urethral stenosis	1%	2%

Conclusions: Conformal radiation therapy for prostate cancer is associated with a low incidence of severe late side-effects. BNED for patients with high risk features remains unsatisfactory after CRT with 70 Gy and short term neoadjuvant androgen ablation.

1114 poster

SPARING THE PENILE BULBUS BY MRI-BASED PROSTATIC APEX DEFINITION IN 3DCRT AND HELICAL TOMOTHERAPY OF PROSTATE CANCER

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Purpose/Objectif: Impotence after radiation therapy for prostate cancer remains a problem: rates of erectile dysfunction range from 20% to 90%. Most evidence suggests that impotence has a vascular aetiology. To decrease the incidence of impotence, it would be logical to decrease the dose to the critical structures involved in erection. These structures can be better defined by MRI.

The aim of this study was to define the prostatic apex and the penile bulbus (PB) by MRI and to evaluate the absorbed dose to this structure from patient underwent helical tomotherapy (HT). For comparison, the absorbed dose to PB in conformal treatment planning was also evaluated.

Materials/Methods: Four patients diagnosed with prostate cancer entered a treatment protocol including acquisition of MRI pelvic sequences and HT. The MRI data sets were registered with the CT images used for treatment planning. Axial MRI T2 sequences were obtained with a pelvic coil using 4 mm slice thickness and no gap. CT images were acquired with 4 mm slice thickness. During CT and MRI acquisition some special skin markers were used in order to facilitate image fusion. The prostate was defined both on MR and CT images; in addition, MRI data sets allowed to better define PB. HT treatment planning was elaborated on MRI defined prostate. Margins for PTV definition were 1 cm in cranial-caudal direction and 0.8 cm in other directions. A dose of 71.4 Gy (2.55 Gy/fraction) was prescribed. PTVs were requested to be covered by the 95% isodose line. The mean dose and V50 of PB were determined. 3DCRT treatment plans were simulated, both on MRI and CT defined PTVs and also employing the caudal limit to the conventional ischiatic tuberosities limit. For comparison to HT treatment plans we used the same criteria of PTV coverage.

Results: Mean PB dose for 3DCRT MR and CT defined PTVs ranged from 14 to 45.2 Gy and 37.8 to 68.4 Gy respectively. Tomotherapy treatments resulted in a mean PB dose ranging from 21.7 to 29.5 Gy. For three of four patients, with a distance between the upper limit of the PB and the caudal limit of PTV around 1 cm, the mean dose to PB was slightly higher with HT compared to 3DCRT. For one patient whit PTV caudal limit very proximal to PB, HT reduced both mean dose (- 15.7 Gy) and V50 (- 32.3%).

Conclusions: We conclude that MRI data sets allowed an efficient sparing of PB with both 3DCRT and HT. Tomotherapy may improve the sparing of PB if this structure is very near to PTV.

1115 poster

THE BIOLOGICAL SIGNIFICANCE OF LONGITUDINAL CHANGERS IN PSA; PSA RESPONSE SIGNATURES (PRS)

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Purpose/Objectif: We sought to determine whether inter-patient variations in pattern of PSA changes during and after radiation ± prior androgen deprivation are prognostically significant.

Materials/Methods: In the TROG 96.01 trial patients with T2b,c, 3, 4 N0 prostate cancer (PC) were randomised to 0, 3 or 6 months maximal androgen deprivation (AD) (goserelin 3.6mg s.c. monthly and flutamide 250mg p.o. tid) commencing 2 and 5 months prior to 66Gy to the prostate and seminal vesicles (XRT). Amongst others, patterns of anatomical site of failure were important trial endpoints. Serial serum PSA and testosterone estimates prior to, during and after therapy were mandated. Pattern recognition software was developed to characterise PSA response 'signatures' (PRS) during and after therapy (but prior to PSA stabilisation or biochemical relapse) in individual patients.

Results: Between 1996 and 2000, 802 eligible patients were randomised. Regardless of treatment arm, individual patient PSA levels were observed to descend according to one of three characteristic signatures (PRS): single exponential (SE), double exponential or polyexponential. In patients randomised to XRT only, those with SE PRS (40% of the group) experienced shorter doubling times on relapse and had significantly higher rates of local and distant failure ($p < 0.00001$ and < 0.0001), deaths due to PC (HR 5.0 [2.1-11.9], $p=0.0002$) and worse overall survival (HR 2.6 [1.5-4.7], $p=0.0007$) than those with the two other signatures. In patients randomised to AD/XRT the reverse was true. SE PRS was associated with longer PSADTs on relapse and lower rates of local and distant failure. PRS retained its powerful prognostic significance in Cox models that incorporated all key pre-treatment co-variates.

Conclusions: PRS reflect the presence of tumour phenotypes that vary substantially in their clinical behaviour and response to both XRT and AD. Molecular characterisation of these phenomena is necessary to understand the underlying mechanisms and to enable stratification prior to treatment.

1116 poster

THE COMPLEXITY OF REPORTING LATE TOXICITY (LT) AFTER CURATIVE HYPOFRACTIONATED RADIATION TREATMENT (RT) IN LOCALIZED PROSTATE CANCER.

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Purpose/Objectif: Late effects are of major concern when hypofractionation is used in curative RT. We report the results of a prospective evaluation of LT in a homogeneous group of prostate cancer patients treated with hypofractionatiated RT.

Materials/Methods: 71 patients with histologically proven low/intermediate risk prostate cancer were treated with hypofractionated

RT alone, without hormones, between October/2002 and April/2004. A 3D treatment plan consisting of five 18MV photon fields was used to deliver 66Gy/22fractions prescribed at the isocenter. PTV was the prostate plus a uniform 7mm margin. Rectum was contoured from anus to sigmoid. Daily ultrasound was used to confirm setup. LT was prospectively registered using the CTC v.3 scoring system. Patients were seen in follow up at regular 3-6 months intervals. Different known factors were calculated from dose-volume histograms to correlate with late rectal toxicity.

Results: The median follow-up for all patients is 30 months (range: 4.6 - 42 months), but 91% had a minimum of 2 years of follow up. Median age=72 years. There was no genitourinary(GU) or gastrointestinal(GI) toxicity > grade 3. The table summarizes the worst acute and late GU and GI toxicity seen during follow-up, and also the toxicity registered at the last visit. Concerning the late rectal effects, there was no relationship between rectal toxicity and any of the dosimetric factors studied. The cumulative incidence of grade 2/3 late GI toxicity at 3 years was 20%.

Discussion: In the literature LT has been reported in many ways. Different definitions of toxicity are used, or known definitions (such as the RTOG system) but with modifications. In some studies toxicity is reported for each grade separately and some report the results with all the grades together. Some mention the total number of patients and others the cumulative incidence using techniques such as the actuarial life table. Recently, reports tend to account for changes over time because toxicity can resolve after treatment.

Conclusions: We found 18% of GU and 23% of GI grade 2/3 toxicity during the whole period of follow up, but only 4% and 7% at the last follow up. Our results seem to go along with the published data about LT after curative RT in prostate cancer. However, the many ways LT has been reported make comparisons of results almost impossible. A consensus meeting should put together the guidelines for reporting LT in this group of patients.

	Acute		Late		Last visit	
Grade	GU	GI	GU	GI	GU	GI
0	7	16	33	46	52	54
1	39	38	26	16	16	10
2	21	17	13	1	4	5
3	5	1	0	9	0	2

1117 poster

THE FULL BLADDER ISSUE IN PROSTATE CANCER RADIOTHERAPY: MEASUREMENTS WITH AN ULTRASOUND BASED BLADDER SCANNER.

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Purpose/Objectif: In many institutions, prostate cancer irradiation is performed with a full bladder, in order to reduce bladder and small bowel toxicity. But daily variation and decrease over time in bladder volume could easily influence prostate position and also render toxicity probability estimations, derived from treatment planning, useless. Daily bladder filling variation, during prostate cancer radiotherapy, and its effect on prostate position were investigated with the use of an ultrasound based bladder volume scanner and an EPID correction protocol. Also a biofeedback protocol, aiming at a more constant bladder filling, was tested.

Materials/Methods: 50 patients were irradiated for localized prostate cancer. Standard treatment (67.5 Gy, 30 fractions) consisted of 3DCRT and an off-line EPID corrections protocol using 4 gold intraprostatic markers. Patients were instructed to have a "comfortably full" bladder during simulation and irradiation. A "comfortably full" bladder was defined as having definite but easily tolerable micturition urge.First, the accuracy of the bladder scanner relative to CT was validated in a group of 26 patients. Next, daily bladder volume variation was evaluated in a group of 18 patients (control group). Another 16 patients participated in the biofeedback protocol. The feedback consisted of telling the patient his daily bladder volume together with a drinking advice. Also EPID data (measured during a mean of 11 ± 2 fractions) were used to study correlations between prostate motion and bladder filling.

Results: A strong correlation between bladder scanner volume and CT volume (R = 0.95) was found. In the control group, bladder volume decrease (33%) and daily variation (1 SD = 47.2%) were very high. Bladder filling and daily variation did not significantly differ between both groups.Only prostate motion in craniocaudal direction showed a significant linear correlation with bladder filling (R = 0.21; p = 0.04). This indicates that only about 5% (R^2) of variance in prostate position is caused by changes in bladder volume.

Conclusions: This study shows large variations in actual daily bladder volume, regardless of a biofeedback protocol. However, no clinically relevant influence on prostate motion was found. Therefore, full bladder radiotherapy of prostate cancer, in order to reduce bladder and small bowel toxicity, can be performed without a negative effect on daily prostate motion.

1118 poster

THE IMPACT OF SET-UP ERROR ON QUALITY CONTROL OF A MULTI-CENTRIC STUDY ON RECTAL TOXICITY DURING 3DCRT OF PROSTATE CANCER (AIROPROS01-02)

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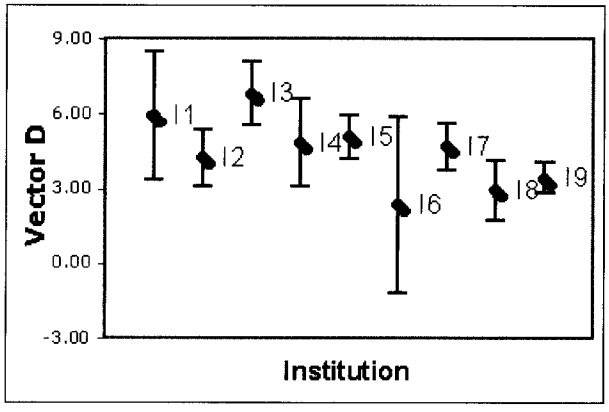
Purpose/Objectif: Geometric uncertainties and setup errors are a critical part in the management of 3DCRT of prostate cancer. This technique delivers high doses to the PTV while attempting to minimize the dose to the surrounding organs at risk (OARs) and precise targeting prostate radiotherapy is primarily dependent on daily setup. The prostate and OARs spatial location can be influenced by changes in the patient position and/or consequential dislocation of the surrounding abdominal organs. In multi-centric studies, all aspects of the treatment are always broached in the agreed upon protocol, but misinterpretations and/or local adjustment are frequent and a careful evaluation of the patient positioning reproducibility should be done.

Materials/Methods: Within an Italian trial, coordinated by the AIRO national working group on rectal toxicity during 3DCRT of prostate cancer, it is in progress the retrospective analysis of a 8% sample extracted form a large population of 1132 patients pooled from 21 Institutions and treated mostly to 68-78Gy 3DCRT. Positioning verification was performed by EPID megavoltage images and portal films. The patient positioning was checked in a collecting reference Centre by measuring the distance of the isocentre from fixed anatomical structures on the reference and verification images taken in anterior-posterior and lateral projection. The total isocentre displacement was also evaluated (vector D).

Results: A number of observers were involved after having estimated their inter-observer variability in assessing the displacements; this variability resulted to be acceptable (6.5% error). Partial results, related to 9 of the 21 Institutions (representing 757/1132 patients), show that setup uncertainties appears to be mainly in the anterior-posterior axis (1.71 ±0.98 mm) and in superior-inferior axis (1.13 ±0.71 mm) than in the lateral direction (0.77 ±0.85 mm), with a vector D mean value of 4.48 ±1.42 mm. Inter-Institution variability seems to be greater than intra-Institution variability (see figure).

Conclusions: This result confirms the conclusion that, even if it is time consuming, setup errors should always be estimated, especially in multi-centric study, where different local realities are involved and this could affect important phases of the study. The considered sample, representative of more than 70 % of the population, suggests that an acceptable set-up uncertainty was reached within the AIROPROS0102 multi-centric study.



1119 poster

THE PRELIMINARY RESULTS OF INTENSITY-MODULATED RADIOTHERAPY ABOVE 70 GY FOR PROSTATE CANCER

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Purpose/Objectif: To investigate the prelimary treatment results in prostate cancer treated with intensity-modulated radiotherapy (IMRT) with or without androgen deprivation therapy (ADT)
Materials/Methods: Between december 2001 and Mach 2004, 92 patients with cancer had undergone primary,curative radiotherapy via IRMT technique. Four patients (5%) were treated to 70.2 Gy, while 74 (805) and 14 patients (15%) were treated to 72 and 75.6Gy. Thirty patients (33%) received pelvic irradiation to 45 Gy as a part of treatment. Seventy-nine patients (86%) also received ADT. Acute and chronic complications were scored and revised by the scale of Common Terminology Criteria for Adverse Events v3.0. The median follow-up time was 37.5 months (20.4-57.8 months).
Results: The grade 3 acute complication rates of urinary and gastrointestinal system were 4% and 1%. No grade 4 or 5 complications were observed and no one had their radiotherapy interrupted due to acute complications. The grade 2 chronic complication rates of urinary and gastrointestinal system were 14% and 6%. No grade 3 or higher chronic complication was observed. Pelvic irradiatino and more than 70 Gy delivered to seminal vasicles were the risk factor of developing acute gastrointestinal complications. No other significant factors were found correlated with other acute or chronic complications. The 3-year sexual function preserving rate was 31%. The 3-year overall survival and disease-free survival rates were 91.8% and 76.4%. High-risk of recurrence was the only significant risk factor correlated to disease recurrence. Besides, some patients with high risk of recurrence received adjuvant ADT but the duration was less than 12 months. We observed that the 3-year disease-free survival in this group of patients (28.6%) was significantly worse, even than the patients with same risk but received no adjuvant ADT (71.6%, p=0.022).
Conclusions: Based on this study, high dose IMRT, with or without androgen deprivation, is safe for treating prostate cancer. The results of survival and disease-free survival need more follow-up time for observation and making any conclusion. And, short-term adjuvant ADT may be a detrimental management for patients with high risk of recurrence.

1120 poster

THREE-DIMENSIONAL CONFORMAL EXTERNAL RADIOTHERAPY VERSUS THE COMBINATION OF EXTERNAL RADIOTHERAPY WITH HIGH-DOSE RATE BRACHYTHERAPY IN LOCALIZED CARCINOMA OF THE PROSTATE: COMPARISON OF ACUTE TOXICITY

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Purpose/Objectif: Radiotherapy represents one of the basic therapeutic methods in treatment of localized carcinoma of the prostate. The current methodology allows us to increase the irradiation dose to the prostate while lowering the dose distributed to critical organs, particularly the rectum. Optimal irradiation dose is the cornerstone of a successful treatment. Along with local control of the disease and overall survival of the patient, possible acute and long-term side effects need to be monitored very closely, as they markedly influence the quality of the patient's life.
Materials/Methods: A non-randomized prospective study comparing the acute genitourinary and gastrointestinal toxicity in patients irradiated for localized carcinoma of the prostate between August 2004 and July 2005. 57 patients treated with three-dimensional conformal external beam radiotherapy (3D CRT) alone represented the first treatment arm (3D CRT arm). In the second treatment arm a combination of external radiotherapy and high dose rate (HDR) brachytherapy (BRT) was employed in 40 patients with localized prostate carcinoma, T1c - T3a (3D CRT+BRT arm). All patients underwent conformal external radiotherapy to the pelvic region or the area of prostate and seminal vesicles at the dose of 45 - 50.4 Gy. Brachytherapy in the 3D CRT+BRT arm was applied in two fractions during the 3rd and the 5th week of external radiotherapy at a dose of 8 Gy per fraction using the interstitial transperineal application technique with iridium Ir^{192} source. Based on the initial PSA levels, Gleason score, and T classification, patients were divided into three groups according to the relapse risk: low risk group (43.9% of the 3D CRT arm vs. 27.5% of the 3D CRT+BRT arm, respectively), medium risk group (26.3% vs. 35.0%), and high risk group (29.8% vs. 37.5%). Average age was 69.9 years in the 3D CRT arm, and 68.7 years in the 3D CRT+BRT arm. Hormonal manipulation was performed in 36.8% of the 3D CRT arm, and in 42.5% of the 3D CRT+BRT arm. The dose volume histogram (DVH) and dose to the anterior rectal wall were evaluated in each patient. Parameters describing the quality of the distribution including the maximum dose to the urethra and rectum were evaluated based on both the calculated and the measured values. Acute toxicity of the treatment was evaluated according to the Radiation Therapy Oncology Group (RTOG) criteria in all patients. Every patient filled out the International Prostate Symptom Score (IPSS) questionnaire both prior to and following the treatment.
Results:
3D CRT
Acute grade 1 genitourinary (GU) toxicity was recorded in 20 patients (35.1%), grade 2 in 13 patients (22.8%), and grade 2-3 in one patient (1.7%).
Acute gastrointestinal (GI) toxicity was experienced by 31 patients (54.4%), evaluated as grade 1 toxicity in 16 patients (28.1%), grade 2 in 10 patients (17.5%), and grade 3 in 5 patients (8.8%), respectively.
3D CRT+BRT
Acute grade 1 GU toxicity was recorded in 37.5%, and grade 2 in 15%

of the patients. In one patient an epicystostomy was performed due to retention. Symptoms in connection with the treatment subsided within one month from therapy in majority of the patients (90%) according to the IPSS. Only grade 1 acute GI toxicity was recorded in 40% of the patients treated in the 3D CRT+BRT arm.

Conclusions: Acute grade 1 GU toxicity was experienced by a similar percentage of patients in both treatment arms (35.1% vs. 37.5%). Acute grade 2 GU toxicity according to the RTOG criteria was more frequent in the 3D CRT arm over the 3D CRT+BRT arm (22.8% vs. 15%, respectively). Higher acute genitourinary toxicity - grade 3 or 4 - was recorded only in one patient per each treatment arm.

Acute GI toxicity was more frequent in the 3D CRT arm over the 3D CRT+BRT arm (54.5% vs. 40%). Higher acute GI toxicity - grade 2 and 3 - was only observed in the 3D CRT arm, not in the 3D CRT+BRT arm. In our group of patients we demonstrated a very good tolerance of the combined external radiotherapy plus HDR brachytherapy treatment in carcinoma of the prostate. The acute toxicity observed was of low grade. The size of the prostate was evaluated as the main risk factor for genitourinary toxicity, while the combination of pelvic irradiation with hormonal therapy was assessed as the main risk factor for gastrointestinal toxicity. The combination of external radiotherapy with BRT resulted in a lower incidence of gastrointestinal toxicity than external radiotherapy alone.

1121 poster

TOXICITY OF PD 103 AND I 125 AFTER INTERSTITIAL BRACHYTHERAPY ? A STATISTICAL ANALYSIS AFTER A FOLLOW-UP OF 5 YEARS

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Purpose/Objectif: Between 07/1999 and 12/2005 225 patients suffering from prostate cancer underwent interstitial brachytherapy at the Donauspital in Vienna.

Materials/Methods: The time depending PSA characteristic is documented as well as scores concerning their overall health, their urological problems and their remaining sexuality by EORTC QLQ-C30 (+3) -, IPSS- (International Prostate Symptom Score) and IIEF-15- (International Index Erectile Function) questionnaires. At each follow-up patients are asked to answer 56 questions by their own, which is accepted in most cases while waiting.

Results: 128 patients were treated with Palladium, 97 with Iodine. The average age at the beginning of the therapy was 68.5 years with a range from 48 to 83 years. The average volume of the prostates was 30.23 cm^3 (12.2 to 66 cm^3). All of these patients were classified by PSA and Gleason score, which leads to a risk classification. 86% I respectively, 77% Pd were low risk, and 14% I respectively, 20% Pd were intermediate risk. Only 3% of Pd-patients have to be classified as high risk patients. During the follow-up of about 5 years, local, lymph-node relapses and bone metastases were observed in a small number . Additionally 10 PSA relapses have been observed. The biochemical relapse free survival is about 95% after a follow-up of about 40 months after brachytherapy.

Conclusions: Brachytherapy of highly selected patients with local prostate cancer is a excellent tool for curative cancer treatment. In most cases toxicity can be scored as mild to moderate. Complimentary questionnaires give additional indicators for the documentation of individual side effects. Data basis for the evaluation of these rankings are of high interest as well as their evaluation. Additionally medical statistic tests of the collected data are introduced.

1122 poster

VARIABILITY OF RECTAL VOLUME DURING RT IS RELATED TO INITIAL RECTAL VOLUME AT SIMULATION

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Purpose/Objectif: To correlate rectal volume (RV) changes during a course of definitive radiotherapy for prostate cancer with RV at simulation

Materials/Methods: 50 consecutive patients with prostate cancer undergoing definitive radiotherapy (RT) for prostate cancer at UTMB were enrolled. At initial consult, patients were counseled on the importance of having a constant rectal volume during RT course and of having a bowel movement the night before or the morning of simulation and each daily treatment thereafter. Each patient was scheduled for a weekly CT during RT. The rectum, from the anal verge to the sigmoid flexure, was contoured by one observer on each available CT. For each patient, the degree of variation of the rectal volume during the course of RT was expressed by both the standard deviation (SD) and the coefficient of variation (CV) of the rectum, the latter defined as the ratio of SD to the mean. Only weekly scans taken during treatment were considered for calculation of SD&CV. Patients were pooled into 3 groups based on RV percentiles on initial planning CT. SD&CV were calculated for each patient and then averaged for each group. Comparison of means among groups were assessed with Wilcoxon two sample test.

Results: 369 scans were performed for a mean of 7.5 scans per pt (SD:1.4). Mean RV at simulation was 76.6 cc (SD:31.4). Based on initial scan, patients were divided into 3 groups: 1. small-S RV (<57 cc) rectum, 16 pts; medium-M RV (57-89 cc), 17 pts; large-L RV (>89 cc), 17 pts. Mean RV, SD, CV data during treatment by group are summarized in the table. If SD change across groups were due only to difference of mean, CV would be similar, but as shown in the table this was not the case.

Conclusions: The magnitude of RV change during treatment is directly related to the initial volume at simulation. The fact that this holds true also when normalizing for the mean is consistent with a lower predictability in RV during treatment for patients who have medium/large rectal volumes at simulation despite instructions.

1123 poster

VOLUME EFFECT FOR ACUTE AND LATE TOXICITY DURING 3DCRT DOSE-ESCALATED RADIOTHERAPY FOR PROSTATE CANCER

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Purpose/Objectif: Study the association between dose-volume parameters and urinary tract (GU) and gastro-intestinal (GI) toxicity in prostate cancer patients treated with 3D CRT dose-escalated Radiotherapy.

Materials/Methods: A total of 341 prostate cancer patients treated between June 1999 and January 2005 were analysed. Toxicity was graded using the RTOG scale. According to tumour stage, Gleason score and pre-treatment PSA, patients were divided into three risk groups. PTV consisted of the prostate plus 6-10 mm of margin with or without the seminal vesicles (SV) and the internal iliac nodes depending on the risk of his involvement (Partin >15%). Hormonal therapy was associated in the worse risk patients. The dose at PTV prostate was 70 - 76 Gy. All the patients were treated using linear accelerator with multi-leaf collimator.

Results: Mean age was 70 years (52 - 85 years). Median follow-up was 22.2 months (3 -76 months). None of the patients experienced grade 4 acute or late toxicity. GI acute toxicity was 39.5 % grade 1, 13.1 % grade 2 and 1.1 % grade 3. GI late toxicity was 14.3 grade 1, 3.8 % grade 2 and 0.3 % grade 3. GU acute toxicity was 56 % grade 1, 9 % grade 2 and 1.1 % grade 3. GU late toxicity was 6.1 grade 1, 2 % grade 2 and 0 % grade 3. The dose-volume histogram shows that in the 66 % of patients with grade 2 late toxicity, the V50 was > 50cc.
Conclusions: Our data shows lower acute and late toxicity using dose-escalated RT for prostate cancer. There is a relationship between dose-volume and grade 2 GI toxicity, with a high association for V50. A longer follow-up is necessary to determine the real local-regional control.

Posters Quality Assurance

1124 poster

3 D IMRT DOSE VERIFICATION BASED ON 2 D MEASUREMENTS WITH A CHAMBER ARRAY

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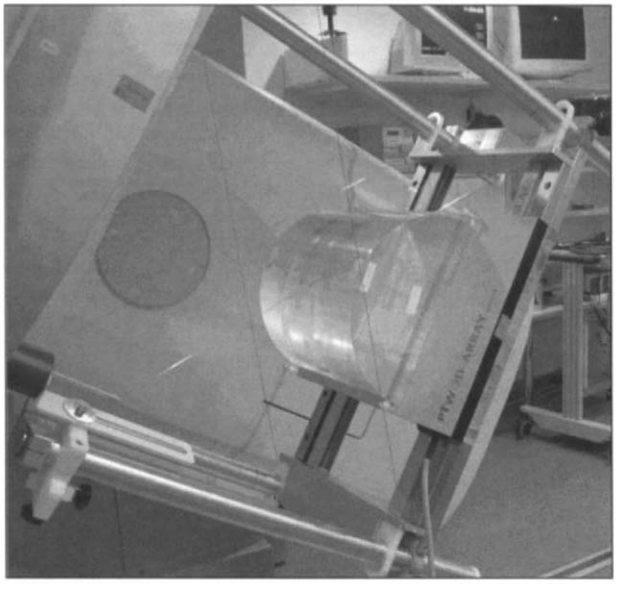
Purpose/Objectif: Individual IMRT patient plan verification is still a task in clinical routine, no matter if radiographic film or other detector and phantom combinations are used. When chamber or diode arrays are in use the main problem is the orientation of the detectors only on one plain and the low spatial resolution. Our method will derive a high resolution 3 D dose distribution from measurements made with a chamber array.
Materials/Methods: Measurements have been made with a PTW array 729, an ionization chamber array with 27 by 27 detectors with a spatial resolution of 10 mm. The array was set to isocenter distance and fixed to a modified PTW air scanner device attached to a Siemens Primus accelerator (Fig 1). On top of the array we mounted a half cylinder made of Perspex with a diameter of 270mm. Phantom plans were generated using the full cylinders geometry and delivered to the device gantry angle by gantry angle. Care was taken that the fluence map exactly matched the center of the detectors. Measured data in absolute doses are loaded to an IDL (RSI) software package where the 3 D dose distribution is derived. A simple projection algorithm then uses the depth dose curves and beam divergence to calculate the dose above and below this plain with a resolution of 0.5mm. Done for all beam directions the sum represents the absolute 3D distribution in the phantom. The software package also includes some tools for evaluation of measurement versus calculation of the treatment planning system like profiles, isodoses and Gamma evaluation.
Results: First measurements taken from 4 patient phantom plans show good results when compared to calculations from treatment plans or verification films. Since ionizations chambers are used and the data along the central axis of the phantom are not touched by the projection algorithm, the agreement is very good on the axis. Larger deviations are found close to the surface of the phantom, witch result from the simple representation of the depth dose curve and of missing scatter in this region. Although almost everywhere in the phantom a 3% of maximum dose and 2mm distance to agreement Gamma criteria could be fulfilled. Drawback of this system is the complex setup and exact positioning of the phantom and detector. We also found some problems in the mechanical stability of the device what resulted in a poor superposition of chamber array and delivered fluence map.
Conclusions: This method combines the high resolution and the potential of measuring several slices of films with simplicity and precision of an ionization chamber measurement to a full 3D verification system. Limitations are of course the difficult setup of the phantom and the poor precision in the build up regions. While these cons can be eliminated by simpler phantom device and a better depth dose representation the fact that non coplanar beams can not be measured is a fundamentally to the system.

Fig.1 : Array and cylinder set up at the linac.



1125 poster

A FAST METHOD TO CORRECT THE PROFILES OF A SEMICONDUCTOR-BASED LINEAR ARRAY FOR REGULAR MEASUREMENT OF VIRTUAL WEDGES

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Purpose/Objectif: Linear arrays are used for regular verifications of virtual wedges. In our hospital we use a Scanditronix LDA-25 array, composed by 25 semiconductor detectors that need regular calibration. In the time between calibrations, the error in measurements increases progressively. We analyze a fast method to correct the measured curves in that interval, because the calibration procedure for LDA-25 is very time-consuming.
Materials/Methods: Scanditronix LDA-25 linear array was used for in-water measurement of Siemens Primus Virtual Wedges®. The control and analysis software were Omnipro Accept v.6.4 and Microsoft Excel. In the first day, linear array was calibrated and measurements were: Reference profiles in the wedge direction and two open field profiles for comparison. Of the open ones, the first was measured using the 25 detectors of the linear array and the second was taken using the central detector only, as if it was a single one, with the same initial coordinate and the same resolution. Reference field was 20x20 cm^2, and scan resolution 2.5mm. This resolution gives a complete profile with 4 lectures per detector. The control of virtual wedges was done weekly. Open field profiles were used to check the loose of calibration an to calculate correction factors. The four readings of each detector in the open profile were compared to the reading of the central one in the same four positions to obtain a correction factor for the given detector. This correction factor was used to correct the wedged profiles. As virtual wedges use low (200-300 MU/min) and high dose rates (30-50 MU/min) to construct the wedge profile, the correction factors were calculated at both dose rates and compared.
Results: For each detector, the differences observed in the correction factor were less than 0.3% between the four positions. In the penumbra region those differences reached higher values, but no

influence in the corrected profiles was observed. When measuring the repeatability of the correction factors in the same day, the maximum observed differences were 0.3%. Measurement of the constancy of factors between high and low dose rates showed maximum values near 1%. These differences were possibly due to the higher deviation over mean for each detector at low dose rates (0.5% to 0.3%). Thus, the same correction factors were used for the wedged profiles and for the open one. To complete the study, the corrected wedged profiles were compared to the calibrated ones, with a calibration done in the same day: the smallest differences were found for the 60° wedge (<0.2% in all detectors). For the 15° wedge the maximum difference was 0.5%.
Conclusions: The presented method can be a practical way to decrease the spend of time due to calibration of linear array LDA25 for regular verifications of virtual wedges. Using it, the time interval between calibrations can be increased with no consequences in the precision of weekly controls.

1126 poster

A RADIOBIOLOGICAL AND CLINICAL ASSESSMENT OF QUALITY ASSURANCE TOLERANCES IN HEAD AND NECK RADIOTHERAPY TECHNIQUES

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Purpose/Objectif: Radiotherapy of the head and neck region can involve a number of complex treatments often involving field matching, matching of electron and photon fields and intensity modulated radiotherapy. Unintended overlap of these fields has the potential to lead to higher than intended doses to the spinal cord. The potential effect of various types of set up error on these parameters has been studied and the suitability of quality assurance tolerances assessed using radiobiological considerations of cord tolerance
Materials/Methods: Unintentional overlap volumes have been simulated using commercial virtual simulation software and dose distributions computed using the Nucletron-TMS treatment planning system. Biological equivalent doses have been calculated bearing in mind the total contribution to the spinal cord from each field, which can exceed intended dose per fraction, assumed 2Gy, given the contribution due to transmission from blocked fields etc.
Results: There is currently limited data in the literature on spinal cord tolerance in these situations. A review by Rampling and Symonds (Current Opinions in Neurol 11:627-632,1998) on the then available clinical data concludes that a spinal cord tolerance of 50Gy is suggested with doses up to 60Gy if clinical need requires, provided dose per fraction is kept at or below 2Gy per fraction. Macbeth et al (Clinical Oncology 8:176-181,1996) recommend that when the computed linear quadratic equivalent dose for 2Gy fractions exceeds 48Gy, consideration should be given to reducing the dose to the cord. In cases where matched fields may unintentionally overlap these tolerances may potentially be exceeded for overlaps as little as 2mm. Bijl et al (Int.J.Radiat.Oncol.Biol.Phys. 64:1204-1210,2006) have also shown in rats irradiated with single doses of unmodulated protons that the high tolerance dose for small regions decrease significantly when adjacent tissue is irradiated with a sub threshold dose.
Conclusions: This study has demonstrated the difficulty of estimating spinal cord dose due to small overlaps of radiation fields and justifies, using radiobiological considerations, the need to ensure geometrical errors due to set up, collimator jaw calibration etc are kept within tight tolerances.

1127 poster

A SIMPLE AND AFFORDABLE METHOD FOR DOSIMETRIC ASSESSMENT AND QUALITY CONTROL OF ABUTTED FIELDS BY USING ASYMMETRIC COLLIMATORS

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Purpose/Objectif: Both junction and match of tangential, lateral and anterior fields are commonly performed techniques in head and neck, breast and other radiotherapy treatments. The introduction of asymmetric collimators provides the possibility to perform treatments by using a common isocentre for all the fields and saves us the need for movement of the couch to join them. In addition, it provides a more reproductive dosimetry in the plane of junction. The aim of this study is to determine *in vivo* the possibility to be out of alignment in the dose distribution across the junction due to the jaw tolerance or the patient movement during the treatment.
Materials/Methods: Two LINAC, a 2100 C/D and a 600 C Varian linear accelerators have been studied. Before treating patients, the alignment of the asymmetric jaws was accurately determined by the exposure of a film, following the technique described by Saw and Husey (Med.Dos. 25 (1) 23-26.2000). The films were digitalized with OmniPro™ IMRT software (IMRT film verification) and the jaws position was adjusted until obtaining a perfect dose matching (within 5 %) on the junction plane (Fig.1). Once jaws calibration was achieved, more than 30 patients were treated with joint fields and were studied by using weekly a little film slice (X-OMAT V) placed on the fields junction on the patient skin.
Results: Two patients showed underdose, due to a dosimetric gap, in the first film obtained. In the following seasons, the dose distribution provided by the films was correct.
Conclusions: Conclusions: The use of in vivo radiographic films allows us to easily control on patient the quality of treatments with joint asymmetric fields, by means of a simple and affordable technique.

1128 poster

AN ANALYSIS OF THE CYBERKNIFE ACCURACY WITH 6D SKULL TRACKING:INFLUENCE OF DIFFERENT THICKNESS AND SHAPE OF HEADREST ON TOTAL CLINICAL ACCURACY

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Purpose/Objectif: 6D skull tracking in CyberKnife gives usually very good results in accuracy and consistency. Measuring monthly the accuracy of CyberKnife system with the E2E test procedure, we found different results when we changed the initial setup (shape or thickness of the headrest). The purpose of this study is to further investigate the influence on total clinical accuracy of using headrests with different thickness and couch plate with different shape.
Materials/Methods: We performed several CT acquisitions of Sheila anthropomorphic phantom, with the "ball cube" inside, each of them with different support device: (1) with the old mask holder attached to the CT couch (2) with the new carbon fiber table top provided with axum for the CT (3) with 1 cm thickness of radiotransparent material between couch and phantom (4) with 1.5 cm

thickness of plastic foam equivalent to air (5) with a wedge with a 9° angle, made of radio-transparent material (6) with a combination of the previous support devices [(4) + (5)]
Afterwards we created the E2E treatment planning, irradiating at least 2 treatments for each of the previous cases, using MD-55 GafChromic films. In treatment we used the same support devices for each case, except for (1) and (2) because we could only use the Axum table top, in the narrower area relating to the head. Initial alignment was with sub-millimetric and sub-degree displacement, the "brightness gain" was about 1.00.
Results: The total clinical accuracy of our center for 6D skull tracking is normally 0.44 ± 0.18 mm, with an average of Left: 0.03 mm, Sup: 0.04 mm, Ant: -0.19 mm. Changing the support conditions we found different results that we are reporting here: (1) Left: 0.03 Sup: 0.04 Ant: -0.19 Avr.Accur.: 0.44 mm (2) Left: 1.03 Sup: -0.49 Ant: 1.20 Avr.Accur.: 1.65 mm (3) Left: 0.83 Sup: -0.78 Ant: 0.12 Avr.Accur.: 1.14 mm (4) Left: 1.03 Sup: -0.66 Ant: 0.54 Avr.Accur.: 1.34 mm (5) Left: 0.75 Sup: -0.56 Ant: -0.39 Avr.Accur.: 1.02 mm
Left: 0.41 Sup: -1.08 Ant: 2.03 Avr.Accur.: 2.33 mm
Conclusions: The system has been calibrated to work optimally with the old mask holder attached to the CT scan, which is our typical clinical situation (1). From all the data reported above we can notice that any variation of the initial setup of the phantom in the CT scan degrades the accuracy of the system; the bigger is the setup difference the bigger is the unsteadiness introduced. A possible explanation of these inaccuracies could be that, between CT scan and treatment, there is a different attenuation and scattering of the diagnostic X-rays. The conclusion of our study is that, even if CyberKnife is a very precise equipment, any variation of the initial setup in the CT scan can introduce an instability in the overall accuracy; further investigation should be performed using a phantom with more skeletal affinity with a real human skull.

1129 poster

CHARACTERISTICS OF RADIOCHROMIC DOSIMETRY FILMS AND EVALUATION OF THEIR USE IN VERIFICATION OF PLANNED DOSE DISTRIUTION IN IMRT

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2 - University of Vienna Medical School, *Division of Medical Radiation Physics, Department of Radiotherapy and Radiobiolo, Vienna, Austria,*
3 - Maria Sklodowska-Curie Memorial Cancer Center and Institute of Oncology, *Department of Medical Physics, Gliwice, Poland,*
4 - Warsaw University of Technology, *Institute of Precision and Biomedical Engineering, Warsaw, Poland*

Purpose/Objectif: The purposes of the work are measurements of sensitometric curves for new radiochromic films in order to asses its potential use in IMRT verification. A method of IMRT verification using films was being developed. The questions on which the authors are going to answer are: Are the sensitometric curves energy dependent? What is the influence of dose rate and processing delay on the signal level recorded on the films? Is the visual density dependent on orientation of the films during digitization? What are advantages of the use of radiochromic films in IMRT verification over the use of radiographic films?
Materials/Methods: GafChromic EBT and RTQA films by ISP International Specialty Products were irradiated with several photon beams 90kV-1.2MV gerated by an X-ray tube, by radioactive isotope sources Am-241, Cs-137 and Co-60, as well as with photon beams in the range 4-25MV from medical linear accelerators . The films were digitized using Vidar and Microtek scanners. In-house developed software was used for IMRT plan verification. Optical densities (OD) were probed using a densitometer.
Results: The measured sensitometric curves differ less than 5% for the whole range of energy. The visual densities of the exposed films were the same for the dose delivered in one fraction and in several fractions. Post-exposure visual density growth up to 20% was observed during few hours after irradiation. The digitization orientation dependence on the readout of the visual density from the films was observed. Sensitometric curves of both radiochromic films are not dose rate dependent.
Conclusions: Radiochromic films seem to be very useful tool for IMRT verification. Digitizing of the films has to be performed at least 3 hours after exposition. The advantages of the use of radiochromic films are related to uniform sensitivity on radiation from different bands and its independence on the dose rate and fractionation. The disadvantages are scanning orientation dependence of EBT type films and required delay before scanning for both types of GafChromic films.

1130 poster

CURRENT STATUS AND ACHIEVEMENT OF KOREAN PATTERNS OF CARE STUDY (PCS) FOR PROCESS OF CLINICAL RADIOTHERAPY BASED ON A WEB-BASED SYSTEM

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8 - Chunnam National University, *Radiation Oncology, Kwangju, Korea*
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10 - Keimyung University, *Radiation Oncology, Daegue, Korea*
11 - Korea University, *Statistics, Seoul, Korea*

Purpose/Objectif: We are to report recent achievements of the 1st Korean Patterns of Care Study (PCS) in radiation oncology using the first web-based system developed in the field of clinical QA.
Materials/Methods: A web-based(www.pcs.re.kr) PCS system and program was developed in mid-2003 for manpower and hardware structures, and for 8 cancer types commonly teated with radiotherapy in Korea. Participants put case data after random sampling into the system using his own PC. We determined the he number of cases to be accrued in each tumors among the patients who started radiotherapy from 1998 to 1999 using power allocation method based on the number of new radiotherapy cases of each tumor.
Results: ore than 70% of the eligible radiotherapy departments participated. The number of randomly sampled and accrued standard cases were 2,996 in total and 623 for uterine cervix ca., 399 for lung ca., 392 for breast(Conservative surgery), 382 for rectal ca., 379 for brain metastases, 343 for breast(mastectomy), 244 for esophageal ca., and 234 for laryngeal ca., . Participating institutes were categorized as A, B, C by the number of new radiotherapy patients as follows; <400, 400-899, >=900. The key simulation images in jpg format were also obtained. The some patterns of radiotherapy process including work-ups, dose, field size, shielding techniques, or QA methods significantly differed by institutional categories in cancers of uterine cervix, esophagus, brain metastases, breast, and rectum while was not definite in laryngeal cancers. There are some clue that end results might be associated with process patterns.
Conclusions: We can obtain overall schemes of radiotherapy practices pattern in detail and variables. Our web-based system was quite effective and optimal for PCS in environment of limited resources like us. We are going to analyze whether differences in process could result in survival or toxicity outcomes or not.

This study was supported by a Long-term Nuclear Research Grant (2006), Korea Science and Engineering Foundation (KOSEF)

1131 poster

DEVELOPMENT OF A METHOD FOR ELECTRON ENERGY CONSTANCY VERIFICATION

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Purpose/Objectif: A novel QA method was developed to ensure electron energy constancy on a monthly basis. This method was compared to other existing methods and all were referenced to measurements made with a scanning water phantom. The aim was to provide a method which meets IPEM recommendations. Electron energies in the range 4-15 MeV were measured.
Materials/Methods: A Delrin wedge was constructed as illustrated below and its dimensions optimised for use with 4-15 MeV electrons. The wedge was driven by an electric motor at variable rotation speeds. A diode placed as shown produced a sinusoidal signal when connected to a virtual oscilloscope. The full width at half maximum (FWHM) of the diode signal can be used as a measure of a shift in electron beam energy. Rotation speed, dose rate, sampling time and sampling interval were optimised to provide a reproducible signal in the shortest time. This approach was compared with existing published methods for reproducibility, easy of use and sensitivity. Sensitivity was determined by placing 2mm of polystyrene in the beam close to the exit window, which produced a shift of 2mm in the depth dose curve.
The methods for comparison included:
1. A double wedge where a change in the width of the profile at half the maximum value indicates a change in energy.
2. 15% and 70% ionisation values taken along the decreasing slope of the depth dose curve.
3. A Cerrobend wedge placed upstream of a 10cm volume CT ionisation chamber.
4. Thin discs of steel placed above an ionisation chamber to reduce the signal by 50%.
A scanning water tank with a Markus chamber provided the reference depth dose curves for all the electron energies.
Results: The water tank readings varied by between 2% and 4% from the commissioning values over a period exceeding six months and the reading with the 2mm polystyrene in place varied by no more than 2.5% from the average reading. The FWHM produced by the rotating wedge varied by between 0.4% and 0.8% over the same period. The 2mm polystyrene in the beam varied the FWHM by between 1.5% for 15 MeV and 10.5% for 4 MeV with all other energies showing a variation between these two values. Reproducibility and sensitivity of the rotating wedge echnique met or exceeded techniques 1-4 listed above over the same period.
Conclusions: An accurate and reproducible technique was developed to measure electron energies. Results have shown it to be as good if not better than other techniques. There is also the advantage of having only one setup and requires only one reading for each energy which makes it a fast method.

1132 poster

DEVELOPMENT OF A SILICON SEGMENTED DETECTOR FOR 2D DOSE MEASUREMENTS

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Purpose/Objectif: The work described in this article was performed in the framework of the European Integrated project MAESTRO which is granted by the European Commission (Methods and Advanced Equipment for Simulation and Treatment in Radio-Oncology, no. LSHC-CT-2004-503564).
Due to the features of the modern treatment techniques, namely IMRT and protontherapy, where high spatial dose gradient are often present, the detectors to be employed for 2D dose verifications have to meet very stringent requirements, in particular they have to show high spatial resolution. The goal of this paper is to develop a dosimetric system adequate for 2D pre-treatment dose verifications.
Materials/Methods: With this aim, we designed a modular dosimetric system, based on a monolitic silicon segmented sensor. The first 6.29 x 6.29 cm^2 module has been manufactured and assembled with the read-out electronic. Each pixel element is 2 x 2 mm^2 and the distance center-to center is 3 mm. In the final configuration nine modules will be assembled together in order to cover an area close to 20 cm x 20 cm^2. A preliminary dosimetric characterization has been performed, using a conventional 6 MV X-ray beam from Linac. The studied parameters were repeatibility of a same pixel, reproducibility between the different matrix elements, response linearity versus absorbed dose and dose rate dependence.
Results: The obtained results are promising because almost all the channels have responses within the project specifications (repeatibility < 0.5%, reproducibility < 1%, deviation from linearity < 1%, dose rate dependence < 1%). Moreover, previous measurements on single diode of the same material have showed a good radiation hardness.
Conclusions: A full dosimetric characterization will be performed in order to establish the suitability of the device for IMRT treatments. A patent is pending on this device.

1133 poster

DIGITAL IMAGE-GUIDED WINSTON-LUTZ TEST FOR A MICROMULTILEAF-BASED RADIOSURGERY SYSTEM

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Purpose/Objectif: To assess the feasibility of the package consisting of a commercial Electronic Portal Image Device (EPID) and in-house developed image analysis software, as an automatic tool to verify the alignment of the radiation isocenter prior the delivery of radiosurgery treatments.
Materials/Methods: A Varian Clinac 2100C/D linac equipped with a Mark II EPID (Varian Inc, Palo Alto, CA) and modified by an attachable micromultileaf collimator (m3, BrainLAB AG, Heimstetten,) was used. A 5mm diameter radiopaque ball (WL Phantom Pointer, BrainLAB) was centered in the "isocenter" defined by the room lasers and portal test shots for selected gantry, collimator and couch angles combinations (Winston-Lutz test) were taken with a m3 collimated

beam (30x30mm, 6MV). The software Rodeo1.1 (written in Fortran) detects the centers of the radiation field and the ball shadow in every 2D image taken. From several portal images the 3D position of the radiation isocenter can be computed and compared with the isocenter defined by the room lasers. The distance between them is a measure of the alignment error. The accuracy of the procedure described was investigated by applying known shifts to the ball and recording the displacements detected by the mentioned software. Twenty gantry isocenter alignment verifications (270, 0, 90 and 180° angles) were performed using EPID and film based methods. The Bland-Altman statistic approach was used to assess the agreement between them. Differences intra and inter-observer was inspectioned for the film case.

Results: The verification system EPID-Rodeo 1.1 shows an accuracy within 0.2mm. Analysis performed on the difference of paired 80 EPID and film radiation field center-ball shadow center distances shows a mean difference of 0.01mm with 95% confidence interval (C.I.) of -0.03mm to 0.04mm. According Bland-Altman analysis, limits of agreement EPID-film methods of -0.3 (95% C.I. -0.4, -0.3) mm y 0.3 (95% C.I. 0.3, 0.4) mm were registered. Inter-observer differences up to 0.3mm were found when we compared the results of several film test registered by three operators. A perfect repeatability was registered with the EPID based method against a value of 0.2mm found for the technique with film.

Conclusions: This study shows the feasibility of using EPID-Rodeo 1.1 in evaluating the isocenter alignment replacing the old film-based procedure with a saving of time and not observer-dependence.

1134 poster

DOSIMETRIC EVALUATION OF A 2D IONISATION CHAMBER ARRAY FOR APPLICATION FOR IMRT QA

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Purpose/Objectif: Two-dimensional ionisation chamber arrays are designed for measurements for external beam therapy. In comparison with other devices like radiographic or radiochromic films, single ionisation chambers and water phantoms the array offers some advantages. They are simple to handle, nearly tissue equivalent, enable a direct reading whereas films must be developed (radiographic) and digitised. Furthermore the array allows a very fast check up of several field parameters with only a few measurements. The purpose of this paper is to evaluate the basic parameters of a new commercial ionisation chamber array (MatriXX, Scanditronix Wellhofer) to use it for quality assurance and for IMRT dose verifications.

Materials/Methods: To verify the ionisation chamber array as an accurate measuring device for the external beam radiotherapy it is necessary to determine all relevant features of the MatriXX. Due to the poor resolution relative to film it is important to analyse the response of a single chamber of the detector to compare correctly IMRT treatment plans and measured dose distributions. The response function was measured by shifting a slit. Also the stability of the internal calibration was checked. Besides the response function dose and energy dependence, initial phase, stability and spatial resolution were investigated. All measurements were performed with 6 and 15 MV photons and the results are compared with film (GafChromic EBT) and water-phantom measurements.

Results: The output of the detector is linear to the dose and independent from the energy. During the initial phase the detector needs a preirradiation of approx. 10 Gy to reach a stable signal. The response functions of a single ionization chamber of the array measured in cross-plane and in diagonal direction show different gradients because of a larger diagonal distance between the chambers and therefore additional scatter material. This characteristic was taken into account for the verification of IMRT fields. The results of the measurements of wedge fields are in good agreement with the results in the water phantom.

Conclusions: The result of our study shows that the MatriXX is qualified as an accurate device for the verification of dose distributions and the ability to facilitate and fasten the measurement procedures in radiotherapy (e.g. verification of IMRT fields).

1135 poster

FACTORY-CALIBRATED MOSFET FOR IN VIVO DOSIMETRY: ?READY TO USE??

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Purpose/Objectif: Several MOSFET detectors have been designed for dosimetry purposes. When used for entrance in vivo dosimetry in high energy x-ray beams they require a build-up cap and to be calibrated to measure entrance dose when placed on the patient's skin. Sicel Technologies calibrate their wireless single-use MOSFET detectors at factory to give entrance dose. These detectors present the advantage of not requiring calibration by the user. Contrary to other MOSFET manufacturers, Sicel has a MOSFET design that incorporates a build-up cap (OneDosePlus). This work aimed to characterise this detector for entrance in vivo dose measurements in 6 and 18 MV x-rays. Measurements were performed to determine the level of accuracy for entrance dose measurements using the manufacturer's pre-set calibration and correction factors.

Materials/Methods: As OneDosePlus detectors can only be used once, a set of 80 MOSFET of the same fabrication batch was used for this study. The intrinsic precision, in this case the homogeneity of the batch, was determined for three dose levels. Linearity of the response with dose was checked. Entrance dose in standard reference conditions for 6 and 18 MV was measured with these pre-calibrated detectors and compared with the dose measured with an ionization chamber at the depth of dose maximum. Correction factors (CF) for field size, SSD, wedge and angle were measured for an 18 MV x-ray beam. The sensitivity variation with temperature (SVWT) was measured. Uncertainty of the entrance dose measurements was estimated.

Results: The intrinsic precision (IP) was about 4% (1SD) and independent of dose level. When used with the manufacturer calibration factors these detectors underestimated the entrance dose in standard reference conditions in about 8% for both energies. Field size, SSD and wedge CF measured agreed with those used by the manufacturer within the uncertainty (2-3%). The detectors presented a strong angular dependence;10% under-response at 45°. No SVWT was found. The uncertainty of entrance dose measurements with OneDosePlus was 7% (1SD).

Conclusions: In conclusion, OneDosePlus MOSFET detectors cannot be used on patients without verification of their pre-set calibration factors. As differences on responses of MOSFET of the same batch can be as high as 8% (2SD IP), more than one MOSFET should be used per patient's measurement point, increasing the perturbation of the irradiation field. Tolerance levels for entrance in vivo measurements should be set to 14% (2SD) when using these detectors.

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1136 poster

IMPLEMENTATION OF A PHOTOGRAPHIC DOSIMETRY SYSTEM WITH EBT GAFCHROMIC AND COMPARISON WITH CLASSICAL KODAK EDR2 IN CLINICAL ROUTINE

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Purpose/Objectif: Film dosimetry is a perfect tool for 2D dose analysis distribution (relative and absolute). This work describes the implementation of a photographic dosimetry system with EBT Gafchromic and compares it with classical KODAK EDR2 in clinical routine.

Materials/Methods: This work presents two different moments: 1- To describe the implementation of a film dosimetry system in the Clínica de Radioterapia e Medicina Nuclear (CRMN) in Faro - , using EBT films together with vulgar scanner and analysis software (free wear). 2- To compare the response of EBT and EDR2 systems for clinical irradiation. Both types of films had been irradiated at "treatment" conditions (for example, placed between plates of a solid water phantom) with beams originated on Varian Clinac 2100C/D accelerator. We used two photon energies (6 and 15 MV), for the fields 6x6, 10x10 and 15x15, in the depths of Dmáx. (14 and 28mm, respectively) and 100mm. After that, we irradiated the films in two different directions (parallel and perpendicular to the beam), allowing us to compare the profiles (symmetry and homogeneity) and percentage depth doses (quality index). For the analysis of the EDR2 films we used a Vidar scanner and the RIT133 software.

Results: The results are very interesting, because they show what are the main advantages and limits of the EBT Gafchromic comparing to the classic EDR2 fims.

1137 poster

IMPLEMENTATION OF AN INDEPENDENT CALCULATION METHOD FOR VERIFICATION OF MONITOR UNITS AND DOSE DISTRIBUTIONS IN IMRT

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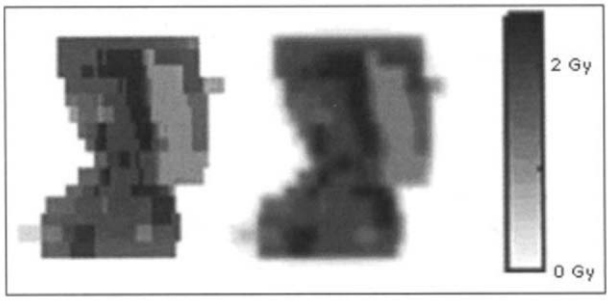
Purpose/Objectif: The use of intensity modulated photon beams in the delivery of highly conformal radiation treatments are growing rapidly. Because of the dynamic nature of the intensity modulated beams new techniques for treatment verification is needed. An essential part of the verification is a secondary calculation of monitor units (MU), independent from the commercial inverse treatment planning system (TPS). Because of the complexity of the IMRT plans, this calculation cannot be performed manually, as in the case of conventional plans. There is also a need to verify 2- or 3-dimensional dose distributions from the TPS. Many institutions perform time consuming and costly measurements because of the lack of effective tools. This study aims to implement and evaluate a calculation engine for independent monitor unit and 2-dimensional dose calculations.

Materials/Methods: A 2D-calculation model has been developed and implemented into a PC application (Radiation Verification Program/RVP). The dose distribution for an IMRT treatment using fixed gantry angles is considered to be a summation of the doses delivered by a number of segments. Each segment is treated as an irregular field and calculated separately. The model is based on the assumption that the energy fluence is homogenous over the field and is a further development of a method previously reported (Knöös et al., RTO, p201, 2001). The method is completely analytical and based on a few measurable physical parameters. The magnitude of the error introduced by the homogeneous-field assumption was investigated by off-axis output measurements for square fields. The measurements were undertaken in water at a depth of 10 cm and a SSD of 90 cm using the LDA-99 diode array (Scanditronix-Wellhöfer). Further, a 2D IMRT dose distribution was calculated by the RVP (left in figure below) and compared with a 2D dose distribution calculated in the TPS (right). The dose distribution from the TPS was previously verified by measurements.

Results: The error introduced by the homogeneous-field assumption was found to be within 2.5% for square field sizes over 4x4 cm^2 and 10 cm off-axis distances. The 2D comparison with the TPS showed an underestimation of the dose and the largest differences were found in the penumbra region of the MLC.

Conclusions: The limitations of the proposed model, resulting in an under-estimation of the calculated dose can potentially be overcome by taking the MLC transmission into account. Replacing the time consuming and costly measurements with an independent calculation could substantially reduce the workload before treating the patient.



1138 poster

IMPLEMENTATION OF INTENSITY-MODULATED-RADIO-THERAPY: MONITORING OF DAILY REPRODUCIBILITY WITH ELECTRONIC PORTAL IMAGING DEVICE TO PTV MARGIN DEFINITION, INTO A QUALITY ASSURANCE PROGRAM

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Purpose/Objectif: Recent imaging studies have demonstrated that there can be significant changes in anatomy from day to day and over the course of radiotherapy as a result of daily positioning uncertainties and physiologic and clinical factors. Positional reproducibility became a crucial aspect in IMRT treatments. The purpose of this analysis is to measure the set-up variations of prostate cancer patients treated with IMRT in our Department.

Materials/Methods: We selected 10 prostate cancer patients fixed in supine position with a set of immobilization devices for external-beam IMRT (Knee-and-Foot Lok™ and Dual Leg Positioner; Medtec, Sinmed). Before each treatment orthogonal localization images from the antero-posterior and from the lateral direction were acquired. Portal images of both were analyzed daily from a physician; corrections of the position of the isocenter were made when its position differed > 5mm from the reference DRR image, according to the Quality Assurance Program adopted in our Center. To minimize the organ motion all patients have been treated with a known filling of the bladder and their rectum emptied.

Results: The set-up fields were calculated in the treatment planning to take in account the overdose administered daily. For each patient 82 electronical portal images have been acquired. In the antero-posterior projection have been measured the shifts in the cranio-caudal

(CC) direction and medial-lateral (ML) direction, whereas in the lateral projection has been measured the shift in the antero-posterior (AP) direction. The median shift in CC direction was 4 mm (0-16), in the ML direction was 2mm (0-18) and in the AP direction was 2 mm (0-8). The limit of 5mm has been exceeded in 5 patients in CC direction, in 5 patients in ML direction and in 6 patients in AP direction. In all patients except two the shifts were less than 10mm. The majority of shifts were recorded in the first week of treatment. The maximum shift in CC direction was recorded in a short patient who didn't fit the immobilization system, whereas the maximum ML shift was recorded in an obese patient.
Conclusions: The immobilization obtained with the system used in our Department seems to be reproducible, even if in patients with a particular anatomical conformation more individualized repositioning system must be adopted. To quantify the set-up margin to be used in our Department we need a higher number of patients. In the next future we are implementing a weekly CT scan to monitor the organ motion, to identify the exact margin from CTV to PTV.

1139 poster

IN VIVO DOSIMETRY DURING TOTAL BODY IRRADIATION : PATIENTDOSE AND TREATMENT REPRODUCIBILITY.

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Purpose/Objectif: Total body irradiation (TBI) for ZNA (Ziekenhuis Netwerk Antwerpen) was clinically started in October 2004. Until today 17 patients are treated with a schedule of 6 times 2 Gy in 72 hours using 18MV photons. Transmission blocks are used to reduce the lung dose to 9 Gy. Quality control of the treatment is done with in vivo dosimetry (IVD). A total of 836 measurements were performed in 84 treatments set-ups.
Materials/Methods: Two EDP20 diodes (Scanditronix) are calibrated for the source skin distance (4meter) and field size (40cmx40cm, col45°) used in TBI. During the TBI diodes are positioned on the central axis (cax) of the treatment field and under the lung block. In this way the entrance dose on the cax and the lung is controlled. The measurements are preformed for the anterior and posterior field separately. After calibration of the TLD's (Thermo 1/8" sq. chips; Harshaw 5500) in treatment conditions the detectors are positioned on the same spots as the diodes; extra TLD's are placed on the head, sternum and leg. The TLD's are packed in a plastic bag. Home made water equivalent build-up caps of 10 mm thickness are used for a selected number of patients.
Results: From in vivo measurements, most stable results are found with diodes: the mean entrance dose measured is 1.57 Gy (1SD=3.5%, N=98); mean entrance lung dose is 1.18 Gy (1SD=4.1%, N=98). The mean ratio of the lung dose and the cax dose with diodes is 0.73 (1SD=5.1%, N=123), for TLD without build-up 0.72 (1SD=6.4%, N=72) and TLD with 1 cm build-up 0.73 (1SD=6.5%, N=19). For TLD measurements without build-up an overestimation of the entrance lung dose is seen because of the scatter of the lung blocks, a correction factor is defined to take this into account. Reproducibility of the total treatment is expressed by the %SD of the day to day result for measurements on the same spot. In 10 cases (7.3%) the %SD is larger than 10%. In 8 out of 17 patients no large variations (>10%) were found. There is no defined measuring place or patient were these large figures are found, although 60% of the large variations were found on the extremities (head and leg). The reproducibility for the TBI set up in our hospital is expressed in the mean %SD : 4.5% (1SD=3.6%) for a total of 57 treatment set-up and 588 TLD measurements. Measurements are also performed in and on the Alderson phantom in TBI treatment position. TLD's in the phantom result in a ratio lung dose and midline central axis dose of 0.73. The entrance lung dose with TLD (with build-up) and diodes are respectively 73% and 74% of the prescribed dose.
Conclusions: In vivo dosimetry in total body irradiation demands a special calibration set-up for as well diodes as TLD, also special corrections for the scatter are needed depending on the build-up used for TLD's. Reproducibility of the treatment and patient dose can controlled by doing IVD during TBI.

1140 poster

IN VIVO DOSIMETRY IN BRACHYTHERAPY OF PROSTATE CANCER

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Purpose/Objectif: The usefulness of the thermoluminesce detectors (TLD) for vivo dosimetry in prostate cancer treatment by HDR brachytherapy was investigated. Treatment plans are based on the 3D data from trans-rectal ultrasound examination (TRUS) of prostate, with 3D planning system SWIFT from Nucletron. The plan consists of two parts: virtual plan providing a proposition of the needles distribution for the moving iridium source, and the live plan based on the second set of the 3D images after insertion of the needles. In order to verify the calculated dose distribution the dose inside the urethra was measured. The prescribe dose for the prostate ranged 10 - 15 Gy.
Materials/Methods: For each measurements the seventeen TLD solid detectors were placed in the bronchus applicator, separated at its tip by 5mm plastic spacers. The detectors are made of sintered hard alloy Lithium fluorine with impurity of magnesium and titanium (Lif: Mg:Ti) in a shape of 3mm length cylinder with diameter of 1mm. The Lif:Mg:Ti is very common and convenient dosimetry material having high sensivity, low background and the density comparable to tissue density. Each detector had an individual calibration factor, differing within the range of over 10%. The length of such detector linear array was 136 mm. The detectors were then inserted into the patient urethra catheters (4.7mm or 5.3mm in diameter) before irradiation.. During the first hour after irradiation the dose absorbed by the TLD were read out in a specially design reader. The TLD rods after irradiation and read-out were placed in special plastic holder with numbered position and calibration factor for individual detectors.
Results: The obtained read-out doses were up to 15% percents lower than calculated by the TPS. It was due to the longer distance of the TLD detectors to the source positions (by 2 to 2.5 mm) than that of the urethra wall position used for calculations.In few cases of a strong calcifications of the prostate, difficulties occurred in accurate establishing the position of the catheter of the TRUS image. This may also be a reason of differences between the calculated and measured doses.
Conclusions: In vivo measurement of the dose received by the urethra using the TLD dosimeters during the HDR brachytherapy treatment of the patients with the prostate cancer is a very useful tool in quality control program of treatment procedure.

1141 poster

KERNEL BASED MODELING OF RADIATION DETECTOR RESPONSE VARIATION IN THERAPEUTIC PHOTON FIELD

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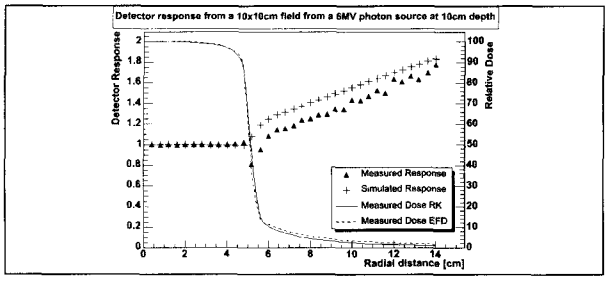
Purpose/Objectif: Modern radiotherapy tends to utilize more of the

available degrees of freedom provided by radiation machines, raising the need for dosimetry to provide reliable measurements for all situations where spectral properties and other beam characteristics vary, and hence, also the detector response. Through a novel kernel based method, spectral dependent detector response can be modeled, and by comparing with experimentally determined response the applicability of these corrections can be assessed.

Materials/Methods: Detector responses vary with beam quality, field shape and position in the irradiated body. Modeling the particle fluence in the irradiated materials enables determination of the detector response. The Monte Carlo package Penelope is used to calculate fluence pencil kernels to fully describe the particle fluence from point monodirectional beams. A published 6MV spectrum is used as input to the simulation. The fluence kernels are scored in 1mm thick cylindrical voxels. The kernels are convolved for incident fluence distributions for different fields. Assuming that the incident particle fluence on a small cavity volume is not significantly altered by the cavity, detector responses for arbitrary positions are calculated using cavity theory. Measurements for validation were performed with an unshielded diode (Scanditronix-Wellhöfer EFD-3G) as test detector and an air ionization chamber (Scanditronix-Wellhöfer RK-chamber) as reference.

Results: Simulated responses agree well with measurements, at different radial distances as well as at different depths. Inside the field the response is rather constant, but increases with radial distance outside the field as the fluence spectrum shifts towards lower energies. Simulations agree with measured data within 1% inside the field, and follow the trend in larger detector response outside the field. Simulated detector response is slightly higher than the measured response outside the field, mainly due to scattering from the flattening filter which is not included in the simulation. Discrepancies in the penumbra region rise from the limited spatial resolution of the reference detector in the measurement.

Conclusions: Kernel based modeling of spectral dependent detector response for arbitrary positions in a, by photons, irradiated body has been developed and validated. The method is fast enough for online response calculation. To improve agreement with measurements, the characterization of the incident beam can be elaborated.



1142 poster

NEW IMAGING DEVICES FOR PRE-TREATMENT PLAN VERIFICATION IN IMRT

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Purpose/Objectif: The objective of a high conformal intensity modulated radiation therapy (IMRT) is to deliver closely defined dose to the planning target volume. However, verification of this method is difficult and time consuming. Till now plan verification procedure required the combination of several tools and different methods to provide an in-depth quality assurance (QA). The promising and direct method can be the use of a new type of flat panel detectors. The aim of the study was to demonstrate the dosimetric capabilities and the usefulness of new imaging tools: an amorphous silicon electronic portal imaging device (aSI EPID) with Transit Dosimetry (TD) module (Varian) in Treatment Planning System (TCP) and Beam Image System (BIS) with OmniPro IMRT software (Scanditronix/Wellhuefer) for IMRT plans verification.

Materials/Methods: A two photon beam 6 and 20 MV linear accelerator Clinac 23EX (Varian) with the flat panel aSI EPID and BIS were employed. 10 treatment plans (60 beams) were evaluated. The dose distribution was detected by both devices separately. The real intensity maps acquired during treatment delivery were compared with an actual intensity map calculated and generated in Eclipse-Heliose TPS. We examined the correlation between readouts from aSI EPID and BIS. Plan verification was carried out on the base of profile measurements and gamma calculation in Eclipse and OmniPro IMRT independently. The similarity of the signal readouts were assessed.

Results: By means of the aSi EPID and BIS the electronic signal can be converted into a dose matrix and acquired intensity map can be compared to the calculated one. The gamma evaluation and profile analysis show good correlation of the calculated and measured intensity maps obtained in both ways. In the evaluated IMRT plans correspondence between calculated and both acquired dose matrix was proven, although it can be lower where the dose gradient is high.

Conclusions: Achieved results showed that the modern imaging devices posses many advantages. The reproducibility and the capability of the method are promising. It was demonstrated that the application of the flat-panel imagers can be applied clinically for pre-treatment QA.

1143 poster

PROSPECTIVE PATIENT RELATED CLINICAL QUALITY ASSURANCE (QA) INDICATORS TO DETECT TREATMENT ERRORS AND POTENTIAL OVERDOSE IN RADIOTHERAPY

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Purpose/Objectif: Despite the execution of modern automated error-minimization methods and QA procedures, serious human systematic mistakes (0,3%-2,5%) remain a source of error in radiotherapy. Dose in excess of 5% leading to increase tissue reactions may not be detected clinically soon enough to prevent significant damage. In order to discrimate potential overdose we have developed two clinical indicators based on the frequency and seriousness of accumulated or single events during radiotherapy treatment. The aim of the study was to assess if these clinical indicators were useful and advisabless in the day to day workload.

Materials/Methods: Two type of indicators were defined: 1-Patients with >7day gap(7DG) due to toxicity during treatment, and 2- Medical Prescription Rest Rate (MPRR) (defined as the number of lost sessions for medical reasons divided by the number of delivered treatments) per month and refered to each treatment unit. In order to define the MPRR cut-off value, we retrospectively analysed the chart data of all patients treated in our department during the 2002. We considered this value plus 2 standart deviation (2SD) as the cut-off value. When MPRR exceeded 7% or there was any 7DG, a clinical and dosimetric QA procedure was activated to detect systematic error related to each treatment unit (MPRR) or individual major mistakes (7DG). From january 2004 to december 2005 we have prospectively registered these indicators.

Results: During the studied period 8632 patients were treated in three units: one cobalt, one 6-18 Mv linac (linac1), one 6Mv linac (linac2). The 7DG indicator was activated in 124 patients (1,43 %). The average magnitude of MPRR (%) over the treatment course was 4,5 %(SD 2,6); 3,3% (SD 1,9); 3,5% (SD 1,8) for cobalt, linac 1 and linac 2 respectively. The MPRR monthly indicator was activated 6 times (11%,10% 9% three times and 8%,), twice in cobalt, three times in linac1 and one in linac2 respectively . The case to case QA review procedure showed that 6 patients loosing each one over 25 ses-

sions. After the individual review no overdose was stated.
Conclusions: Despite that the MPRR or >7d gap due to toxicity indicators did not show any overdose, prospective patient related clinical QA procedures are very recommended to detec systematic errors that could escape from established QA process.

1144 poster

QUALITY ASSURANCE (QA) IN A UK RANDOMISED CONTROLLED TRIAL (RCT) OF RADIOTHERAPY IN PATIENTS WITH STAGE I-II NON-SMALL CELL LUNG CANCER (NSCLC) UNFIT FOR SURGERY

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Aims:
To assess quality of radiotherapy planning and treatment delivery in a RCT in patients with medically inoperable stage I-II NSCLC.
Background: GRiN is an ongoing NCRN-badged RCT investigating the addition of weekly low dose gemcitabine to radical radiotherapy in patients with medically inoperable stage I-II NSCLC. This abstract describes the QA procedures of that study, designed and set up before the creation of a national QA service for radiotherapy trials in the .
Methods: All material was reviewed by 3 radiation oncologists (the Chief Investigator and 2 members of the Trial Management Group) and the Trial Coordinator. Participating centres were asked to submit for central review of their first and every fifth subsequent participant a paper record of planning data including contouring, the record of treatment delivery (prescription sheet) and copies of treatment verification, using either films or electronic portal imaging,. These were matched against pre-set criteria of minor and major protocol violations, comprising GTV outlining, dose distribution, treatment time, spinal cord dose, lung V_{20}, length of oesophagus irradiated and set-up error.
Results: To date 111 participants have been randomised in the trial from 22 centres. The planning and treatment records of 34 participants have been reviewed. 8 (24%) met all 7 criteria set, 8 (24%) had incomplete data sets (6 verification, 5 treatment time, 3 contouring), 9 (26%) minor (7 dose distribution ± 7-10%, 2 set-up errors 5-10 mm) and 9 (26%) major violations (8 dose distribution > 10% and 1 contouring > 5mm error). Among the 9 with major violations, 1 also had a minor set-up error and a further 4 provided incomplete verification data.
Conclusions: Conclusion Central review of planning and verification indicated that a minority of treatments met all the criteria set in the trial protocol. Set-up verification data was frequently unavailable. This data will be fed back to participating centres and QA repeated to assess whether this will improve future treatment quality.

1145 poster

QUALITY ASSURANCE AND QUALITY CONTROL IN RADIOTHERAPY: PRACTICAL ASPECTS OF THE SYSTEM IMPLEMENTATION AT THE DEPARTMENTAL LEVEL

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Purpose/Objectif: Procedures, codes of practice and guidance are available on the technical aspects of radiotherapy treatments, maintenance of which is achieved by quality control checks within a quality assurance approach to radiotherapy. Our goal is to report the development, structure, and implementation of QA and QC system in a radiotherapy department of a comprehensive cancer center.
Materials/Methods: This paper is discussing the underlying principles of quality management covering service provision as well as technical radiotherapy treatment delivery and by providing some guidance based on experience in the practical implementation of quality management through three stages of development: (a) QA programme including checks on essential parts of the technical treatment delivery chain, (b) formal documented certified QA system focusing on technical treatment delivery, (c) comprehensive quality management system covering all parts of radiotherapy treatment prescription and delivery.
Results: In the first 2 years of the application of the QA, QC system we paid great attention on radiotherapy equipment. In the third year radiotherapy treatment plans were audited by a real-time peer-review process. A total of 2400 treatment plans were audited. Of these, 5% were not approved by the audit due to some errors in planning. The majority of the non approved plans (>80%) were modified before to initiating treatment; the audit provided important clinical feedback about individual patient care in these instances.
Conclusions: The results after 3 years of experience in our department highlight the principle that with planning, some resources and commitment, a comprehensive quality of service management system is achievable in radiotherapy in a country with limited resources.

1146 poster

QUALITY CONTROL OF LINEAR ACCELERATORS: AN OBJECTIVE APPROACH TO STANDARDS OF PERFORMANCE

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Purpose/Objectif: To explore the application of an outcome surrogate -the Equivalent Uniform Dose (EUD)- to the objective setting of standards for linear accelerator performance.
Materials/Methods: Volumetric CT data sets for four prostate patients were, following Ethics Review Board approval, available for this study. Each data set included contours of the prostate, bladder and rectum. A series of plans for each data set was generated using a conformal 4 field geometry with MLC defined apertures. The first plan in each series used reference beams, fields and geometries. Subsequent plans in each series were generated by altering, one at a time, parameters of the modeled beams so as to simulate performance deviations which might be encountered during routine linac quality control. These performance parameters were: output, flatness, field size, laser positions (3) and gantry and collimator angle. The ranges over which these performance parameters were varied were sufficient to encompass the tolerances and action levels specified in the Canadian Association of Provincial Cancer Agencies (CAPCA) standards documents (www.medphys.ca). The EUD's of the target and organs at risk were calculated as a function of deviation of these key parameters from their reference values while keeping the monitor units per beam constant.
Results: The CAPCA standards are broadly consistent with those promulgated in other jurisdictions. At the action levels defined in the CAPCA standards, the EUD's of the three structures studied were equally sensitive to beam output and flatness; a 2% change in EUD for a 2% change in either output or flatness. The CTV was relatively insensitive to field size compared to the bladder and rectum (less than 1% compared to more than 3% for 2mm on the field edge). These latter two structures also exhibited sensitivity to laser (isocentre) accuracy but the sensitivity depended on direction. There was almost no sensitivity (<0.3%) of any EUD on the collimator or gantry

angle within CAPCA and commonly accepted tolerances.
Conclusions: Within the context of conformal 4-field prostate plans, commonly accepted standards on linear accelerator performance are inconsistent when viewed from the perspective of their impact on the Equivalent Uniform Dose as an outcome surrogate. Confirmation of our observations for other anatomical sites could lead to the establishment of a more consistent set of standards for linear accelerator quality control.

1147 poster

TLD AUDITS IN NON-REFERENCE CONDITIONS IN RADIOTHERAPY CENTRES IN POLAND

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Purpose/Objectif: The Secondary Standard Dosimetry Laboratory (SSDL) of the Medical Physics Department of the Centre of Oncology in Warsaw has become a member of the IAEA/WHO international network of such laboratories in 1988 and is periodically audited by the IAEA. The SSDL has been carrying-out the external postal TLD audits in teletherapy centres since 1991. Regular yearly audit runs have been carried out in reference conditions. A significant numbers of deviations in non-reference situations, as used clinically on patients, have been observed in international audit networks operating world-wide. The aim of the study is to develop a general strategy for the TLD-based quality audit program for radiation dosimetry in non-reference conditions at the national level. Regular yearly audit runs have been extended to non-reference conditions since 2003. The results of subsequent runs are presented.
Materials/Methods: TLD system consists of PCL3 TLD automatic reader (FIMEL) and Niewiadomski &Co. (LiF:Mg,Ti) powder. TLD runs for on axis measurements in non-reference condition were performed in Co-60 beams, in X-ray beams and in electron beams from linear accelerator. The TLD were irradiated at 10 cm and 5 cm depth for open fields (8x8, 10x10, 10x20 cm^2) and wedge field (10x10 cm^2) in Co-60 and X-ray beams. In electron beams the TLD were irradiated at depth of dmax for 6x6 cm^2 and 10x10 cm^2 fields.Pilot studies were performed in order to test the methodology for the dosimetry measurements and the documentation for the practical operation of the audit system in a variety of non-reference conditions: off-axis (symmetric and asymmetric fields) and for fields formed by MLC.
Results: The results of the audit in non-reference conditions for on axis measurements are in the majority within the 3.5% tolerance limit which is usually used for reference conditions.The results of the pilot study for off-axis (symmetric and asymmetric fields) measurements and measurements for fields formed by MLC show that it is possible to keep the dose determination within tolerance limits by the implementation of correct methodology and carefully carried-out measurements and calculations of doses.
Conclusions: The results of pilot measurements and prepared documentation permit to introduce the audit program in non-reference conditions, for on axis and off-axis measurements, at national level.
Support: IAEA CRP 11918/RO

1148 poster

WATER PHANTOM FOR FILM DOSIMETRY

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Purpose/Objectif: Aim of this paper is to present a new phantom for arc therapy, IMRT and tomotherapy treatment plan dose verification. The phantom uses water as filling material together with a technical solution specifically designed to support radiographic or radiochromic films and ionimetric chambers in the desired position.
The phantom is intended to be used for pre-treatment verification purposes: the plan prepared for the patient treatment is imported on the phantom CT study and the dose distribution in water is evaluated.
Materials/Methods: The phantom here presented is a Plexiglas container with shape and dimensions able to simulate an human torso which can be filled with water, opening the upper cover. In the inner side of the cover four carbon bars, equipped with millimetric scales are fixed. To compare the measured and the planned dose distribution a reference system is defined on the film using four reference points. The dosimetric film, fasten on a thin plastic sheet using a film pack, is then positioned at the desired coronal plane inside the phantom using the carbon bars. With four further bars is also possible to arrange the film along axial or sagittal planes. At one of the two phantom ends a movable system of two disks allows a Plexiglas finger to be positioned, parallel to the rotation axis of the accelerator gantry, in all the possible positions inside a 20 cm diameter cylinder. Therefore an ionization chamber can be inserted in the finger, thus allowing to measure the adsorbed dose in a point for film calibration purposes. The phantom is positioned on the accelerator bed using the positioning lasers and the irradiation is performed.
Results: The comparison between the measured and the computed dose distributions is performed for the global plan in a realistic condition along axial coronal and sagittal planes. The reference system defined on the film allows to perform the comparison with a millimetric accuracy.
Conclusions: The use of water makes it possible to realize extremely versatile phantoms completely compliant with the dosimetric reference standard (1). If materials simulating lungs or other tissues are put inside the phantom, a comparison between measured and planned dose distribution in presence of inhomogeneities is also possible. The work described was performed in the framework of the European Integrated project MAESTRO granted by the European Commission (Methods and Advanced Equipment forSimulation and Treatment in Radio-Oncology, no. LSHC-CT-2004-503564). Patent pending.

Posters Radiation Technologists

1149 poster

A CROSS-SECTIONAL STUDY OF THE IMMOBILISATION OF PAEDIATRIC PATIENTS FOR EXTERNAL BEAM RADIOTHERAPY

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Purpose/Objectif: To investigate the types and availability of immobilisation devices for paediatric patients in the radiotherapy department, and to compare practice with a view to establishing the most prevalent immobilisation techniques or any in- house practices not known in the wider community. To compare the use of General Anaesthesia and sedation on paediatric patients undergoing radiotherapy in different radiotherapy departments.
Materials/Methods: In a cross-sectional study, the immobilisation of paediatric patients for radiotherapy in 14 different radiotherapy departments was reviewed by postal questionnaire.
Results: A variety of immobilisation devices were used during paediatric radiotherapy procedures. The types of immobilisation devices used reflect the influence of clinical research into immobilisation for radiotherapy on clinical practice. The availability of immobilisation and positioning devices on the market influences the types of immobilisation devices used on paediatric patients during radiotherapy procedures. The number of paediatric patients treated and departmental experience treating any particular types of paediatric

cancers did not appear to influence the availability and types of immobilisation devices used.
Conclusions: Although there was consistency in the use of general anaesthesia and sedation for paediatric patients, different immobilisation techniqes were used for the same patient groups both between and within the departments surveyed.

1150 poster

ACTIVE BREATHING CONTROL, A FEASIBILITY STUDY

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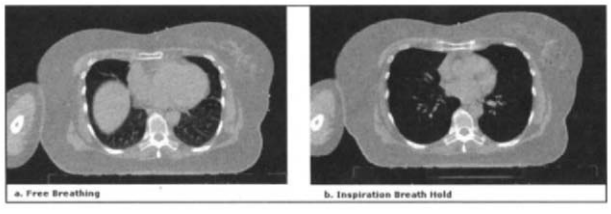
Purpose/Objectif: During the respiration manoeuvre the location of the target volume can vary 1-3.0 cm resulting in a suboptimal target coverage. Also the probability of cardiac damage is increased with the radiation of a larger amount of heart volume (as might be the case in left sided irradiation of the female breast). Active Breathing Control (ABC) might be a solution to both problems. The patient breaths through a mouth-tube, which is connected to the ABC computer for registration of the respiration. ABC is achieved by breathholding during several seconds, either on inspiration or on expiration. During the breath hold the movement of the tumour is stopped. A better target coverage is achieved and less normal tissue will be radiated.
Materials/Methods: In order to evaluate the benefits of ABC, we first started a literature search. We gained experience with the ABC-equipment by visiting the Centre Leon Berard Lyon, France.
Finally we examined a number of left-sided breast cancer patients in our department, who would benefit from the post-operative radiation treatment with ABC rather than our standard treatment without ABC.
Results: Breath holding shows a reduction in radiating critical structures, which can clearly be seen on a CT scan. A clear difference can be observed between a breath holding scan and a free breathing scan (fig 1). The heart-breast distance increases with the breath hold. There will be more lung volume included in the radiation field with a breath hold, but the density of the lung will reduce. Several studies point out that moderate Deep Inspiration Breath Hold (mDIBH) is the best way to treat breast cancer patients with ABC. mDIBH is defined by 75% of the maximum lung volume. ABC can easily be used in a radiotherapy department; the treatment time will increase, 15-30 minutes. In our department we noted that in 56.3% of the left sided breast cancer patients, more than 1.5 cm of the heart volume was included in the tangential fields. So these patients might benefit from the post-operative radiotherapy with ABC.
Conclusions: From the literature search we found that mDIBH using ABC is feasible in a radiotherapy department and that the dose in the critical structures can be decreased significantly. With increasing experience ABC treatments could be performed within a 15-30 minute time slot.
In our department we found that 56.3% of the patients with left-sided breast cancer might benefit from ABC.

Fig 1: CT scan of a left-sided breast cancer patient.



1151 poster

ANALYSIS OF NEEDLE DISPLACEMENT DURING HIGH DOSE RATE BRACHYTHERAPY FOR PROSTATE CANCER

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Purpose/Objectif: To improve treatment results of High-Dose Rate (HDR) brachytherapy for prostate cancer, we evaluated the displacement of needles among the treatment fractions.
Materials/Methods: Ninety-three patients were treated with HDR brachyterapy followed by external beam conformal radiotherapy (EBRT) for organ-confined prostate cancer at our hospital. The total dose given to the prostate was 37.5Gy in 5 fractions over approximately 50 hours by HDR and 30Gy in 3 Gy daily fractions for 2 weeks by EBRT. All patients were studied by the pre-treatment verification radiographs everyday. Computed tomography (CT) was also taken for 39 patients everyday, and 54 patients had CT verification only prior first fraction. The metallic marker seeds were placed into the base and apex of the prostate for evaluating the deformity of the prostate. We determined the mean displacement distances of marker seeds placed in the prostate and of the implanted needles between HDR fractions.
Results: Mean displacement distances in the caudal direction were documented up to 8.1 mm (1^{st}-2^{nd}, 2^{nd} day) and 8.6 mm (1^{st}-4^{th}, 3^{rd} day), for the implant needles. Mean displacement distances in the cranial direction were documented up to 7.1mm (1^{st}-2^{nd}) and 7.8 mm (1^{st}-4^{th}), respectively, for the marker seeds on the base side. Mean displacement distances in the caudal direction were documented up to 1.0mm (1^{st}-2^{nd}) and 1.0 mm (1^{st}-4^{th}), respectively, for the marker seeds on the apex side. All displacement of implant needles occurred in the caudal direction. The displacement distances of seed pairs (inter-seed distance) were increased to 10.0mm (1^{st}-2^{nd}, 1^{st}-4^{th}) from verification films. As a result, an average of 20 mm caudal displacement of needles occurred prior to HDR brachytherapy. The displacement for both marker seeds and needles in the greatest degree most frequently occurred between the first and second fractions due to hemorrhage and edema caused by the insertion of needles.
Conclusions: Obtaining verification films with CT and making adjustments in the treatment volume prior to each fraction is necessary to improve inaccuracies in treatment. It is appropriate to treat the first fraction approximately 20 hours after needle implantation.

1152 poster

CLINICAL IMPACT OF A NEW DEVICE - EXSIGHT ™ MACULAR IRRADIATION SYSTEM

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To determine the practical and safety issues within the clinical arena, a new device called the eXsight™ Macular Irradiation System (MIS) has been investigated at the Radiotherapy Dept. Northern Ireland Cancer Centre, Belfast . This system has been developed to treat wet macular degeneration using a combination of small focused fields,

targeted at the retina of the eye avoiding the lens. The device may have the potential to treat ocular tumours in the future. An investigation to evaluate how the MIS technique should be incorporated into our radiotherapy department working practice and procedures was undertaken. The Clinical trial Radiation Therapist's primary role in the implementation of this new technique was to ensure that patient safety and clinical treatment parameters could be achieved and replicated. Relevant documentation for the multi-professional team was produced. A patient pathway was developed with the assistance of a 'healthy volunteer' who had a thermoplastic mould prepared, fitted to the MIS tilt board on the Varian Linac and set up in the 6 field positions. This demonstrated the feasibility of patient's visualisation on the target in the MIS collimator mount, during treatment and field alignment using the pupil for reference anteriorly and the surface of the cornea laterally. Eye motion is recorded by the MIS and the technique is verified using Varian VARiS. The practical implementation of the eXsight™ Macular Irradiation System was deemed to be successful within the radiotherapy department. The use of a volunteer to demonstrate the impact on each area in the patient pathway proved invaluable. A pilot study employing this device in the treatment of wet macular degeneration is in progress.

1153 poster

COMPARISON OF TWO MATERIALS IN THE IMMOBILISATION OF PATIENTS WITH HEAD AND NECK CANCER

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Aim: to establish any difference in immobilisation/reproducibility between 2 types of immobilisation materials available in the Beatson Oncology Centre (BOC) and assess patient acceptance.

Background: The purchase of a new commercial system for head and neck immobilisation in the Beatson Oncology Centre led to a review of current processes and a study on how thermoplastics compare to the conventional Vivac shells in terms of set-up reproducibility. Currently the BOC uses Vivak BDS's as standard with the Sinmed baseboard system. The use of thermoplastics in the immobilisation of Head and Neck patients is becoming increasingly popular as time demands increase in radiotherapy service delivery. There are a number of obvious advantages, mould room only require one session for the construction and fitting of the shell compared to the time and labour intensive two sessions required when creating a Vivac shell. A number of studies have been carried out looking at reproducibility of thermoplastic systems showing that there is no significant difference in set-up accuracy (Lord et al 2003).

Methodology: Patients were selected for the study on a diagnosis of T1 Larynx. Twenty patients were randomised into each arm of the study; 10 immobilised using thermoplastic shells and 10 using the conventional Vivak BDS. Five-fixation points were used. All patients had EPI's taken on the Lateral field during the first 5 treatments and then weekly thereafter, unless additional images were required due to random errors. A total of 140 images were reviewed using the Vision 7.0 image software package. Displacements in the cranio-caudal (C-C) and antero-posterior (A-P) direction were recorded. One radiographer reviewed these images to reduce inter-observer error. An end of treatment questionnaire was issued designed to assess the patient's experience of the immobilisation material used.

Results: The range of field accuracy deviations for the thermoplastic and Vivac system were very similar. The mean displacement was higher among those patients where thermoplastic material was used; however the median values were almost identical with only the posterior displacement in the Vivac group of patients being higher. The standard deviation in the C-C and A-P for the Vivac shells is lower (0.67, 0.8, 1.0, 1.2) than that of the thermoplastic material (0.88, 0.86, 1.1, 1.5) analysing a scatter plot of the results demonstrates this is possibly due to a greater incidence of random errors among patients immobilised with the thermoplastic material. Patient satisfaction questionnaires generally demonstrated an equal tolerance of the two systems however the authors recognise that the patients were unable to make a comparison.

Conclusions: In conclusion this study has demonstrated that both systems provide adequate immobilisation the results have been influenced by the incidence of random errors in the thermoplastic arm of the study. On analysis of the datasets it was shown that these random errors in both groups occurred during initial fractions and were adjusted accordingly, patients then continued treatment without any further displacements outwith the 3mm action level. It is recommended that with the agreement of the clinical teams thermoplastic material be used as standard for head and neck patients. The continuous review of set-up errors should allow us to ensure we are using appropriate CTV-PTV margins for treatment.

1154 poster

DEVELOPING AN IMRT TECHNIQUE FOR RECTAL CARCINOMA TREATMENT

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Purpose/Objectif: Patients with rectal carcinoma are traditionally irradiated with a standard 3- or 4-field technique, resulting in a large volume of small bowel (SB) receiving a high dose. The main objective of this study was to develop a class solution IMRT technique to reduce the volume of SB receiving more than 40 Gy in order to minimize acute and late side effects.

Materials/Methods: The CTV consists of the primary tumor, the perirectal fat, presacral nodes and nodes along the a. iliaca interna and is delineated by the treating physician on the CT scan. The CTV is expanded with 1 cm in all directions to create the PTV. The prescribed dose to the PTV is 50 Gy in 25 fractions. The constraint for the PTV is that at least 99% of the PTV has to receive more than 95% of the prescribe dose, with a maximum dose of 107%. The SB is considered the most important organ at risk. Because of the mobility of the SB the whole area where the SB may reside was considered as organ at risk (OAR-SB). From the OAR-SB the PTV plus 0.5 cm margin was subtracted. This area is used in the optimization process to reduce the dose in the whole bowel area. Maximum dose in OAR-SB minus the PTV is 40 Gy. For this area we defined an objective using a maximum generalized equivalent uniform dose (EUD) to act on the high dose and an objective with a max. EUD to act on the average dose. The dose delivered to the bladder and volumes outside the PTV were considered as further inputs to the optimization. Besides different objectives to the PTV and OAR's, the effect of IMRT parameters, such as the maximum number of segments and minimum segment area and the number of beams were investigated.

The treatment planning was performed in Pinnacle version 7.4f, using the inverse planning tool Direct Machine Parameter Optimization.

Results: By using a 7-beam technique, a good conformal coverage of the PTV is reached. So far we looked at 6 patients to compare the 3-field technique with the IMRT technique. We found that for the IMRT technique we could use a maximum of 40 segments and a min. segment area of at least 16 cm^2. A max. EUD of 30Gy was used to act on the high dose and a max. EUD of 19 Gy was used to act on the average dose. The area of the small bowel outside the PTV, with an average volume of 860 cc, that receives a dose of 40 Gy or higher is reduced from 25.4% (sd=6.9%) to 12.6%(sd=2.4%). For the bladder we used a max. EUD of 2500 to act on the average dose. Compared to the 3-field technique, the dose in the bladder remained approximately the same in most cases, but was sometimes even a

little higher. This is because with a 3-field technique, a large part of the bladder is outside the lateral beams.
Conclusions: By systematically changing the beam set-up, IMRT parameters and objectives, a 7-beam IMRT class solution for rectum patients was found and is now clinically used. By using this technique the volume of small bowel that receives a dose higher than 40 Gy is significantly reduced.

1155 poster

DOSE MEASUREMENT IN THE URETHRA DURING HIGH DOSE RATE BRACHYMONOTHERAPY USING THERMOLUMENISCENCE DOSIMETERS.

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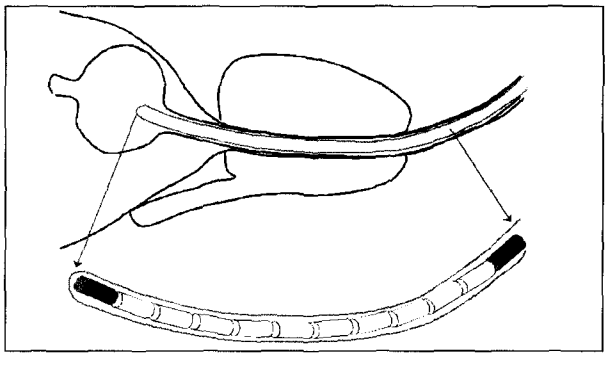
Purpose/Objectif: The urethra is one of the organs at risk during radiotherapy but is generally considered to be more resistant than rectal mucosa. However, during HDR brachymonotherapy the dose distribution is more critical since small displacements can generate large differences in dose to critical organ compared to the one predicted from the pre-treatment dose plan.
Materials/Methods: The dose to the urethra was measured in 12 patients with prostate cancer receiving HDR brachymonotherapy. The measured dose was compared to the predicted dose from the pre-treatment dose plan. The prescribed dose to the clinical target volume (CTV) was 15 Gy per fraction given twice with 2 weeks interval. The volume of the urethra was defined as the volume of an 18 Gauge catheter ad demeur placed in the urethra both during the preplanning examination and the treatments. The maximum dose to this volume was 15.5 Gy. To measure the dose during the treatment, 10 thermolumeniscence dosimeters (TLD), rod shaped (1x1x6 mm), were used. They were put into a thin sterile catheter with X-ray markers in both ends. This catheter (æ 2.6 mm) was inserted into the urinary catheter and was in position during the whole treatment. Fluoroscopy was used to position the most cranial X-ray maker in the urinary bladder. The TLDs covered a length of 6 cm.
Results: Out of 24 measurements 22 were successful. During two treatments the inner catheter with TLD came lose from the fixation. In total 134 TLDs were used for measuring the dose in the prostatic part of the urethra. In 79 TLDs (59%, 79/134) the measured dose with TLDs was within ± 5% of the dose according to the dose plan. In 12 TLDs out of 134 (9%) the measured dose differed more than 2 Gy compared to the dose plan. In one patient the measured dose with TLD was 20 Gy in the cranial part of urethra. The discrepancy was found to be due to a misinterpretation of the urethra position at ultrasound images in the pre plan situation.
Conclusions: Measuring dose with TLD in the urethra is feasible and provides valuable clinical information. Dose measurements should be considered as a part of the quality assurance program at a department of brachytherapy.



1156 poster

EVALUATION OF RADIATION THERAPISTS EDUCATION GROUP LUNCHTIME LECTURES

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Background: Radiation Therapists (R.T.s) at St. Luke's Hospital established the "Radiation Therapists' Education Group" because there was a perceived need to promote CPD in our Dept. The aim is to promote and encourage Radiation Therapists' educational and professional development by providing the infrastructural support for monthly lunchtime lectures. The lectures are delivered by R.T.s for R.T.s. It was envisaged that lectures would provide an opportunity for R.T.s to learn about a relevant research initiative; to discuss published articles relevant to our work; that ideas would be generated, discussed and possible solutions proposed; and that this initiative would tap into and support the enthusiasm in our profession and daily work in St. Luke's.
To date, the wide range of lectures delivered to R.T.s have included new technology developments, psychosocial care, health promotion initiatives, health care management, and reports on seminars/courses. We feel that the lunchtime lecture is an ideal medium for learning and sharing information with our colleagues in a relaxed environment and provides encouragement for R.T.s who have not previously presented to an audience. The Group will shortly be in existence for one year, and it was decided to evaluate the lectures to provide evidence that we are delivering our intentions, to determine their benefit and if they can be improved to meet the needs of R.T.s.
Aims: To determine whether the monthly lunchtime lectures being provided by the Radiation Therapists' Education Group are meeting the aims of the Group as set out when it was established. This evaluation process will establish a quality standard for the Group's activities that can be further improved in the future.
To evaluate staff satisfaction with the monthly lunchtime lectures.
To determine if and how we can improve the monthly lunchtime lectures in the future
Materials/Methods: A questionnaire designed by the Radiation Therapists' Education Group, currently being piloted, will be administered to all Radiation Therapists in St. Luke's in June 2006. N=66. Some key areas being investigated include satisfaction with the content/topics of the lectures; the standard of presentations; the timing and duration of the lectures; the environmental facilities; positive and negative aspects of the lectures; any recommended changes.
Results: This study is on-going. Final results will be available for presentation at the ESTRO conference in October. To date, observations suggests that Radiation Therapists welcome the opportunity to have the lunchtime lectures as a protected forum for them to learn about new developments, and to discuss updates on these developments, and question specific aspects of their work & profession

1157 poster

FLAWLESS STARTING OF PATIENTS

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Purpose/Objectif: To start new patients as smoothly as possible. The reasons for problems at the start are rather diverse.
Materials/Methods: We started a registration of all mistakes. This is based on the FONA system (Fauld, accident, near accident). We add a score form to the patient radiation chart of every patient that is simulated. This form follows the entire path between simulation and start of the treatment on the radiation machines. The document

is separated into two parts. One part is filled in by the physicists. They score everything that happened before the planning. The second part is filled in by the nurses during the treatment. They score everything that can go wrong when starting up the treatment. The score form is taken out of the patient radiation chart after the start of the treatment. All documents are evaluated and a code is given to each problem or mistake. Every two months a general evaluation is performed. We then look how many patients started without any problems. Besides that, we also see which mistakes or problems occur the most. The codes that receive the largest score are connected to actions or agreements that have to make sure that the problem is resolved in the future. The next scoring periods serve as an indicator to show if the agreements that were made do work.
Conclusion: By doing so, we optimized the quality of our work. We used to have a lot of stress, frustrations, tensions and rework, but now it is better. To be able to start patients completely flawless is probably an utopia. Working with the thought of achieving this is a strong thought for us.

1158 poster

GASTRIC CANCER: IMRT VERSUS CONVENTIONAL RADIOTHERAPY

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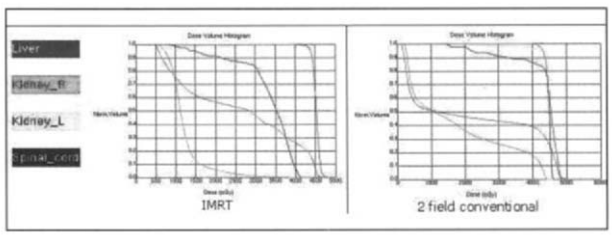
Purpose/Objectif: IMRT (Intensity Modulated Radio Therapy) is a promising new technique in postoperative chemoradiation of gastric cancer. IMRT has the ability to conform the dose to concavities and to better avoid critical organs, particularly for the treatment of large volumes.We have started a clinical routine for treatment of gastric cancer with IMRT. The purpose is to compare IMRT and conventional (AP-PA) radiotherapy with respect to doses in organs at risk (OAR).
Materials/Methods: For one patient irradiated with IMRT (45 Gy/ 25 fractions) on an (Elekta SL 18) accelerator, both a conventional plan (two field conformal technique) and an IMRT plan were constructed (Pinnacle®). Dose volume histograms (DVH) for the right and left kidney and the liver were compared to evaluate the benefit of IMRT.
Our patient received 45 Gy, in 25 fractions 5 days a week over a period of 5 weeks, which was combined with daily chemotherapy (cisplatinum 5 mg/m^2 i.v. and capecitabine 800 mg/m^2 bid orally). Patient tolerated treatment well and increased in weight during radiotherapy.
Results: The DVH below show that the doses to the OAR decrease partially with IMRT. The volume irradiated to ≥ 20 Gy (V20): V20 of the left kidney with IMRT is 97% and 99% for the conformal technique. The V20 of the right kidney with IMRT is 5.7% and for the conformal technique 22%. V20 of the left kidney decreases with 2%, and the right kidney with 16.3% by using IMRT. With IMRT the mean liver dose is 25.6 Gy, and for the conformal technique 19.9 Gy. The mean liver dose increases with 29% when using IMRT, which is clinically non significant.
Conclusions: In postoperative chemoradiation of gastric cancer, IMRT is able to reduce doses to critical organs, which ultimately can result in better tolerance of this treatment and a decrease in long-term toxicity.



1159 poster

HIGH DOSE RATE BRACHYTHERAPY FOR THE TREATMENT OF SKIN CANCERS

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Purpose/Objectif: To assess the use of HDR surface applicators as an alternative radiotherapy modality to external radiation for the treatment of skin lesions.
Materials/Methods: A total of 17 patients were treated to 18 sites, which included lesions of the face, scalp, trunk and extremities. Thermoplastic casts were fitted with Leipzig Surface Applicators and custom molded to the patient for non-melanomatous carcinomas < 2cm in diameter. A custom surface mold applicator (Freiburg Flap) was used for lesions up to 4cm. PTV included the tumor plus a 5mm margin. Photographs of the treatment volume were taken for monitoring of reactions. Prescribed dose was 5Gy/fraction, twice per week for four weeks to a 5mm depth. TLD's were placed at the center of the treated volume under the applicator and at critical structures (i.e. lateral canthus) twice during the course of treatment.
Results: Patients' setup and reproducibility were accurate and treatment time was short. With the HDR surface applicators, dose distribution was uniform at the skin surface and at 5mm depth in the whole area of the applicator. Differences between the areas of maximum and minimum dose at this depth did not reach values higher than 5% of the prescribed dose. At the edges of the applicators, the dose gradient was sharp, with the detected dose at 5mm from the applicator negligible. An exudative radiation reaction was noted in some patients, which reversed with appropriate therapy.
Conclusions: HDR Brachytherapy offers a highly effective treatment of skin carcinomas. Surface applicators, used with HDR brachytherapy equipment, enable a uniform dose distribution and sharp dose gradient at the edge of the treatment field. Surface applicators are easy and safe to use and offer reproducibility for subsequent treatment fractions. These applicators have the ability to become the standard treatment for skin carcinomas in the near future.

1160 poster

INVERSE PLANNING IN PROSTATE CANCER

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Purpose/Objectif: To evaluate the use of inverse planning in 3-dimensional conformal radiotherapy (3DCRT) of prostate cancer patients and analyse the dosimetric results by comparing with the forward planning 3DCRT and inverse planning of intensity modulated radiotherapy (IMRT).
Materials/Methods: For each of the ten prostate cancer paitnes, forward 3DCRT, inverse 3DCRT and inverse IMRT plans were produced using the XiO treatment planning system. The dosimetric results, tumour control probability and normal tissue complication probability, and the optimisation time of earch treatment plan were recorded for comparison.
Results: The inverse 3DCRT plans showed comparable TCP with the forward 3DCRT plans ($p = 0.133$) but were inferior to that of the IMRT plans ($p < 0.001$). Relative to the forward plans, the inverse 3DCRT plans deliverd lower doses to the bladder and rectum. When compared to the IMRT plans, no significant difference was observed in the bladder dose ($p = 0.355$) whereas the mean rectal dose was significantly lower in the IMRT plans ($p = 0.006$). The average optimisa-

tion time for inverse 3DCRT was the shortest. However its difference with the IMRT plans was insignificant (p = 0.150).
Conclusions: Inverse planning for 3DCRT is a reasonable alternative to the forward planning for prostate cancer with reduction of the optimisation time. However, IMRT has better potentials for further reduction of rectal dose and target dose escalation.

1161 poster

KNOWLEDGE, USE AND ATTITUDES OF COMPLEMENTARY AND ALTERNATIVE MEDICINE (CAM) AMONG IRISH ONCOLOGY HEALTH CARE PROFESSIONALS

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Purpose/Objectif: As no studies have been carried out in to investigate the knowledge, use and attitudes of CAM among oncology health care professionals, the primary aim of this project is to investigate the knowledge, use and attitude of CAM among Irish oncology health care professionals.
Materials/Methods: An anonymous questionnaire was designed to contain questions addressing these three variables. Questionnaires were distributed within the radiotherapy departments of six Irish hospitals. In order to fill out the questionnaire participants must have been involved in the cancer patient's care, management and/or delivery of their treatment.
Results: Overall, participants seemed to have a poor knowledge of CAM . 90% of participants who had used some form of CAM therapy to treat their own illness, found the therapy they had used beneficial, suggesting that they would have a positive attitude towards cancer patients using CAM therapies. On the whole, participant's attitudes towards CAM were positive, with the exception of the oncologists, who in the majority showed negative attitudes towards patients using complementary therapies. Negative attitudes towards the patient's use of alternative therapies were reported among the majority of participants, with 43% of participants believing that there were no benefits to patients using alternative therapies.
Conclusions: The results from my questionnaire correlate with other studies in the same area. As CAM usage among cancer patients is continually increasing, this lack of knowledge among oncology health care professionals and negative attitude among oncologists towards CAM needs to be addressed.

1162 poster

ON BOARD IMAGING - NEW DEMANDS FOR NURSES WORKING AS RADIATION THERAPISTS, TO SECURE THE BEST QUALITY FOR THE PATIENT.

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In April 2005, two new accelerators with On Board Imaging (OBI) were installed.At the same time a new treatment technique for treating prostate cancer was implemented. This technique is based on Image Guided Radiotherapy: Gold seeds, already implanted in the prostate gland, are used as markers and, using the OBI technology, the patient is screened, and the image obtained is then matched with a CT-reference image. The accelerator couch - with patient - is then moved to the correct position determined by the image match. Consequently the treatment is very precise and true to the treatment plan, reducing both ITV and PTV and - subsequently - the normal tissue damage. In nurses have always been involved in both the nursing care and the radiotherapy treatment of cancer patients. With the introduction of Image Guided Radiotherapy, a new area has been added to the nurses field of work.The image analysis and resulting treatment is a new responsibility and has required additional training.The reduced nurse-patient contact during treatment, due to automation, has increased the need for thorough information prior to the treatment.Conclusion:On Board Imaging makes it possible to deliver a more precise daily radiotherapy treatment, and thereby minimize normal tissue damage (secondary effect/side effects).Reduced nurse-patient contact during treatment demands better information prior to treatment to ensure patient understanding and sense of security.The introduction of a new treatment technique has required further training, and resulted in increased responsibility for the nursing staff.

1163 poster

OPTIMIZED SEGMENT-APERTURE MONO-ARC THERAPY (OSAMAT) AND ITS APPLICATION IN CONFORMAL RADIATION OF OLIGOMETASTATIC PROSTATE CANCER: A PHASE I STUDY.

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2 - Gent University Hospital, Nuclear Medecine, Gent, Belgium,
3 - Gent University Hospital, Radiology, Gent, Belgium

Purpose/Objectif: For patients who develop M1a-b disease after primary treatment for prostate cancer, androgen deprivation (AD) is the standard of care nowadays, but has an important impact on quality of life. Singh demonstrated that the number of metastatic sites is a significant prognostic factor for survival (cut-off: 5) and hypothesized that aggressive treatment (e.g. radiosurgery) of oligometastatic prostate cancer might improve survival (1).
OSAMAT uses a single radiation arc collimated with multiple leafs and creates highly focused dose distributions to the metastatic site(s).
We want to evaluate acute gastro-intestinal (GI) and genito-urinary (GU) toxicity of OSAMAT as treatment for oligometastatic prostate cancer and test the hypothesis generated by Singh et al (1).
Materials/Methods: Eight patients who developed <5 metastases after primary treatment for prostate are the subject of this study. Primary treatment (PT) consisted of radical prostatectomy + postoperative radiotherapy in 7 patients, and radiotherapy alone in 1 patient. Six patients received concomitant AD at the time of PT.
All patients developed PSA relapse after PT. Using bone scan, MRI and ^{18} FDG-PET -CT imaging, the metastatic sites were revealed. Table 1 depicts the characteristics of patients (n=8) and the metastatic site(s) (n=12). Using OSAMAT, a median dose of 45 Gy (9 x 5 Gy, 3 times/week; n=7) or 50 Gy (10 x 5 Gy, 3 times/week; n=1) was prescribed to the metastatic spot(s) (=GTV). In 6 patients, a concomitant AD was initiated for a period of 6 months. Two patients refused.
The RTOG toxicity score supplemented with an in-house toxicity score was used to score acute GI and GU toxicity (2).
Results: All treatments were delivered successfully without interruption. Median dose to the GTV was 45 Gy, 46 Gy and 51 Gy in 6, 5 and 1 case respectively. Minimal dose was >95% of the prescription dose in all cases. Two patients developed a transient grade 2 GI toxicity during OSAMAT. In 1 of these patients, also grade 2 nocturia was present. Six patients remained asymptomatic during OSAMAT. With a median follow-up of 6 months, all OSAMAT-induced acute toxicity disappeared. In all but 1 patient, PSA dropped after OSAMAT. Both patients who refused AD had a normalization of their PSA.
Conclusions: OSAMAT is feasible for treating oligometastasis of prostate cancer. There were no technical problems and acute toxicity was low.
References
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2. De Meerleer G et al. Intensity Modulated Radiotherapy as primary

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	primary treatment (PT)	relapse characteristics		PSA at relapse	grade of toxicity		duration of toxicity	follow-up
		number	site		GI	GU		
patient 1	RP + salvage RT + LHRH (6 mo)	1	external iliac left	1.5 ng/ml	1	1	during - M3 3	6 months
patient 2	RP + adjuvant RT + LHRH (6 mo)	1	internal iliac left	7.1 ng/ml	0	0	not relevant	9 months
patient 3	primary RT + salvage RP + AA (10 mo)	2	internal iliac right precaval	11.1 ng/ml	0	0	not relevant	6 months
patient 4	RP + salvage RT	4	common iliac left external iliac left external iliac right paurectal	n/a ng/ml	2 1	2 1	during during - M3 6	6 months
patient 5	RP + adjuvant RT (64 Gy)	1	internal iliac right	2.2 ng/ml	0	0	not relevant	6 months
patient 6	RP + salvage RT	1	external iliac right	X.X ng/ml	0	0	not relevant	1 month
patient 7	RP + salvage RT + LHRH (6 mo)	1	external iliac left	2.1 ng/ml	2	0	during	4 months
patient 8	RT	1	acetabulum right	18.9 ng/ml	0	0	not relevant	1 month

1164 poster

POTENTIAL BENEFIT OF IMRT VERSUS CONFORMAL RADIATION FOR UNRESECTABLE HEPATIC MALIGNANCIES

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Purpose: 1) To compare intensity modulated radiotherapy (IMRT) and conformal radiotherapy (CRT) normal tissue sparing for the same PTV coverage in patients treated on a hypofractionated isotoxicity study. 2) To explore the potential for dose escalation using IMRT.

Methods: CRT plans of 21 patients with unresectable liver cancer treated with a median of 6 beam angles (3-10), 1 segment/beam (1-4) and minimal path-lengths through normal liver and other normal tissues were investigated. The dose delivered using CRT was individualised, based on effective liver volume irradiated to maintain a 5% or less risk of radiation induced liver disease (RILD), with a maximal permitted dose of 54Gy in 6 fractions. Doses to 0.5cc of bowel and stomach could not exceed 30Gy. Maximal dose to spinal cord was 25Gy. Up to 140% was permitted in the PTV. Plans were divided into 2 groups: 1) PTV overlapping (n=6) or directly adjacent to (n=3) serial functioning normal tissues and 2) liver as dose limiting normal tissue (n=12). IMRT plans were generated in Pinnacle treatment planning system using direct machine parameter optimization with the CRT plan beam angles. EUD based optimization was used to maximize PTV dose and/or improve normal tissue sparing. Dose escalation was investigated in IMRT plans with the same or higher minimum dose to 0.5cc of the non-overlapping PTV without exceeding normal tissue tolerances.

Results: The median CRT dose was 40.8Gy in 6 fractions (range: 25.2 - 54). 12/21 (57%) IMRT plans had improved PTV coverage compared to CRT plans and met normal tissue constraints (5/9 overlap, 6/12 non-overlap). Of these 12, 4 plans with a prescription dose of 54 Gy (maximal) had an improved PTV EUD by an average of 1.3Gy with IMRT. For the other 8 CRT plans, IMRT permitted dose escalation in 6 (3 overlap, 3 non-overlap) by an average of 3.3 (0.6 - 6.6), for a 5% RILD risk.

Conclusions: UD based IMRT can facilitate normal tissue sparing and dose escalation in patients with liver cancer. The robustness of these IMRT to geometric uncertainties needs to be investigated.

Research is funded in part by an Elekta clinical research grant.

	Mean (range) change with IMRT (Gy)		
	Min PTV dose	PTV EUD (a=-20)	Max duodenal dose
Overlap	+1.0 (-11.4, +7.9)	+2.9 (-1.0, +9.4)	-0.3 (-7.2, +9.1)
Non-overlap	0 (-7.2, +7.6)	-0.2 (-10.1, +11.4)	-0.3 (-13.8, +9.6)
All	+0.4 (-11.4, +7.9)	+1.1 (-10.1, +11.4)	-0.3 (-13.8, +9.6)

1165 poster

PRACTICAL IMPLEMANTATION OF VIRTUAL CT SIMULATION AND ADVANTAGE SIM SOFTWARE BY RADIATION THERAPISTS

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Purpose/Objectif: Virtual simulation of radiotherapy treatment planning, replaces the real simulator, and uses 3D CT patient data, including the external skin marks instead of a real patient body. A Virtual simulation system simulates all the motions of the physical simulator and displays the digital reconstructed radiograph (DRR). Virtual simulation permits interactive work with high quality image manipulation and advanced contouring tools to define treatment beams and blocks, to control the simulator, to find the appropriate gantry position and to investigate the tumour and organs at risk. Another significant benefit of virtual simulation is that all of the planning procedures are performed without the presence of the patient. Virtual simulation provides more functions than a conventional simulator in order to produce an effective and efficient treatment plan.

A GE Lightspeed CT Scanner with Advantage Sim 6.0 Software was recently installed in St. Luke's Hospital. The following research will ensure the safe and efficient transition from conventional to virtual simulation in our dept.

Aims:

- Ensure a smooth transition from conventional simulation to Virtual CT Simulation by establishing protocols for the implementation of Virtual CT Simulation and the use of Advantage Sim Software for radiotherapy treatment at St. Luke's Hospital. These protocols will then be used as training tools for radiation therapists.
- Determine patient information needs related to Virtual CT Simulation and implement necessary changes to meet these needs.

Materials/Methods: Protocols for Virtual CT Simulation will be created beginning with Breast and Prostate techniques and ultimately all treatment sites. These protocols will include detailed instructions for acquiring the planning CT scan, including the topogram, single check slice to determine patient movement prior to scan and image selection to include anatomical coverage required for treatment planning. Optimal immobilisation techniques, skin marking methods, additional treatment set-up parameters e.g. table-top height, will also be examined with regards to reproduction of the patient position from CT sim to daily treatment. Initially, radiation therapists will be supervised by a radiation oncologist in the use of Advantage Sim 6.0 Software. All alterations made to the simulation, by the oncologist, will be recorded and used to create a protocol which will be used directly for on-going R.T. staff training. Specific patient information leaflets will be prepared regarding the Virtual CT Simulation pathway.

Conclusions: This research is on-going. Detailed results will be available for poster presentation at the ESTRO Conference in October 2006.

1166 poster

QUALITY ASSURANCE OF INDIVIDUAL SEGMENTS OF STEP-AND-SHOOT IMRT

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Purpose/Objectif: Absolute point dose measurements as part of the quality assurance of step-and-shoot intensity modulated radiation therapy (IMRT) often reveales unexpected deviations. This study investigates the feasibility of IMRT-QA of individual segments to explain these deviations, and the efficacy of different evaluation

methods.
Materials/Methods: The dose in a small volume around the point of interest (POI) was calculated for the individual segments of an IMRT plan for which a software script was added to our treatment planning system (Pinnacle^3 7.6c, Philips). Furthermore, two input parameters for analysis of the measurements, i.e. the dose per monitor unit (D/MU) and the maximum dose gradient (dD/dr), were calculated for each segment. A software application was developed for automated data acquistion and analysis. The analysis was carried out either disregarding measurement data with a low confidence level (dD/dr or D/MU outside a critical range), or using g-evaluation.
Results: IMRT-QA was performed for 10 prostate and 5 head and neck patients. We found significantly higher deviations for segments at which the detector turned out to be located within the penumbra, which was consistent with 0.15 < D/MU < 0.55 cGy/MU, or dD/dr > 0.25 cGy/mm. When these data were filtered out, the total dose deviation ranged from -2% to 3% (not filtered: -5% to 5%). However, only 78% of the fraction dose was verified on average due to filtering. When g-evaluation was used, 93% of the fraction dose was within acceptance criteria (2.5% D_{segm}; 2.5mm) on average. Datapoints outside these acceptance criteria were predominantly related to measurements behind jaws or leafs (D/MU < 0.15).
Conclusions: IMRT-QA of individual segments revealed that penumbral ionometric uncertainty is the main cause of deviations in overall IMRT-QA. This method is feasible in daily clinical routine and provides more insight in deviations between measurements and calculations.

1167 poster

RESPIRATORY MOTION IN RADIOTHERAPY FOR LUNG PATIENTS PRIOR TO THE IMPLIMENTATION OF GATING TECHNOLOGY

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Purpose/Objectif: To (a) establish a methodology for patient set-up verification during radiotherapy treatment based on the registration of electronic portal images and (b) investigate the clinical appropriateness of commercially available gating systems for minimizing respiratory-induced anatomic motion in patients with lung cancer.
Materials/Methods: In our department all linear accelerators (Varian) are equipped with EPIDs (electronic portal imaging devices) capable of acquiring cine-vision images during treatment. Our study involved the "real-time" acquisition of cine-vision images for a cohort of lung patients receiving curative radiotherapy during the delivery of treatment to determine the maximum extent of tumor displacement in both the superior-inferior and lateral aspects. GTV was defined as tumor as identified at CT simulator and PTV included the GTV plus 10 to 15 mm margins. An analysis of tumor motion within the treatment field was performed to assess the need for a complex respiratory-gating system.
Results: 21 patients treated using AP/PA 18 MV parallel-opposed photon beam radiotherapy were analyzed using the EPID cine-vision option for tumor motion during treatment. Every 2 seconds the EPID recorded a portal image. 168 portal images were analyzed. Superior-inferior movement ranged from 3 to 20 mm with a standard deviation of 4.7 mm, and lateral movement ranged from 3 to 6 mm with a standard deviation of 2.5 mm. Under these treatment conditions tumor coverage was found to be acceptable in all patients excepts for one.
Conclusions: During this investigation a practical methodology of using the cine-vision option to access organ motion was developed. In general, lung tumors do not exhibit much motion, but the use of a gating system to account for respiratory-induced motion during treatment may allow for the use of reduced margins for the CTV. However, a careful choice of patients may be required for this particular technique. The introduction of gating equipment into our clinic will give us the opportunity to further investigate the use of this technology.

1168 poster

RISK ESTIMATION FOR THE INDUCTION OF SECONDARY CANCER IN THE CONTRALATERAL BREAST FOLLOWING 4-FIELD RADIOTHERAPY TREATMENT OF PRIMARY BREAST

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3 - Norwegian Radium Hospital, *Department of Medical physics, Oslo, Norway*

Purpose/Objectif: To predict the risk for secondary breast cancer in CB (contralateral breast) following radiotherapy of the breast and regional lymph nodes by a 4-field technique, approaching a nonlinear and linear risk estimating models. In addition, it was of interest to investigate the influence of dose inhomogeneity in predicting the risk for secondary cancer induction.
Materials/Methods: Data from dose volume histograms and mean dose in CB calculated by the treatment planning system for 8 patients using a collapsed cone algorithm are used to predict the risk for cancer induction in CB by employing a competition nonlinear and linear model.
Results: The results from the linear approach together with the mean CB dose indicate a risk prediction which is 3-9 times higher than the prediction of the risk with nonlinear approach using the dose volume histograms. It is also found that risk increases with increasing $\alpha 1$ (from 0.001-0.1 Gy-1) independent on other chosen parameter values.
Conclusions: Choice of risk estimation model has a considerable effect on the predicted risk and should be considered carefully.

1169 poster

SKIN DOSE: COMPARISON OF INTENSITY MODULATED RADIOTHERAPY AND THREE FIELD CONFORMAL TECHNIQUES FOR HEAD AND NECK CANCER

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Purpose/Objectif: Intensity modulated radiation therapy (IMRT) and three field conformal radiation therapy (3 Fields conformal RT) are the optimal radiation therapy techniques used to deliver maximum dose to the target volume and minimum dose to the surrounding normal tissue. With IMRT treatment, each radiation field is divided into small segments with different intensities of radiation to account for irregular shape tumours and surrounding tissues. It has been shown that intensity modulated radiation beams can produce an optimal distribution where the target volume is an irregular shape. Recent literature has raised the issue about the skin dose of IMRT treatment which is reported to be higher than that of conformal therapy.
Materials/Methods: A Varian 600CD linear accelerator with 80-leaf multi leaf collimation (MLC) was used to provide the 6MV photon beam for the measurements. This study shows the skin dose measurement for both IMRT and 3 Field conformal treatment techniques for one identical patient ('Rando' phantom) using the method of thermo-luminescent dosimeters (TLD) measurements.
TLD packets were used to measure the dose at skin regions at entry points of each IMRT treatment field (7 fields) and 2 TLD packets on each of 3 Field conformal treatment fields (total of 6 TLD packets).

Results: The TLD results of both IMRT and 3 Field conformal plan show that the bolus effect of the stabilisation shell is effecting the skin dose and thus raising skin toxicity. The average dose difference of the IMRT plan with and without shell is 21.83%.The average dose difference of 3 Field conformal plan with shell when all fields were exposed is 27.16% and that of individual field difference is 39.7%.
Conclusions: several factors are responsible for the high dose at the skin region in the IMRT treatment. The factors that influence skin dose in an IMRT plan are summarised as follows:
- The bolus effect of shell
- The multiple tangential beams of IMRT plan
- Physical and mechanical properties of MLC cause specific delivery issues such as leakage radiation and rounded leaf tip effect.

1170 poster

THE AIO SOLUTION STABILIZATION SYSTEM-BREAST PRONE AND SUPINE POSITION

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2 - Centre of Oncology-MSC Memorial Istitute, Branch Gliwice, *Radioteraphy Department, Gliwice, Poland*

Purpose/Objectif: In Radioteraphy and Brachyteraphy Planing Department in Gliwice the AIO Solution stabilization system by Orfit Company is used. This new stabilization system provides breast cancer irradiation in two different ways: standart-supine and new-prone position. The new approach of prone position may be useful in patients with specific big breast.The aim of this work is an assesment of dose in critical organs in patients immobilized by new stabilization system in comparison with the standard one.
Materials/Methods: In years 2005-5006 fifteen patients immobilized with the AIO Solution system in prone position had been irradiated. The treatment plans were done in Eclipse-Varian Treatment Planing System.In every patienst the smallest "X" size was 10cm.The dose in critical organs: lung and heart was estimated by mean of dose-volume histograms. The dose distribution was compared with this for patients in supine position.
Results: The use of new stabilization position coused dose reduction in both critical organs.The difference was from few to a dozen per cent.
Conclusions: The prone position helps to lay patients in more comfortable position. Moreover the position gives good effects in dose distribution

1171 poster

THE CLINICAL IMPLICATIONS OF THE IMPLEMENTATION OF IMRT FOR THE TREATMENT OF PROSTATE CANCER FROM THE PERSPECTIVE OF THE RADIATION THERAPIST.

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Purpose/Objectif: Intensity Modulated Radiation Therapy (IMRT) represents one of the most significant advances in radiation therapy in recent times. IMRT is based on the use of non-uniform radiation beam intensities which conform to the tumour volume and greatly reduce the dose to surrounding critical structures. This leads to a greater reduction in acute and chronic radiation toxicities. Due to the limited amount of published data on the implementation of IMRT for prostate cancer treatment it is important to review what has been done in other departments to see how the different issues have been managed clinically. This research was undertaken to determine the issues that affect radiation therapists when implementing IMRT.
Materials/Methods: This study involves six hospitals where IMRT is in use for the treatment of prostate cancer. Semi-structured interviews and questionnaires were used as the research tools in an attempt to gain insight into what IMRT for prostate cancer treatment entails.
Results: There doesn't appear to be any true consensus on the implementation of IMRT for prostate cancer treatment. From a Radiation Therapist's point of view, the main areas of concern when implementing this technique are training, immobilisation, daily patient set-up verification and the time element involved in each step. Pre-treatment quality assurance is also a major issue with respect to training and time.
Conclusions: There is a need for more published data in every area involved in IMRT for prostate cancer treatment, from selection criteria through to treatment delivery. There needs to be more sharing of knowledge gained so that this can be improved on in order to achieve the most effective and efficient system.

1172 poster

THE HEALTH AND SAFETY OF PREGNANT EMPLOYEES IN THE REPUBLIC OF IRELAND

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Purpose/Objectif: To investigate the awareness of female radiation therapists (RTTs) in the Republic of Ireland regarding the health and safety of pregnant employees.
Materials/Methods: Anonymous questionnaires were distributed to 59 female radiation therapists (response rate 75%). Participants were questioned regarding the potential risks that a pregnant radiation therapist may be exposed to in the RT department and the legislation that protects the pregnant employee.
Results: Results were analysed and compared between two age groups-under 25s and 25+. Both age groups had a reasonable knowledge of the potential physical and radiation type risks that a pregnant radiation therapist may be exposed to in the RT department. Knowledge of chemical and biological risk types was lower. Overall knowledge of the legislation that protects the pregnant employee was poor-only one participant (u-25) was aware of the exact legislation that protects the pregnant employee.
Conclusions: There is a need for radiation therapists to become more aware of the risk types that one may be exposed to in the RT department. Greater compulsory training relating to H&S should be introduced in departments

1173 poster

THE NEW IMMOBILIZATION SYSTEM FOR BREAST CANCER PATIENT IRRADIATION ? PATIENT?S AND TECHNICIAN?S SUBJECTIVE NOTE

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2 - Medical University, *Computer Laboratory, Lodz, Poland*

Purpose/Objectif: The irradiation after breast conservative therapy (BCT) is the standard therapy for all patients. It's necessary to use immobilization system to provide the same breast position during every fraction. There are many immobilization systems made by different companies.
The aim of study: To compare subjective note, given by patients and radiotherapist, for 3 immobilization system.
Materials/Methods: 30 specially prepared questionnaires were fulfilled by breast cancer patients treated with three different immobilization systems (10 patients for each systems): Standard ther-

moplastic Mask (STM), Breast in prone position (BPP) and Breast in supine position (BSP). Patients wrote notes from 1 to 5 as a positioning comfortable at 1st and 5th week of treatment. We had measured time of patient positioning and we had asked technicians, performing irradiation about their subjective notes of each system. ANOVA rang Kruskal-Wallis and U Mann-Whitney Tests were used for statistical analysis.
Results: We observed statistically important difference between STM and BSP comforts of positioning at 5th week of irradiation (p=0,002). We also observed that BPP is more comfortable for patients then STM and BSP is the most comfortable all of it at both 1st and 5th week although there were not statistically important different. Median time of positioning was 123 sec. for STM, 198 sec. for BPP and 299 sec. for BSP). We observed statistically significant difference between time positioning of patients using each system (p=0,0005 for STM and BPP, p=0,00001 for STM and BSP, p=0,00004 for BPP and BSP). We did not observe statistically significant difference between notes given by technicians, but notes for BSP were quite divergent.
Conclusions: The new breast positioning systems give patients more comfort but are more time consuming.

1174 poster

UTILISING A HYPOXIA-INDUCIBLE SUICIDE GENE THERAPY STRATEGY IN COMBINATION WITH RADIATION TO TARGET PROSTATE CANCER CELLS

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Purpose/Objectif: Hypoxia is an inevitable feature of solid tumours and a common cause of treatment failure. We have chosen to exploit the hypoxic nature of prostate tumours to gain a therapeutic advantage. Gene therapy targeted to hypoxic tumour cells may allow selective killing of malignant cells. The induction of gene expression under hypoxic conditions is governed by the activation of hypoxia- inducible factor 1 and its subsequent binding to hypoxia responsive elements (HREs). Tandem repeats (5) of the HREs of the oxygen-responsive gene vascular endothelial growth factor (VEGF) were cloned upsteam of the cytosine deaminase (CD) gene. This construct drives the expression of this prodrug activation enzyme, which converts inactive 5-fluorocytosine (5-FC) to active 5-fluorouracil (5-FU), allowing selective killing of vector containing cells. 5-FU is also a radiosensitising agent, so specific expression of this agent in prostate cancer cells could also potentiate radiotherapy approaches in prostate cancer. This study therefore aimed to assess the effect of combining this hypoxia-induced suicide gene therapy with ionising radiation, delivered as single or fractionated doses.
Materials/Methods: Prostate cancer cells (22Rv1) were transfected with three plasmids; pCMV-CD (positive control), p0HCD (negative control) and pH5V-CD (test vector). The cells were then treated in one of four ways. One group was treated in air with radiation alone (2Gy in two fractions). Three groups were treated in hypoxia with either 5-FC treatment alone, 5-FC treatment plus 2Gy in a single fraction or 5-FC treatment plus 2Gy in a split dose (1times 2Gy). Percentage cell growth was then assessed.
Results: A cytotoxic effect was observed with the combination of 5-FC and radiation treatment. Radiation did not, however, induce the increased cytotoxicity expected. Radiation given in a split dose was more effective than when given in a single dose. At clinical concentrations of 5-FC (1mM), the use of pH5V-CD did not result in a large difference in cytotoxicity between the treatment conditions, yet at larger doses a variation was seen.
Conclusions: The combination of hypoxia-induced suicide gene therapy has the potential to help overcome hypoxia in radiotherapy. Its use clinically could lead to a reduction in late side effects as well as the possibility of introducing new treatment schedules.

Posters Radiosensitisers

1175 poster

AT-101, A SMALL MOLECULE INHIBITOR OF BCL-2 FAMILY PROTEINS, ENHANCES RADIATION-INDUCED APOPTOSIS IN HNSCC

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Background: Bcl-X_L and Bcl-2 are important inhibitors of apoptosis and are frequently overexpressed in a variety of human tumors including head and neck squamous cell carcinomas (HNSCC). Increased levels of Bcl-X_L and Bcl-2 confer radio- and chemoresistance and are associated with poor clinical outcome. AT-101 ((-)-gossypol) is a pan-Bcl-2 inhibitor of Bcl-X_L, Bcl-2, and Mcl-1 and induces apoptosis in a large series of tumor cell lines. Furthermore, it has been shown to overcome cisplatin resistance in HNSCC *in vitro*. We investigated the potential of AT-101 to enhance radiation-induced apoptosis in HNSCC cell lines.
Materials/Methods: Four human HNSCC cell lines (UM-SCC-11B, UM-SCC-14C, UM-SCC-22A and VU-SCC-OE) were treated with increasing doses of AT-101, radiation and different combinations of both. FACS analysis and Quantitative nuclear Fluorescence Morphology assay were used to quantify apoptosis. The expression levels of relevant Bcl-2 family proteins were measured by Western blot and correlated with cellular sensitivity to AT-101 and radiation. The type of interaction between radiation and AT-101 was evaluated by isobolographic analysis.
Results: Both radiation and AT-101 induce apoptosis in a time- and dose-dependent manner. ED50 values for radiation and AT-101 range from 4 to 15 Gy and 16.5 to 49 μM, respectively. Because all cell lines tested markedly express the anti-apoptotic proteins Bcl-X_L and Bcl-2, and also the pro-apoptotic proteins Bad and Bax, a clear correlation between expression levels and sensitivity could not be determined. When radiation was combined with AT-101, especially when AT-101 was given 24 hours after radiation, apoptosis was strongly enhanced. Isobolographic analysis revealed a synergistic interaction between both stimuli.
Conclusions: AT-101 enhances radiation-induced apoptosis in human HNSCC cells. The sequence of delivery appeared to be important, with radiation given prior to AT-101 being the most effective schedule. Inhibition of the anti-apoptotic functions of Bcl-X_L and Bcl-2 by AT-101 represents a promising strategy to overcome resistance to radiotherapy.

1176 poster

CI-1033, A PAN-ERBB TYROSINE KINASE INHIBITOR, ENHANCES THE RADIATION RESPONSE OF HUMAN GLIOMA CELL LINES

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Purpose/Objectif: EGFR is a member of the ErbB family of growth factor receptors. Amplification and overexpression of EGFR frequently occur in malignant gliomas. Radiation can directly activate ErbB receptor signaling and this activation forms part of the survival response to ionizing radiation. Increased EGFR expression has been demonstrated to correlate with relative radioresistance in patients with astrocytic gliomas and glioblastomas. The pan-ErbB tyrosine kinase inhibitor CI-1033 has been shown to achieve radiosensitization in several cell types, including breast and colon. The present study is aimed at determining whether CI-1033 can enhance radiation-induced cell death of human glioma cell lines in vitro.

Materials/Methods: A panel of human glioma cell lines (D384, Gli-6, U251 and U87) were used for this study. ErbB expression levels were determined by Western blotting and quantitative RT-PCR (Taqman). The effect of CI-1033 on proliferation was examined by cell growth assays and the radiosensitizing potential was assessed by clonogenic assays.

Results: CI-1033 (0-25 μM) inhibited proliferation of all cell lines in a dose- and time-dependent manner, with significant cytotoxic effect at doses higher than 10 μM. CI-1033 treatment of D384 (5 μM), U251 (6 μM) and U87 (8 μM) cells 24 hours before radiation did not result in radiosensitization, however addition of 8 μM CI-1033 resulted in a clear radiosensitizing effect in Gli-6 cells. If CI-1033 incubation was prolonged to 48 hours prior to irradiation, a marked enhancement of radiation-induced cell death of D384 cells was demonstrated.

Conclusions: CI-1033 clearly enhances radiation-induced cell death of Gli-6 and D384 cells. The timing of CI-1033 addition seems important and will be investigated in more detail.

1177 poster

GOSSYPOL ACTIVATES THE SAPK/JNK PATHWAY AND ENHANCES RADIATION-INDUCED APOPTOSIS

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Purpose/Objectif: Gossypol is a small molecule inhibitor of Bcl-X_L and Bcl-2 and induces apoptosis in a wide range of tumor cell lines. Moreover, Gossypol has been shown to enhance chemotherapy- and radiation-induced cytotoxicity *in vitro* and *in vivo*. Racemic (±)-Gossypol has two enantiomer forms: R-(-) and S-(+). AT-101, a derivative of R (-)-gossypol, is a pan-Bcl-2 inhibitor of Bcl-2, Bcl-W, Bcl-X_L and Mcl-1 that had previously been shown to be more potent than racemic gossypol as a single agent or in combination with chemo- or radiotherapy in vitro and in vivo. Because activation of the SAPK/JNK pathway is important for apoptosis induction by a variety of different stimuli, we investigated the role of this signaling cascade in AT-101-induced apoptosis.

Materials/Methods: Human Jurkat T and U937 leukemic cells were treated with increasing doses of AT-101, radiation and the combination. Apoptosis was quantified by FACS analysis; SAPK/JNK activity was measured by Western blot; isobolographic analysis was performed to characterize the interaction between radiation and AT-101.

Results: AT-101 induces apoptosis in a time- and dose-dependent fashion, with ED50 values of 2 and 1.5 mM in Jurkat T and U937 cells, respectively. Like radiation, AT-101 rapidly activates SAPK/JNK which can be blocked by the kinase inhibitor SP600125. To demonstrate the critical role of SAPK/JNK activation in AT-101-induced apoptosis, U937 cells stably expressing the dominant negative mutant of c-Jun, TAM-67, were used. In these U937-TAM-67 cells both radiation- and AT-101-induced apoptosis was significantly reduced as compared to vector-only controls. By combining radiation and AT-101, in particular radiation given 24 hours before AT-101, apoptosis was strongly enhanced. Isobolographic analysis revealed a synergistic interaction between both stimuli.

Conclusions: AT-101 strongly enhances radiation-induced apoptosis in human leukemic cells. Our studies also indicate a requirement of the SAPK/JNK pathway in this response. This type of apoptosis modulation may lead to the development of new effective combination therapies.

Posters Signal Transduction

1178 poster

A ROLE FOR THE LIM-ONLY FOCAL ADHESION PROTEIN PINCH1 IN RADIATION SENSITIVITY

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Purpose/Objectif: Molecules of focal adhesions including integrins and their signaling cascades participate in the regulation of cell survival and proliferation. Pinch1 is a recently identified adapter protein of the integrin b1/integrin-linked kinase/a-parvin signaling cascade. To analyze the role of Pinch1 in radiation sensitivity, pinch$1^{fl/fl}$ and pinch$^{-/-}$ mouse embryonic fibroblasts (MEFs) were irradiated on different substrata, in suspension or in three-dimensional Matrigel cell cultures.

Materials/Methods: Clonogenic survival was determined in irradiated (0-15 Gy) cell cultures growing without adhesion (suspension), under adhesion (fibronectin, 2D-Matrigel, poly-l-lysine) or in 3D-Matrigel. Expression and/or phosphorylation of Pinch1, Akt, GSK3b, FAK, Paxillin, p130Cas und Src were evaluated after 2 Gy using Western blotting. For evaluation of adhesion and spreading, laser scanning microscopy was employed under the different conditions at various time points.

Results: pinch$1^{-/-}$ MEFs showed a significant ($p<0.01$), substratum-independent enhancement in radiation sensitivity at radiation doses ^{3} 2 Gy relative to pinch$1^{fl/fl}$ MEFs. 3D-Matrigel further increased radiation survival by over 10-fold in both cell lines. Intriguingly, the significant difference in radiation survival between pinch$1^{fl/fl}$ versus pinch$1^{-/-}$ MEFs remained unchanged in 3D. Irradiation in suspension led to a slightly reduced clonogenic survival in both cell lines. Concerning protein and phosphorylation analysis, pinch1 knockout status stabilized FAK, p130Cas and Paxillin in suspension. While phospho-Akt was induced in 3D and after irradiation, Paxillin, p130Cas and GSK3b showed strong dephosphorylation in 3D and less radiation-mediated activation relative to 2D. Cell adhesion and spreading of pinch$1^{-/-}$ MEFs was evidently derogated compared to pinch$1^{fl/fl}$ MEFs.

Conclusions

The data indicate the focal adhesion protein Pinch1 as strong modu-

lator of cell survival after radiation-induced genotoxic injury. Future studies will elucidate the impact of this molecule on adhesion-mediated radioresistance of tumors or radioprotection of normal tissue.

1179 poster

BORIS EPIGENETICALLY INFLUENCES SURVIVAL TRANSCRIPTION FACTORS

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Purpose/Objectif: Many pro-survival factors which are known to be oncogenes are used by tumor cells to evade the cytotoxicity of anticancer therapies, thus they are potential molecular targets. CTCF and a recently described paralog (BORIS) are 11-zinc finger (11-ZF) motif DNA-binding insulator proteins that appear to regulate aspects of proliferation, enhancer blocking, growth, X-chromosome inactivation and imprinting. While these proteins share the same 11-ZF motif, BORIS is expressed only in primary spermatocytes where it is believed to function in germ line epigenetic reprogramming. In addition, BORIS is also expressed in a number of cancers including breast suggesting a possible role in tumor cell pro-proliferation and pro-survival pathways.

Materials/Methods: Immunohistochemical analysis was used to demonstrate expression and localization of BORIS. High-throughput yeast two-hybrid assay was used to identify several BORIS interacting protein. Immunoprecipitation (IP) was used to confirm these interactions. Finally, experiments were also done to assess the oncogenic and/or transforming potential of BORIS by constitutively overexpressing BORIS using the CMV-BORIS plasmid in NIH/3T3 mouse fibroblasts.

Results: BAT3 (BAG-6), a nuclear protein involved in apoptosis was identified to interact with BORIS along with several proteins. BAT3 is the human homolog of Scythe that is necessary for normal development, likely due to the normal regulation of apoptosis and proliferation. Immunoprecipitation confirmed that BORIS physically interacts with and binds BAT3. Transient overexpression of BORIS upregulates a reporter plasmid containing only three CTCF-binding sites up stream of the tk-promoter. In addition, transient expression of BAT3 activates CTCF-tk-LUC and co-transfection of both CMV-BORIS and CMV-BAT3 further increased luciferase activity. Immunohistochemical analysis demonstrates that BORIS and BAT3 are co-expressed and co-localized in the nucleus. No distinct foci formation, which indicates cell transformation, was observed in overexpressed BORIS cell line. Since our results suggest that expression of BORIS may also require expression of BAT3, these experiments are being repeated in cells genetically altered to overexpress both. Growth curves and clonogenic survival curves showed no difference in survival after exposing exogenous agents in cells overexpressing BORIS versus control cells.

Conclusions: These results suggest BORIS is overexpressed in tumors and that BAT3 may be required for its role in transformation and tumor cell resistance. Since BORIS is a testis-specific protein it may be a promising molecular target with a favorable therapeutic index due to the testis-restricted expression of this gene. Furthermore, these experiments strongly suggest that BORIS can activate CTCF-dependent gene expression and further suggests, but does not prove, that BAT3 is involved in the process.

1180 poster

INTERACTION OF THE RADIOPROTECTOR O-PHOSPHO L-TYROSINE (PTYR) WITH THE EPIDERMAL GROWTH FACTOR RECEPTOR (EGFR)

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Purpose/Objectif: The aim of this study was to investigate the molecular mechanism of the new radioprotector O-phospho-L-tyrosine (pTyr) in different cell types after irradiation. Moreover we want to assay the effect relationship between pTyr and the EGFR.

Materials/Methods: Nuclear proteins were isolated and seperated by SDS-page and detected by specific antibodies. Cellular survival was determined by colony formation assays and DNA-repair was quantified by the amount of residual γ H2AX-foci.

Results: Based on earlier studies describing the Bowman Birk Protease inhibitor (BBI) and BBI-derived peptides as radioprotectors, we investigated the radioprotective potential of pTyr in cultured human cells with different TP53 status. We observed that pTyr shows a radioprotective effect in clonogenic assay for cells with TP53 wild type status, when exposed to ionizing radiation. This effect could not be observed in transformed or human tumor cell lines characterized by mutated or functional inactivated TP53. As shown in the present study treatment with pTyr induces an increase in nuclear EGFR protein. After such a pTyr pre-treatment we were also able to observe an increased phosphorylation of EGFR at T654. Interestingly, this phosphorylation could be detected within the nuclear protein fraction predominantly and correlates with the increase of EGFR protein in the cell nucleus. Thus, we hypothesize, that T654 phosphorylation is involved in regulation of nuclear EGFR transport.The molecular function of nuclear EGFR is not resolved, but the observation that EGFR translocation into the nucleus can be triggered by several genotoxic treatments, e.g. radiation, argues for a function during cellular stress response. The increase of nuclear EGFR protein after pTyr treatment also correlates with increased DNA-PK protein. Although the exact interaction of EGFR and DNA-PK has to be resolved in future experiments, we can provide evidence, that pTyr pre-treatment stimulates DNA-repair processes in irradiated cells. Quantification of residual DNA-damage 24 hours after irradiation, indicated a significant reduction of γ-H2AX-foci after pre-treatment with pTyr .

Conclusions: Taken together the presented data suggest that pTyr pre-treatment interacts with the accumulation and interaction of nuclear EGFR and DNA-PK and can thus stimulate DNA-DSB repair processes.

1181 poster

IRRADIATION LEADS TO SENSITIZATION OF HEPATOCYTES TO TNF-ALPHA- MEDIATED APOPTOSIS BY UPREGULATION OF IKB EXPRESSION

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Purpose/Objectif: Due to the danger of development of radiation-induced-liver-disease, the liver is a dose-limiting organ in abdominal irradiation. However, hepatocytes in primary culture are highly radioresistant. In previous studies, we showed that irradiated hepatocytes undergo apoptosis when cultured in presence of TNF-a whereas TNF-a has no effect on viability of non-irradiated hepatocytes. The aim of the present study was to reveal pathophysiological signalling responsible for radiation-induced sensitization of hepatocytes to TNF-a mediated apoptosis.

Materials/Methods: Hepatocytes were isolated from rats and irradiated with doses of 2, 8, and 25 Gy on the first day after isolation. Thereby, hepatocytes were additionally exposed to TNF-a (100 U/ml; 6, 12, and 18 hours after irradiation) with or without administration of IkB antisense oligonucleotides or transfection of IkB expression

vector. Apoptosis was measured by annexin staining and FACS analysis. Western Blot analysis was used to detect IkB expression on the protein level. Active NFkB in nuclear extracts was detected by EMSA. Activities of caspase 3, 8, and 9 were measured by ELISA.
Results: Whereas irradiation alone did not lead to apoptosis of hepatocytes, TNF-a administered 6 or 12 hours after irradiation lead to a statistically significant increase of radiation-induced apoptosis. However, TNF-a administered 18 hours after irradiation had no effect on apoptosis of hepatocytes. Western Blot analysis revealed an up-regulation of IkB in irradiated hepatocytes compared to sham-irradiated controls. As expected, active NFkB was down regulated simultaneously.Administration of IkB-antisense oligonucleotides to hepatocytes prior to irradiation significantly inhibited occurrence of apoptosis after TNF-a administration. However, overexpression of IkB in hepatocytes was not able to sensitize these cells to TNF-a mediated apoptosis. In isolated hepatocytes, activities of caspase 3, 8, and 9 were increased due to irradiation and TNF-a administration. By IkB antisense oligonucleotides, this effect could be abrogated for caspase 3 and 9 but not for caspase 8.
Conclusions: IkB upregulation and consecutive downregulation of active NFkB are required for TNF-a mediated apoptosis of irradiated hepatocytes. However additional changes besides caspase 8 activation are required for initial induction of the proapoptotic signalling of TNF-a.

1182 poster

LACK OF CORRELATION BETWEEN RADIOSENSITIVITY AND INHIBITION OF AKT ACTIVATION BY PROTEIN KINASE INHIBITORS IN GLIOBLASTOMA CELLS.

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Purpose/Objectif: The PI3K/Akt signalling pathway is involved in proliferation and survival and is constitutively activated in many cancers owing to lack of the endogenous antagonist PTEN. Therefore, it has been suggested that inhibitors of the PI3K/Akt pathway may be particularly efficient in sensitizing such cells to cytotoxic therapy. The purpose of this work was to test the relation between Akt activation and modulation of radiosensitivity by protein kinase inhibitors in glioblastoma cells lacking PTEN.
Materials/Methods: U87MG, U251MG and U343MG human glioblastoma cell lines were used. Different concentrations of Wortmannin (WM), erlotinib (Roche Diagnostics, Penzberg, Germany) and AG1478 were dissolved in DMSO and added 1h before irradiation, and DMSO was added to the controls. Phosphorylation of Akt was determined by Western blotting. The sensitivity to 6 MV x-rays was determined by the colony formation assay and analysed by the linear-quadratic model. Statistical analysis was performed by JMP 5.0 statistical software (SAS Institute, Cary, N.C.).
Results: Akt was constitutively activated in all three cell lines and irradiation alone did not significantly increase the level of P-Akt further. Phosphorylation of Akt could be inhibited by 50-500 nM WM in U87 and U251. By contrast, sensitisation to radiation required a much higher concentration (20 µM) of WM. In U343 cells, the effect of WM on P-Akt was biphasic with partial down-regulation by 50-500 nM. However, at these concentrations a small but significant radioprotective effect was observed. EGFR inhibitors had no effect on constitutive Akt-phosphorylation but caused a moderate enhancement of the radiosensitivity in U251 which did not depend on the presence of the inhibitor during irradiation. Instead, the enhancement appeared to be associated with a reduction in the proliferation rate during colony formation.
Conclusions: Down-regulation of constitutive Akt-activation by low concentrations of WM did not confer radiosensitisation which required high, non-specific concentrations in these cells. Thus, a critical role of constitutive Akt activation in mediating radioresistance was not confirmed under the present conditions. Conversely, inhibiting upstream receptor tyrosine kinase activity enhanced the radiosensitivity without affecting P-Akt. Together, these data suggest an uncoupling of survival from Akt-activation in these cells. We are presently studying downstream effectors of Akt and the role of the MAP kinase signalling pathways.

1183 poster

LOSS OF DNA BINDING ACTIVITY OF MULTIPLE TRANSCRIPTION FACTORS IN CHRONIC RADIATION DAMAGE OF THE LUNG

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Purpose/Objectif: Radiation damage leads to long term effects on cell proliferation and tissue structure. Since transctiption factors are the central regulators of gene expression, we tested the time course of the DNA binding activities of multiple transcription factors in a model of chronic radiation damage to the lung.
Materials/Methods: The right lungs of female Fischer rats were irradiated with a dose of 20 Gy. DNA binding activity was determined by Electrophoretic Mobility Shift Assays (EMSAs) using oligonucleotidess with consensus DNA binding sites for AP-1, Sp1, NF-kappaB, c-Myc, CREB and ARNT. Protein expression in lung cells was determined with Immunohistochemistry.
Results: In this model, pulmonary fibrosis develops 8 weeks after irradiation. Whereas DNA binding activity of Sp1, c-Myc, CREB and ARNT remain stable until four weeks after irradiation, AP-1 and NF-kB show an increase in DNA binding activity. The DNA binding activity of NF-kappaB is further increased until 8 weeks after irradiation. In contrast, the DNA binding activity of AP-1, Sp1, c-Myc, CREB and ARNT is strongly decreased at time points after four weeks. In contrast, the proteins that are part of the DNA binding complexes are still detectable in the cells.
Conclusions: The tissue reorganization in the long term response to irradiation is accompanied by dramatic changes in the DNA binding activity in a several transcription factors. There is an imbalance between increased DNA binding activity of NF-kappaB and the decreased activity of the other factors studied. Therapeutic approaches to normalize this imbalance should alleviate the radiation induced damage to normal tissue.

Posters Skin Cancer

1184 poster

HDR BRACHYTHERAPY WITH STANDARDIZED SURFACE APPLICATORS (THE LEIPZIG APPLICATOR) AS AN ALTERNATIVE RADIOTHERAPY TREATMENT FOR SUPERFICIAL MALIGNANT SKIN LESIONS

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Purpose/Objectif: More than 90% of skin cancers develop in exposed areas such as the head, neck and extremities. Most non-melanomatous skin cancers begin as small superficial lesions. These lend themselves to successful treatment using variety of modalities. The principal objective of treatment is the complete regression of the lesion, while minimizing functional and cosmetic impairment.

The aim of this study is to investigate the use of HDR surface applicators as an alternative radiotherapy modality for the treatment of skin lesions.

Materials/Methods: Only patients with histologically proven epithelial skin cancer, in various sites (face, scalp and lower extremities) were included. Treatment was delivered by HDR Brachytherapy (Ir-192), with standardized Leipzig surface applicators. The appropriate applicator was fitted in thermoplastic casts, dimension chosen so that the lesion fell within 80% of the nominal field diameter; thus the maximum lesion size is about 2.5 cm in diameter. India ink was used to verify the planning target volume (PTV), (lesion plus 0.5 cm margin) coverage. A total dose of 40 Gy (5 Gy twice weekly for four weeks) was prescribed to the surface. TLD chips measurement were used twice during the course of treatment. Acute skin toxicity was evaluated twice weekly during radiation using the modified RTOG morbidity criteria. Local response was monitored at periodic intervals after treatment completion.

Results: Between January 2003 to January 2006, 20 patients with a total of 21 lesions were treated. Eleven male and nine females, with a median age of 69 years. Out of twenty one lesions treated, twelve were squamous cell carcinoma and eight were basal cell cancers. Ten lesions involved the nose, six in face and scalp, ear pinna in two and three in the lower extremities. Eleven patients were treated for pathological positive margins, close margin in two and seven with gross disease. After a median follow-up of 18 months, nineteen lesions underwent complete remission with excellent cosmesis and partial remission in two. Grade 1 acute skin toxicity was detected in sixteen patients and grade 2 in four.

Conclusions: HDR Brachytherapy (Ir-192), with standardized surface applicators (Leipzig applicators) offer an alternative in treatment of small superficial skin carcinomas. Patients' setup and reproducibility were accurate and treatment time was short which added great convenience for the patients.

1185 poster

HIGH DOSE RATE BRACHYTHERAPY (HDRB) AND NEW TREATMENT SCHEDULE IN SKIN CANCERS: 4 YEARS RESULTS.

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Purpose/Objectif: To evaluate outcome and toxicity in patients (pts.) treated with high dose rate brachytherapy, and with minimum follow up of 48 months.

Materials/Methods: From August 1999 to February 2005, 96 consecutive pts. with skin cancer (20% squamous cell) were enrolled in this perspective study: HDRB treatment consisting of twice-daily fractionation of 350 cGy each, 6 hour apart final dose delivered 49 Gy as esclusive modality or postoperative treatment for positive margins; as postoperative treatment for squamous cell with clear margins the final dose delivered was 42 Gy. To provide the maximum coverage of the tumor the implants were performed with afterloading catheters embedded in personalized surface molds or interstitial implant planned with a semi-3-D technique aided by simulator. Radiopaque markers for target definition were obbligatory. The follow up consisted in clinical examination. We studied the pts. with a minimum follow up of 4 years. For failure cases a rewiew of dosimetry was performed.

Results: The eligible pts. were 71, the median follow up 65 months (range 48-72). The cosmetics results were poor in 5% of cases; the most important toxicity was a telangectasia of the skin. The local relapse were 10% (7), for 2 of these cases a full-dose reirradiation was performed without severe toxicity. The cases of missing target 4% (3).

Conclusions: This treatment schedule is effective and can be used in skin cancers with a good compliance of the treated pts. HDRB is a tecnique with a good learning curve. To test new treatment schedules clinical settings are ongoing. Actually this schedule is the standard for skin cancer in our Center.

1186 poster

MERKEL CELL CARCINOMA; TREATMENT RESULT AND PROGNOSTIC FACTORS IN 23 PATIENTS

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Purpose/Objectif: To report treatment results of the rare neuroendocrine Merkel cell carcinoma of the skin and to identify prognostic factors for survival.

Materials/Methods: Retrospective analysis of treatment results of 23 patients (pts), treated with surgery (S) and/or radiotherapy (RT) and/or chemotherapy (CT) in our Centre from 1990-2004 with curative or palliative intent Patient characteristics: Age: 55 to 93 years (mean 76). Sex: female 12, male 11.

Stage (Yiengpruksawan) Ia: 9 pts, Ib: 7 pts, II: 6 pts, III: 1 pt.

Location of tumor: head and neck 18 pts (78 %), extremities 3 pts (13%), trunk 1 pt (4%), no primary tumor 1 pt (4%).

Treatment characteristics: 17/23 pts were treated with curative intent.

S consisted of a primary local excision in 18 pts.R0, R1, or R2 resections were performed in 7, 7 and 2 pts respectively. In 2 pts surgical margins were not recorded. Regional S: 8 pts, 4/8 primarily.

Local RT:13 pts, 9/13 postoperatively (postop). Regional RT: 11 pts, 6/11 postop. Locoregional RT : 7 pts. Local doses: 7-60 Gy in 4-30 fractions of 1.8-3 Gy . Regional doses: 30-60 Gy in 10-30 fractions of 2-3 Gy.

Palliative CT: 5 pts (Cyclofosfamide, Doxorubicin and Etoposide in 3 pts and Etoposide in 1 pt, in 1 pt the type of CT was not recorded).

Results: For all stages: actuarial median overall survival (OS) 25 months, 1 yrs OS: 76%, 2 yrs OS: 53%, 5 yrs OS 34%. Univariate prognostic factors for OS were: stage (I vs II / III, p= 0.003), tumorsize (≤ 2 cm vs > 2 cm, p= 0.05), tumor location (H&N vs extremities, p=0.003), local or regional recurrence (p=<0.001).

14/23 (60%) pts had a local or regional recurrence, 9/16 stage I and 5/7 stage II or III.

Conclusions: Merkel cell carcinoma is an aggressive tumor, with a high chance of local and regional recurrence in all stages.

Poor prognostic features for OS are high stage (II and III), tumor size >2 cm, local or regional recurrence.

Also stage I warrants optimal locoregional treatment to improve OS. This means in our opinion: if possible, radical local surgery followed by postoperative radiotherapy with a localregional dose of 50 Gy and a local boost up to 60 Gy. The role of chemotherapy is not clear but in fit patients with poor prognostic features chemoradiation is to be thought of.

1187 poster

RADIOTHERAPY PRESERVES FINGERS IN THE MANAGEMENT OF SUBUNGUAL SQUAMOUS CELL CARCINOMAS; NO NEED FOR AMPUTATION.

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Purpose/Objectif: To evaluate the role of primary radiotherapy in the local management of subungual squamous cell carcinoma (SSCC) as an alternative to amputation of the affected finger.

Materials/Methods: We irradiated 12 fingers in 12 patients; 3 females and 9 males, median age 71 years (range 42-82 years). Histology showed SSCC is all: 8 patients grade I, 2 patients grade II and 2 patients grade III. In 8 patients the thumb was affected. Radiotherapy was applied in various regimens with curative intent; median dose 54Gy (range 49-66Gy), median fraction size 3Gy (range 2-3.5Gy). Median follow-up was 29 months (range 4-156 months).
Results: Local control was achieved in 11 patients (92%); 1 patient showed a recurrence after 11 months, was salvaged by amputation of the finger and died 4 years later of an unrelated cause. During follow-up none of the patients experienced regional or distant failures. Function was preserved in all but 1. For this patient an amputation was performed because of radiation necrosis of the distal phalanx; histology showed no residual tumour.
Conclusions: Radiotherapy is an adequate management for SSCC with a local control of 92%. Amputation of the finger can be preserved for the rare local failures and/or complications.

1188 poster

SUPERFICIAL HYPERTHERMIA COMBINED WITH HYPOFRACTIONATED RADIOTHERAPY OF MALIGNANT MELANOMA METASTASES TO SKIN AND LYMPH NODES

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Purpose/Objectif: Effectiveness of different treatment modalities (excluding surgery) of malignant melanoma metastases is very limited. Because surgery is not always accepted by patients or possible to perform, some others ways of treatments, as hyperthermia and radiotherapy combination are used.
Purpose of this study is an evaluation of combined radiohiperthermia in the treatment of skin and lymph nodes malignant melanoma metastases.
Materials/Methods: Material comprises of 10 skin and 11 lymph nodes melanoma metastases (13 patients) treated with combined superficial hiperthermia and irradiation. Tumor diameter before the treatment varied from 0,5 to 7 cm (mean 2,9). All patients were treated using three 1 hour hiperthermia sessions and three 9 Gy radiation doses delivered within 8 days. Gaps between hiperthermia and radiotherapy sessions were shorter than one hour. Follow up period varied from 1 to 18 months (mean 4.6). Patients were examined in the day of treatment completion, 2 and 6 weeks later and next every three months. The skin reaction and tumor regression were evaluated. Impact of different biological factors for skin reaction and treatment result were checked.
Results: The most frequent skin reaction was erythrema (51% of cases in the day of treatment end) and blisters (19% of cases 6 weeks after the treatment). Means of tumor diameter 0.5, 1.5, and 4.5 months after the treatment were 2.3, 2.3 and 2.4 cm respectively. The biggest percentage of complete regressions was observed 1.5 and 4.5 months after the treatment, 33.5% and 43% respectively. Significant dependencies between skin reaction 2 weeks after the treatment and red blood cells count in this time and before the treatment were found.
Conclusion: The combined radiohiperthermia is safe and effective treatment modality of superficial melanoma metastases and could be an valuable alternative for palliative surgery.

1189 poster

TECHNICAL FEASIBILITY OF CT ASSISTED 3D HDR BRACHYTHERAPY IN THE TREATMENT OF SKIN CANCERS

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Purpose/Objectif: Cross-sectional image based brachytherapy becomes more and more popular in the treatment of certain type of cancers especially at the gynaecological and urological sites. Since brachytherapy plays a crucial role in the curative treatment of skin cancers our goal was to introduce the feasibility of 3D CT assisted HDR brachytherapy (HDR-BT) in the complex treatment of these tumors using individual molds.
Materials/Methods: Between December 2003 and January 2006 20 patients (9 male, 11 female) with 21 basal cell or squamous cell carcinomas on the face were treated with 3D CT assisted HDR-BT. Mean age was 70 years (range 59-85). 18 patients received brachytherapy as a boost treatment after external beam radiotherapy (EBRT), while in the remaining 2 cases brachytherapy was used alone. A total of 8 patients were irradiated as first-line therapy, while the remaining 12 patients had local recurrences or incomplete R1 resection. In all cases individual molds were constructed to get a well reproducible, fix geometric arrangement for the catheters. After clinical placement of the moulage planning CT was performed. After delineation of the PTV and organs at risk 3D conformal planning was carried out using dose point optimization. The average dose of EBRT was 41 Gy (39,6-50,4 Gy). The mean of HDR-BT dose administered was 23 Gy (8-50,4 Gy) with a mean of 13 (4-28) fractions. The average fraction size was 1,9 Gy (1,6-2,5 Gy).
Results: All patiens with macroscopic tumors had complete remission. During the median of 14,2 months (range 2,5-26) follow up period there were no local recurrences as well as regional or distant failure. According to the RTOG scoring system no grade 3-4 acute and late side effects were observed. The reproducibility of the catheters and the treatment tolerance were excellent in all cases. The average time needed for treatment planning was 20 minutes, while the total time of brachytherapy procedures in the daily routine was only 15 minutes.
Conclusions: In the treatment of skin cancers HDR-BT boost via custom made molds combined with CT based 3D treatment planning seems to be feasible, safe and accurate facilitating its application as a sole modality. Individual, precise and well reproducible placement of the catheters allows appropriate target coverage with individual sparing of critical organs at the same time. Higher number of patients and longer follow up are needed to properly establish local tumor control, functional and cosmetic results.

Posters Stereotactic Radiotherapy

1190 poster

A DANISH PHASE II TRIAL ON STEREOTACTIC BODY RADIOTHERAPY FOR COLO-RECTAL METASTASES

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Purpose/Objectif: Surgical resection and radiofrequency ablation are widely used in the treatment of colo-rectal metastases (CRM).

Stereotactic body radiotherapy (SBRT) has been shown to be effective in treatment of limited stage lung cancer and also for CRM it may be an alternative to the more widely used treatments.
Materials/Methods: The effect and toxicity of SBRT was tested in the treatment of patients with CRM in a phase II trial conducted in two Danish university radiotherapy units. Sixty-five patients with a median of 2 (range 1-6) and a total number 142 CRM in liver, lung or suprarenal gland were included into the trial. Sixty-one patients had metastases in one organ and 4 patients had metastases in 2 organs. All patients were considered inoperable by a multi-disciplinary hepato-biliary team. The patients were immobilized by the Elekta stereotactic body frame (SBF) or a custom made body frame. SBRT was given on linear accelerator with standard multi-leaf collimator. Central dose was 15 Gy x 3 and overall treatment time 5-8 days.
Results: Local control 2 year after treatment was 79% in an individual tumour based analysis. However, due to development of new metastases, only 19% were without progression after 2 years. Overall survival was 36% and 14% 2 and 4 years after SBRT, respectively. No difference in survival was observed between patients treated for hepatic- or extra-hepatic CRM and neoadjuvant chemotherapy did not influence survival. One patient died 7 weeks after SBRT due to hepatic failure, 1 patient had a colonic and 2 patients duodenal ulceration caused by the treatment. Grade> 2 toxicity was observed in 47% of the patients within 6 months after SBRT. Most frequent side effects were nausea, diarrhoea, pain and skin reaction.
Conclusions: In conclusion, SBRT in patients with CRM results in a high probability of local control and acceptable survival rate. The toxicity after SBRT of CRM is moderate.

1191 poster

ACOUSTIC NEUROMA: TOXICITY AND LOCAL CONTROL WITH FRACTIONATED STEREOTACTIC RADIOTHERAPY

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Purpose/Objectif: Radiosurgery (RS) in acoustic neuromas (AN) is limited to small size tumours due to the neighbouring to cranial nerves and other cranial structures. The complications rates depend on total dose and target volume. Fractionated stereotactic radiotherapy (FSRT) combine the precision offered by RS and the fractionated radiotherapy radiobiological advantages. The aim of the present study is to analyse toxicity and local control in patients with AN who have been treated by FSRT.
Materials/Methods: Between May 1998 and June 2005 FSRT, 35 patients were treated. 13 were male and 22 female. Median age was 57 years. Nine patients (26%) had an intracanalicular tumour, three (8%) an extracanalicular one and twenty-three (66%) both intra- and extracanalicular. Median tumour size was 17mm (range 6-25mm). FSRT was performed as initial treatment in 32 patients and 3 patients were relapse after surgery. The total dose administered was 56 Gy in fractions of 2 Gy in five fractions per week. 22 of 35 patients preserved useful hearing before FSRT. The median follow up was 37 ± 24 months. Radiological control and hearing preservation rates were calculated by the Kaplan-Meier method. Toxicity was evaluated by CTC 2.0 scale.
Results: Radiological control rates (evaluated by MRI) were 96%. In 58% patients, tumour decreased and in 38% of the patients were a stabilization of the disease. Mean time free of progression was 36 ± 25 months and both 3-year and 5-year actuarial rates were 94.3% ± 4%. After the treatment with FSRT, 46% patients referred a regression in their symptoms. In our series, acute cutaneous toxicity G1 appears in 3% patients and no patients developed toxicity G≥2. Acute CNS toxicity G1 in 20% and G2:3%, no toxicity G≥3 was observed. Chronic CNS toxicity G1: 12%, there wasn't chronic CNS toxicity G≥2. Facial and trigeminal G1 neuropathies were developed in 4% patients, these neuropathies were temporarily and disappear in 19 months (R: 10-26 months) and no G≥2 neuropathies were observed. Useful hearing preservation rates were 77% and 3-year and 5-year actuarial preservation rates were 90% ± 6.5% and 64%± 16% respectively.
Conclusions: FSRT is an effective and well-tolerated treatment for acoustic neuroma and provides low toxicity rates and non permanent V and VII neuropathies. Hearing preservation rates are better than those reported with surgery.

1192 poster

ACUTE PULMONARY MORBIDITY FOLLOWING STEREOTACTIC BODY RADIOTHERAPY FOR NON-SMALL CELL LUNG CANCER: A PROSPECTIVE STUDY OF ITS ASSOCIATION WITH DOSE-VOLUME HISTOGRAM PARAMETERS

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Purpose/Objectif: Stereotactic body radiotherapy (SBRT) is acknowledged as an effective treatment for patients with medically inoperable NSCLC. It involves the delivery of radiation doses of high biological potency to patients with frequent pre-irradiatory compromise of pulmonary function. Care must be taken for pulmonary toxicity not to outbalance the benefits of tumor control. If they predict the risk of pulmonary toxicity, DVH parameters may serve as tools for optimised dose planning and patient selection.
Materials/Methods: The study population consisted of 28 patients with medically inoperable stage I NSCLC. Between 2000 and 2003, the patients received SBRT at our department with a central dose of 45 Gy delivered in 3 fractions in 5-8 days. Using the WHO scale for dyspnea, acute pulmonary morbidity was prospectively recorded at follow-up visits within the first 6 months after completed SBRT. DVH parameters for pulmonary tissue were retrieved from the three-dimensional dose distributions.
Results: Radiation exposure of the tumor-bearing lung mounted to a median physical MLD of 5.4 Gy (range 2.6-14.7 Gy). Acute pulmonary morbidity was registered in 11 patients during follow-up. Four patients experienced aggravation of dyspnea corresponding to an increase of $^{3}1$ grade above baseline. The dyspnea in seven patients increased by $^{3}2$ grades above baseline. The time-course showed pronounced intra- and inter-individual variability. No clear relation to the onset of radiation exposure was observed. We found no association between DVH parameters and acute pulmonary morbidity. When accounting for potential confounders, we identified COPD as the factor showing the closest association with acute pulmonary morbidity after SBRT.
Conclusions: The observed aggravation of dyspnea during a 6-month-follow-up after SBRT reflects habitual exacerbations of COPD rather than treatment-related toxicity. The study supports our notion of SBRT as being not only an effective, but also very safe treatment for NSCLC. Concern about acute pulmonary toxicity should not be prohibitive for future studies targeting current limitations to radiation dose, irradiated volume, and tumor localization in SBRT for NSCLC.

1193 poster

ANALYSIS OF THE ACCURACY OF THE CYBERKNIFE

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Purpose/Objectif: The use of stereotactic radiosurgical systems to treat intracranial and extracranial tumors and other lesions requires a high degree of accuracy in target identification and localization. CyberKnife can deliver, with a high degree of precision, a single or several fractions of radiation dose to a well-defined small intracranial or extracranial target. The accuracy of the output factor directly affects the accuracy of dose delivery in CyberKnife system. The purpose of this study was to evaluation the total system accuracy of the CyberKnife and also to estimate an output factor for CyberKnife using the several detectors.

Materials/Methods: Accuracy of target localization was measured in anthropomorphic head phantom containing a spherical target, fiducial markers, and two pieces of film. The accuracy measured is the displacement of the dose contours from the treatment plan to that measured in the exposed phantom.

All measurements of the output factors for all 12 collimators were performed by six different detectors: diode detector, X-Omat V film, Gafchromic EBT film, 0.015 cc, 0.125 cc and 0.6 cc ionization chamber. The diode detector and three ionization chambers performed using water phantom at 80 cm SSD and 1.5 cm depth. When the film measurements were performed, the water phantom was replaced with a solidwater phantom. Each collimator normalized with respect to the output factor of the largest collimator (60 mm).

Results: The targeting error of the skull tracking mode and fiducial tracking mode were 0.956 mm and 0.923 mm. For the collimators over than 30 mm, the output factors from the different detectors showed a good agreement within 0.5% except 0.6 cc ion chamber. For the collimators less than 15 mm, there were substantial differences in the output factors among different detectors. That is, the value of output factor for the 5 mm collimator of a diode and Gafchromic film was each 0.656±0.009 and 0.777±0.013.

Conclusions: In this study, the total system accuracy of image-guided radiosurgery in the CyberKnife is less than 1 mm. In the ion chamber and diode detector, those difference were due to the presence of large dose gradients and lack of electronic equilibrium in narrow megavoltage x-ray beams. Therefore, the Gafchromic EBT film were considered more accurate than the others detectors.

1194 poster

BRAIN METASTASES: EFFECTIVENESS OF THE TREATMENT WITH RADIOSURGERY

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Purpose/Objectif: Brain metastases (BM) represent a mayor and common clinical problem, affecting up to 40% of all cancer patients. Recent data reveal that Radiosurgery (RS), alone or in combination with whole brain radiotherapy (WBRT), has emerged as an effective, non-invasive, treatment modality in prolonging survival and improving the quality-of-life (QOL), functional status (FS) and local control in these patients. We aimed to analyse our results.

Materials/Methods: Between April 1997 and September 2006, a total of 67 patients, 44 men and 23 women, were treated with RS. The median age at the diagnosis was 53 years. Most of the primary tumour types were lung (57%), breast (21%) and others (22%). Most common histologic features were: adenocarcinoma (54%), squamous carcinoma (21%) and others (15%). At the time of the diagnosis of the BM, 49% patients had no evidence of extracranial extension in comparison with the other 51% with known active local and/or metastasic disease. The distribution of patients by RTOG RPA class revealed that 31% were in class I, 67% in class II, and 2% in class III. The number of BM identified by MRI when the diagnosis was stabilised was one in 63% of patients, two in 27% and >3 in 10%. WBRT was delivered 15 days before RS, with a median external beam dose of 30 Gy in 10 fractions. The median dose with RS was 15 Gy. The prognostic factors were analysed using univariate analysis with log-rank tests and the actuarial survival with the Kaplan-Meier method.

Results: Median follow-up was 12 months (R 1-79 months). At the time of analysis, 54/67 patients had died. Local control: 41,8% patients presented intracranial failure. Functional independence: mean KPS observed at the time of diagnosis was 95%, 90% 6 months later and decreased to 87% after a year. 66% patients showed neurological functional class 0-I at the time of diagnosis, increasing to 72% 12 months after treatment. Medication: mean dose of dexametasone required before RS was 8 mg. However, no corticoid need was observed 6 and 12 months after treatment. Actuarial relapsed-free survival was 58% + 6,25 and 27% + 5,9 in 12 and 24 months, with a mean time of 19 months + 3% for the whole group.

Conclusions: RS applied as a boost with WBRT significantly increases overall survival in patients with brain metastases, improves QOL and functional status, as well as reduces the need of corticoids and its subsequent morbidity.

1195 poster

DOSIMETRIC IMPACT OF GEOMETRIC UNCERTAINTIES DURING GAMMA KNIFE RADIOSURGERY FOR TRIGEMINAL NEURALGIA

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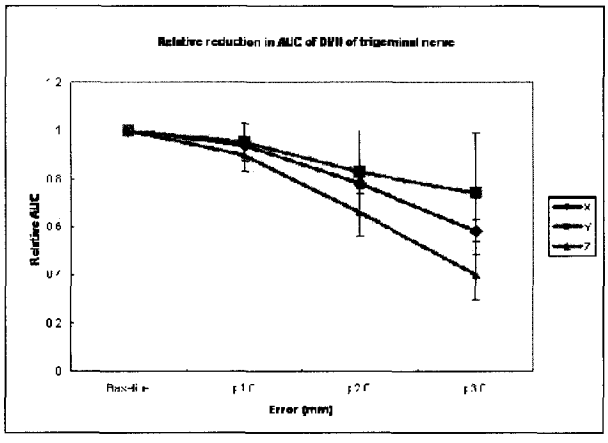
Purpose/Objectif: Trigeminal neuralgia is a disabling condition that may be treated by Gamma Knife radiosurgery (GKS) when refractory to medical or other surgical interventions. However, the relapse rate following GKS is reported to be as high as 30-50%. GKS requires high targeting accuracy given the high doses of radiation delivered to a very small target, proximity of target to critical structures at risk of radiation injury, and absence of a PTV margin. Typically, GKS is dependent on CT and MRI fusion for provision of both geometric accuracy and anatomical detail. However, MRI is prone to spatial inaccuracy, with reported spatial differences between CT and MRI data being up to 3mm. We hypothesize that the high relapse rate following GKS may be due to target under dosage resulting from the geometric error introduced by MRI data. The purpose of this study was to determine the dosimetric impact of geometric inaccuracies during GKS for trigeminal neuralgia.

Materials/Methods: The Gamma Knife database was reviewed for all trigeminal neuralgia cases. A test case was randomly selected and 0.5mm incremental errors on localization were modeled, up to a total of 3mm, in the X (lateral), Y (anterior-posterior) and Z (inferior-superior) planes in a positive (p) and negative direction. These shifts

represented potential imaging geometric errors in the expected range of MRI inaccuracies. Dose volume histogram (DVH) analyses were generated for all modeled errors to determine the dosimetric impact of geometric error to the target. These data enabled a more directed introduction of localization errors for a further 7 cases. These cases utilised 1mm incremental errors on localization in the X, Y and Z planes in the positive direction only, as direction did not substantially impact on the dose to trigeminal nerve in the test case. Errors of 0.5mm in magnitude generated similar data to the baseline planning test case, therefore errors of greater than 0.5mm in magnitude were used for the subsequent 7 cases.

Results: Analysis of DVH data for all 8 cases was undertaken and the relative change in mean area under the curve (AUC) was calculated for the trigeminal nerve DVH. For positive shifts in the X direction, mean AUC (SD) decreased to 94%(±3) of target coverage for 1mm shifts, 78%(±4) for 2mm shifts and 58%(±4) for 3mm shifts. In the Y plane, mean AUC (SD) decreased to 95% (±8) of target coverage for 1mm shifts, 83%(±17) for 2mm shifts and 74%(±25) for 3mm shifts. For positive shifts in the Z direction, mean AUC (SD) decreased to 90%(±7) of target coverage for 1mm shifts, 66%(±10) for 2mm shifts and 40%(±10) for 3mm shifts.

Conclusions: Our data confirm that geometric errors of 1mm or greater in magnitude substantially reduce dose delivery to the trigeminal nerve. This is most evident in the Z plane. This error is comparable to the reported inaccuracy of the Gamma Knife delivery system. Therefore, a stringent evaluation of the geometric error introduced by MRI is critical to the clinical interpretation of dose-response relationships.



1196 poster

EXTRACRANIAL STEREOTACTIC RADIOTHERAPY FOR TREATMENT OF MULTIPLE LESIONS IN THE LUNG

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Purpose/Objectif: Lung provides the most challenging area for delivering stereotactic radiotherapy. As technology evolves, opportunities will arise for improving the clinical outcome and reducing toxicity. The two main issues with respect to the lung continue to be: a) set up errors and b) breathing motion. There are now a few reports of clinicians resorting to the use of SBRT in the treatment of lung lesions. We report here the use of the Radionics XKnifeRT system for treating mutiple lesions in the lung using their Body Localizer. At this time breath-hold technique is used to adequately restrict tumor motion.

Materials/Methods: The Radionics' Body Localizer consists of a whole body Vac-Lok bag that conforms to the patient's body when evacuated. This fits onto a carbon fiber board which is attached either to the CT couch or the linac couch. The stereotactic localizer has 9 rods that define the coordinate system for the CT scans. A new feature within XKnifeRT does not require the CT localizer to be used. Three fiducials are placed on the chest so that they are visible on a single CT slice. These determine the origin for XKnifeRT planning system as well as for setting up the patient at the linac. The treatment delivery is on a Varian linear accelerator using a 120-leaf MLC that has the inner leaf width of 5 mm. Both conformal and IMRT delivery is feasible using the 120 leaf MLC integrated into the XKnife stereotactic system. Currently orthogonal electronic portal imaging is utilized for verifying the patient setup. The total time needed for the patient to be on the linac couch when treating three lesions has been reduced to about one hour.

Results: The Body Localizer has several limitations including the size of the patient. Also, due to the inherent inaccuracy of placing the patient in the Vac-Lok bag on a day to day basis, the external marker system is providing exceptional reproducibility and is within 2 mm when referenced to bony landmarks. Although generally six conformal beam arrangement is preferred, IMRT has been used in many situations where three lesions were treated simultaneously. A margin of 15 mm appears to be adequate for upper lung lesions whereas 20 mm is certainly needed when dealing with lesions in the lower lung for patients that are cooperative and have been educated in the breath-hold technique. Clinical outcomes have been excellent with no report of any toxicity.

Conclusions: The Radionics stereotactic technology is being implemented successfully in treating multiple lesions in the lung. Future direction includes Siemens PET-CT imaging directly linked to the XKnifeRT planning system and Image Guided Radiation Therapy for improved setup verification.

1197 poster

FRACTIONATED STEREOTACTIC RADIOTHERAPY IN MENINGIOMAS: LOCAL CONTROL AND TOXICITY RESULTS.

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Purpose/Objectif: Meningiomas are the most common intracranial tumours arising from the meninges. Despite of surgery is the primary treatment of choice in most of them, the use and indications of fractionated stereotactic radiotherapy (FSRT) are increasing in patients who had performed a subtotal resection and those with non surgical tumours or after relapse, reporting optimal results. The purpose of this study is to analyse local control, acute and late toxicity in a prospective group of patients with intracranial meningioma treated by FSRT

Materials/Methods: between October 1997 and November 2005 FSRT was performed in 58 patients with intracranial meningioma. Median age was 54 years (range 22-77), and the male/female rate was 1/3.8 (12 male/46 female). 60.3 % (35) were catalogued as WHO grade 1, and 39.7% (23) was inaccessible to histological study so in these cases the diagnosis was established by radiological criteria. FSRT was performed as primary therapy in 39.7% (23), as adjuvant therapy after subtotal surgery 27.6% (16), and as salvage treatment for relapse after surgery 32.8% (19). PTV was defined as GTV + 5mm. The total dose applied was 56 Gy in fractions of 2 Gy, 5 fractions per week. Radiological control rate was calculated by the Kaplan-Meier method , and the toxicity was evaluated by the RTOG scale.

Results: Median follow up was 42months (range 3-92). Global radiological control rate (by CT/MRI) was 96.4% (56/58), partial remission was observed in 32.7% (18) and tumour remained unchanged in 65.5% (38). 94.8% (55/58) had neurological symptoms before FSRT, with total or partial remission in 29.1% (16), stabilisation in 69.1%

(38) and progression in 1.8% (1). The mean time free of progression was 88 months (IC 95% 83-93 months) and both 3-year and 5-year actuarial rates was 94.5% (IC 95% 87.5-100). The rate of acute cutaneous toxicity G1 was 24.1% (14), neurological acute toxicity G1 in 5.2% (3) and G2 in 1.7% (1). Late toxicity was reported in 10.4% (6), G1 in 5.2% (3) and G2 in 5.2% (3). No patients developed G≥3 toxicity.

Conclusions: FSRT is an effective and safe treatment for local control in meningiomas.In our serie the global control rate was 96,4% with an acceptable late toxicity

1198 poster

FRACTIONATED STEREOTACTIC RADIOTHERAPY IN THE MANAGEMENT OF FUNCTIONING AND NON-FUNCTIONING PITUITARY ADENOMAS: A 8-YEAR EXPERIENCE AT HU ? 12 DE OCTUBRE

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Purpose/Objectif: To evaluate the efficacy and safety of stereotactic fractionated radiosurgery (FSRT) delivered using CT/MRI-based treatment planning for functioning (F) and non-functioning (NF) pituitary adenomas.

Materials/Methods: Between May 1997 and January 2005, 40 patients were treated with FSRT for residual or recurrent pituitary adenomas at HU "12 de Octubre". Twenty-nine patients presented with biochemical evidence of residual or recurrent Cushing disease (N=12), acromegaly (N=10), prolactinoma (N=6), or FSH-secreting tumour (N=1). Eleven patients had NF adenomas with evidence of local progression. Median age was 45,5 years (range 21-73). The follow-up was 53.1 months (range 11-107 months). Toxicity was reported according CTC2. 36 patients had prior surgery with a subtotal resection, 3 patients had relapse and one patient had none. FSRT was delivered by LINAC. Treatment planning was based on fused CT/MRI images in all cases. The dose was 46 Gy. Endocrine follow-up included serial testing of urine free cortisol for Cushing disease, IGF-1 for acromegaly, prolactin for prolactinoma, and FSH for FSH-secreting tumour. The endpoint for F tumours was normalisation of endocrine testing without medical suppression (complete response) or normalization of endocrine testing on continued medical suppression (partial response). The primary endpoint for NF tumours was local control based on both MRI and clinical follow-up.

Results: All patients achieve local control (stable disease in 24 and shrinkage in 16). Endocrine symptoms were resolved in ten patients (24,4%), improved in 18 (43,9%) and obtained stabilisation in 12 (29,3%). Hormone response was observed in 25 patients of F adenoma (86,2% of F adenomas). We describe hormone response by kind of F adenoma. Acute toxicity observed was grade I-III. Chronic toxicity was (percent expressed relative to evaluable patients for each symptom): Migraine, grade I, 3 (7,3%) and psychiatric, grade I, 3 (7,3%). Pituitary dysfunction after FSRT was observed, in different grade, in six patients (15%). with pituitary function, 9 (18%) had partial pituitary failure and 2 (4%) had complete pituitary failure after treatment. No visual complications were reported.

Conclusions: FSRT is efficacious in the management of residual or recurrent pituitary adenomas. FSRT is advantageous by joint stereotactic precision with know radiobiological effect by classical dose fraction. The tolerance was good and chronic toxicity was minimal.

1199 poster

HEARING PRESERVATION FOLLOWING STEREOTACTIC FRACTIONATED RADIOTHERAPY FOR ACOUSTIC NEUROMAS: PROGNOSTIC IMPLICATIONS OF COCHLEAR DOSE.

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Purpose/Objectif: To evaluate hearing preservation rates and to determine its prognostic factors following fractionated stereotactic radiotherapy (FSRT) of acoustic neuroma (AN).

Materials/Methods: Between May 1998 and December 2003, 34 patients with serviceable hearing who received FSRT were identified. Clinical and audiologic data were collected prospectively. Serviceable hearing was defined as Gardner-Robertson (G-R) Grade I or II. The median tumour volume was 2.2 cc (0.3-17.9). The prescription dose was 50 Gy in 25 fractions prescribed to the 100% isodose. Tumour control, toxicity and hearing preservation were recorded. Radiation doses (V90, V80, V50, max, min) to the cochlear and cochlear nucleus were analysed.

Results: The 34 patients, 19 male and 15 female, median age 54 years (17-71) had a median follow-up of 36.5 months. The actuarial 2 year and 4 year local control rates was 100% and 95.7% respectively. Permanent trigeminal and facial nerve preservation rates were 100%. The actuarial 2 and 3 year serviceable hearing preservation rate was 63.0% and 63.0% respectively. The actuarial pre FSRT G-R grade preservation rate at 2 and 3 years was 53.8% and 45.5% respectively. The median loss in speech reception threshold (SRT) was 15 dB (range -10 to 65). Patients were split into two groups: deteriorated hearing (≥ 15 dB loss of SRT) and preserved hearing (< 15 dB loss of SRT). By bivariate analysis, the radiotherapy doses to the cochlear were significantly different between the deteriorated and preserved hearing group for all cochlear dosimetric parameters measured. At median cochlear V90, the median loss of SRT was 25 dB (≥ median cochlear V90) and 10 dB (< median cochlear V90) p= 0.038. Radiotherapy dose to cochlear nucleus, age, gender, pre-GK hearing grade, tumour volume, cochlear volume and cochlear nucleus volume failed to show any significance as prognostic factors. Using BrainLAB software, 5 cases in which the lateral extent of the PTV did not overlap the cochlear, and thus had the potential for lower cochlear doses, were replanned with four different radiotherapy techniques, namely: arcs, dynamic arcs, static conformal and IMRT, with the cochlear defined as an OAR. In all cases, replanning resulted in statistically significant reduction in radiation to the cochlear (p= 0.001), however no one replanning technique was found to be superior.

Conclusions: The radiation dose to the cochlear is strongly predictive for subsequent hearing deterioration. It is essential for the cochlear to be outlined as an organ at risk, and radiation techniques optimized, to improve long term hearing preservation.

Characteristics	Deteriorated (SRT loss>15 dB)		Preserved (SRT loss<15dB)		p value
	mean	median	mean	median	
cochlear V90	71.25	86.8	41.33	30.56	0.043
cochlear V80	88.99	99.9	58.99	68.5	0.006
cochlear V50	99.94	100	81.6	100	0.012
cochlear min	75.42	79	52.47	51	0.01
cochlear max	97.68	98	90.93	96	0.007

1200 poster

ISOLATED LYMPH NODE METASTASIS FROM COLORECTAL CANCER TREATED BY STEREOTACTIC RADIATION THERAPY

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Purpose/Objectif: Although metastases from primary tumors are usually considered to be fatal, the patients with isolated metastases from colorectal cancers can be expected to have a relatively long survival if treatment is performed adequately. As treatment for isolated liver or lung metastasis from colorectal cancer, the role of aggressive local modality like surgery was defined well. However, in cases of isolated lymph node (LN) metastasis, the role of local modality was not defined exactly and chemotherapy was considered for the only treatment option. The aim of this study is to evaluate the role of stereotactic radiation therapy (SRT) as local modality treatment for isolated lymph node metastasis from colorectal cancer.
Materials/Methods: From September 2002 to August 2004, among 42 patients with recurrent colorectal cancer treated with SRT using CyberKnife (CK), 19 patients were proven to have isolated LN metastasis and enrolled for this retrospective analysis. They all received chemotherapy as first line or combined with CK. The recurrence sites were pelvic LN in 10 patients, presacral or rectal lesion in 6, and periaortic LN in 3. Four patients received previous RT on treatment site. The patients who were in the status of first and second relapse at the time for CK were 16 and 3, respectively. The range of the longest diameter of the tumor was 2-11 cm (median 4 cm). Four patients were treated with a single fraction of 13 to 18 Gy as a boost following external beam radiation therapy (RT) of 40 to 45 Gy. Fifteen patients received 3 fraction SRT of 33 Gy to 42 Gy. Overall survival (OS), tumor progression-free survival (TPFS) and disease progression-free survival (DPFS) rate were calculated from the date of SRT using Kaplan-Meier method. The median follow-up duration was 26 months (range 7-39 months).
Results: The 3-year OS rate was 67.5% and DPFS rate was 45%. The overall median survival time was 37 months. Tumor response evaluated by 12 months after CK were complete response (CR) in 9 patients (47%), partial response (PR) in 3 patients (16%), stable disease (SD) in 6 patients (32%), and progression (PD) in 1 patient. The cases with first relapse, smaller planning target volume (≤26 cc), or long progression free time from operation to first relapse (>23 months) had significant better OS ($p<0.05$). Also response group (CR+PR) after CK had significant better OS ($p=0.06$) than that of non-response group (SD+PD). In aspect of TPFS, the cases that first relapse occurred within 24 months after initial operation had significant poor prognosis ($p<0.05$). The diameter of tumor (≤4.5 cm vs. >4.5 cm) was marginally significant factor on DFS ($p=0.07$). Treatment related severe complication was not found during follow-up period.
Conclusions: Even though follow-up period is not enough to evaluate its effectiveness, the OS or DFS rate were outstanding and showed similar to the results of cases performed surgery for isolated liver or lung metastasis. Isolated LN metastasis from colorectal cancer would be good candidate for aggressive local modality including SRT in aspect of improving survival rate as cases of isolated lung or liver metastasis.

1201 poster

LINAC-BASED STEREOTATIC RADIOTHERAPY FOR BRAIN METASTASES : A PALLIATIVE TREATMENT ?

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Purpose/Objectif: The aim of the study is to report the outcome of 24 patients with 32 brain metastases (BM) from solid tumors treated by stereotatic radiotherapy using a 6MV photon beam and Brainscan TPS .
Results: Mean age is 65 years, 71% are female and the median of Karnofsky Performance Score is 89%. A total of 17 patients were treated for a single newly diagnosed BM, 6 for 2 BM and 1 for 3 BM. The most common histology is non-small cell lung (33,5%) and breast carcinoma (29,5%). The other tumor histologies were rectosigmoid (12, 5%), bladder (8, 5%), oesophagus (4%), ovarian (4%), cervix (4%) cancer and small cell carcinoma (4%).Headache was the only sign of initial symptom in 9 patients. Additional symptoms, usually included motor deficit, dizziness, change in mental status, visual deficits and seizures in order of decreasing frequency. Asymptomatic BM was found during staging procedures in 4 patients. Radiosurgery was used as sole management (8 patients) or in combination with WBRT (4 patients).Single shot treatment is not always affordable in case of large tumors: 9 patients received hypofractionated stereotatic radiotherapy (hfSRT) and 3 patients with a large and small BM a combination of hfSRT and radiosurgery. 14 patients remain alive with a median follow-up of 4 months: 12 without cranial evolution, 2 with new BM received salvage treatment. Of the 4 patients with neurological function >2, 2 improved, 1 remained stable and 1got worse. Of the10 patients with a baseline neurological function of 1, 6 remained stable and 4 got worse. Brain tumor progression was the cause of death for 2 patients only but 8 died due to an extracranial evolution and /or chemotherapy toxicity.
Conclusions: Stereotatic radiotherapy required no hospitalisation and lead to earlier symptom palliation. The incidence of radiation-induced dementia was far lower than with standard treatment.

1202 poster

LUNG CANCER STEREOTACTIC BODY RADIOTHERAPY: THE DOSIMETRIC EFFECT OF HETEROGENEITY CORRECTION ON NORMAL TISSUE TOLERANCES AND TARGET COVERAGE

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Purpose/Objectif: High radioablative doses used in Lung Stereotactic Body Radiotherapy (SBRT) pose an increased risk of normal tissue toxicity. Accurate calculation of doses received by organs at risk (OARs) is critical in ensuring the safety of SBRT. Heterogeneity correction (HC) of dose is not used in SBRT protocols. The aim is to examine the effect of HC on the OARs and target dose distribution.
Materials/Methods: The 4DCT datasets of 10 pts with stage I non-small cell lung cancer, treated with 60Gy in 3 fractions, were analyzed retrospectively. The CTV (CTV=GTV) was contoured on the maximum exhale and maximum inhale datasets and fused to form the internal target volume (ITV). ITV was uniformly expanded by 5mm into a PTV. OARs (heart, esophagus, proximal airway, distal airway, spinal cord, lung) were contoured on the maximum exhale dataset. HC is well characterized for our system and known to be a good model. The protocol plan was calculated with and without heterogeneity correction, using identical beam arrangements and monitor units. Two standard conformality indices were calculated on both plans; the ratio of the prescription isodose volume to PTV (CI_1) and the ratio of the volume of PTV receiving the prescription isodose to the PTV (V100); ideal score for both =1.0.
Results: The mean GTV was 5.61±4.36 (1 SD) [range: 1.26-15.51] cm^3; the mean PTV was 27.30±12.28 [10.87-48.36] cm^3. HC increased the mean dose to heart by 1.20±1.81 [-0.77-4.39] Gy; esophagus by 1.92±1.04 [0.67-3.70] Gy; proximal airway by 0.91±0.85 [0-2.50] Gy; distal airway by 0.80±1.05 [-0.10-3.00] Gy; spinal canal by 1.46±1.40 [-0.29-4.30] Gy; lung by 0.25±0.36 [-0.56-0.88] Gy; V20 by 0.34±0.72 [-1.54-1.17] %. In 1/10 pts, HC resulted in the spinal canal dose exceeding protocol dose limits. The mean uncorrected CI_1 was 1.26±0.12 [1.11-1.50] while the mean HC CI_1 was 1.05±0.20[0.65-1.25]. The mean uncorrected V100 was 0.97±0.02 [0.95-1.00] while the mean HC V100 was 0.87±0.10 [0.65-0.99].
Conclusions: Heterogeneity correction typically causes a small increase in OAR dose, which was not clinically relevant for most cases examined; this is critically dependent on tumor location in rela-

tion to OAR, and may result in unacceptable doses if OAR is close to PTV. Effect of HC on conformality indices was greater, and more unpredictable. To ensure appropriate target coverage and safety of all SBRT plans, optimized plans using heterogeneity corrections are preferred.

1203 poster

LUNG TUMOR TRACKING DURING STEREOTACTIC RADIOTHERAPY TREATMENT WITH THE CYBERKNIFE: MARKER PLACEMENT AND EARLY RESULTS

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Purpose/Objectif: Lung tumor tracking during stereotactic radiotherapy treatment with the CyberKnife requires the insertion of markers in or close to the tumor. However, in this group of inoperable patients, it is associated with high risks like pneumothorax. To reduce the risks, 3 different methods of marker placement were used: 1) intravascular coil placement, 2) percutaneous intrathoracal and 3) percutaneous extrathoracal placement (for fixed tumors to the thorax). To evaluate these techniques, we investigated the toxicity of the marker placement and the tumor response.

Materials/Methods: Markers were placed in or around 22 tumors in 20 patients: 13 patients were treated with curative intention (T1-2N0M0 lung cancers), and 7 with palliative intention (2 with recurrent lung cancer, and 5 with metastasis). Five patients had the Charlson comorbidity score of 1-2, 6 patients 3-4 and 9 patients more than 4. Platinum fiducials (4 mm by 0.9 mm) and intravascular embolisation coils were used as markers. In total, 78 markers were placed: 37 intrathoracal, 25 intravascular and 16 extrathoracal. Seven days after marker placement, a planning CTscan was made and the GTV was contoured on a 4-D CTscan. The PTV equaled the GTV plus 5 mm. For curative treatment, a total dose of 36 Gy (1 patient), 45 Gy (8 patients) or 60 Gy (4 patients) was prescribed to the 80-85% isodose line and was given in 3 fractions. For palliative treatment, a median dose of 45 Gy (range: 30-49 Gy, 3 Gy/fraction) was prescribed to the 70-80%. The response was evaluated with a CTscan 6-8 weeks after the last treatment and routinely thereafter. The median follow up was 4 months (range 2-11).

Results: No severe toxicity due to the marker placement was seen. Only 1 patient complained of severe intrathoracal pain several hours after intravascular coil placement. Pneumothorax was not seen. Two patients complained of intrathoracal pain 2-3 weeks after the treatment that disappeared with NSAIDs. The local control was 100%. Three tumors in 3 patients had a complete response after a median time of 6 months, 16 tumors in 15 patients had a partial response after a median time of 2.4 months. Three tumors in 2 patients with metastatic disease had stable disease after a median time of 2 months.

Conclusions: No severe toxicity of marker placement was seen due to the 3 methods. CyberKnife tumor tracking with markers is feasible and resulted in excellent tumor response. Longer follow up is needed to validate the local control.

1204 poster

PRELIMINARY PLANNING COMPARISON BETWEEN GAMMA KNIFE AND HELICAL TOMOTHERAPY TREATMENTS IN CASE OF SMALL BENIGN BRAIN DISEASE

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Purpose/Objectif: Gamma Knife (GK) is considered the eligible irradiation technique in treating small brain lesions, due to its capability to create very high dose gradients and thanks to the use of a stereotactic frame during all the diagnostic and therapeutic procedures. Helical Tomotherapy (HT) is a new irradiation modality able to provide a better dose painting (target coverage while sparing healthy tissue) compared with CRT and Linac-based IMR; the daily acquisition of a MV_CT reduces random and systematic set-up errors.

Materials/Methods: A few patients affected by (a single) small benign brain disease (Vtarget<10cc), previously treated with Gamma Knife, were selected and re-planned for HT. Same organs at risk (OARs) contours were considered and the target volume defined for GK was not expanded. Patients had coregistered CT and MRI images acquired in treatment position with stereotactic frame in place. GK plans were optimised to deliver the prescribed dose (13-15 Gy) at a reference isodose (usually 50%), by limiting the dose to OARs according to the dose volume constraints adopted in our clinical practice. HT plans (Tomotherapy Inc.) were inversely optimised to deliver the same GK prescribed dose at („d) 95% of target volume, by satisfying the same GK dose-volume constraints for OARs. For HT plans these user selectable parameters were considered: field width equal to 1 cm, a pitch of 0.1 and a modulation factor equal to 3. GK plans were made using 4 and/or 8 mm collimator helmets. HT TPS, but not GK TPS, was able to apply inhomogeneity correction during 3D dose calculation. Plans were compared in terms of DVHs and dose statistics. As an appraisal of the conformation of the dose distribution to the target and the body involvement to high dose, the conformity index (CI) was defined as: CI=(V2PTV/(VPTV(reference dose)*VTOT(reference dose)).

Results: A good dose conformity was reported both for GK and HT plans: the Conformity Index values were in the range 0.8-0.9. HT plans improved dose homogeneity in the target volume with a SD<3% and Dmax always less than 107% of the prescribed dose. Brain stem (most critical OAR) dose constraints were satisfied both with GK and HT: Dmax< 14 Gy, V12< 0.025cc (HT) and V12< 0.01cc (GK).

Conclusions: Preliminary results suggest that, in cases of small and "simple" brain disease, HT is able to produce dose gradients comparable with that obtained by GK TPS.

1205 poster

RE-IRRADIATION WITH STEREOTACTIC RADIOSURGERY IN PATIENTS WITH HEAD AND NECK TUMORS USING HYBRID FDG-PET/CT TO IMPROVE TARGET LOCALIZATION ? PRELIMINARY RESULTS

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Purpose/Objectif: Re-irradiation of locally recurrent head and neck carcinomas still poses a challenge especially due to dose limitation and precise target definition on a previously irradiated and/ or surgically violated tissue. Stereotactic radiosurgery (SRS) is a relatively new treatment modality allowing precise delivery of the radiation beam to cancer tissue. The purpose of this study was to evaluate the use of positron emission tomography and computed tomography

(PET/CT) using [F-18] Fluorodeoxyglucose (FDG) for target definition prior to stereotactic radio surgery.
Materials/Methods: Sixty-seven patients with a total of 74 recurrent head and neck tumor lesions were treated with SRS using the CyberKnife Frameless Radiosurgery System (Accuray Inc., Sunnyvale, CA). All patients had a FDG-PET/CT for whole body staging and a planning CT-based simulation. Lesions visually identified as local tumor recurrence by FDG-PET/CT were contoured as the clinical target volume (CTV) without a margin on the planning CT scans by an experienced radiation oncologist. Patients were followed clinically and/ or by serial FDG-PET/CT or other scans to evaluate response.
Results: Ninety seven percent of the patients had received at least one course of irradiation treatment and 52% had undergone surgery previously to SRS. Most of the local tumor recurrences were poorly visualized on the treatment planning CT due to fibrosis, necrosis, and edema from previous treatments. All recurrent tumors had increased FDG uptake and the tumor definition obtained from hybrid FDG-PET/CT was superior to both the diagnostic and planning CTs in determining the exact target location and extent. Fifty-seven percent of the patients have died after a median follow-up of 10 months, 32 patients are alive and had been followed for an average of 12 months. Forty-two out of 67 patients progressed locally, of the 74 lesions, 21 (27%) progressed inside the treatment volume, 12 outside (15%), and 9 (11%) both inside and outside of the treatment volume. Fourteen patients developed distant metastasis.
Conclusions: FDG-PET/CT was invaluable for stereotactic radiosurgery planning in patients with local recurrence of head and neck cancer. The precise tumor localization and extent was accurately determined by FDG-PET/CT in this cohort. Despite the lack of a margin around the CTV, only 9 out of 74 lesions failed both inside and outside the treated volume. All other failures were either inside the treated volume or entirely outside the treated volume. This may advocate that FDG-PET/CT augment target definition for this group although there's clearly a potential for dose-escalation to further minimize in-field failures.

1206 poster

REDUCING TREATMENT TIME FOR EXTRACRANIAL ROBOTIC RADIOSURGERY

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Purpose/Objectif: With the CyberKnife robotic organ tracking system, early stage non-small cell lung cancer patients are treated with 3x20 Gy at our institution. In current practice, delivery of 20 Gy may require as much as 10787 monitor units (MUs). A new planning strategy has been developed to substantially reduce the treatment time by reducing the required number of MUs.
Materials/Methods: The CyberKnife system uses many non-coplanar and non-isocentric beam directions to produce highly conformal treatment plans with a cone beam (5-60 mm diameter). The inverse treatment-planning algorithm minimizes the number of MUs by beam weight optimization within the imposed clinical constraints. For 5 patients, we systematically investigated the relationship between the number of MUs, the plan quality, the selected cone diameters, and the beam direction setup. In clinical practice one cone size is usually used, which is aimed at random surface points of the PTV. For optimal conformity, the cone diameter is relatively small. As an alternative we investigated a two-cone technique. A larger cone is aimed at an inner surface of the PTV. With this cone the bulk of the tumor is irradiated efficiently. A small cone is aimed at the PTV-surface, and is used to increase the conformity of the dose distribution. The plan quality was assessed by the conformity index, mean lung dose (MLD), V20 and by visual inspection. The reduction in MUs was determined by comparing the two-cone plan with a one-cone plan with equal MLD.
Results: With the new two-cone technique the required number of MUs was reduced by an average 39% (range 24-52; $p = 0.009$), while the quality of the treatment plans was not compromised. The combination of cone sizes for the most optimal plan was 25 or 30 mm for the small cone and 35 or 40 mm for the large cone. The average PTV-volume was 36 cm^3 (range 34-51). Typically, the diameter of the large cone was equal to the minimum diameter of all beams eye view projections of the PTV. The large cone was aimed at the PTV-volume that was shrunk with 8 or 10 mm.
Conclusions: With the new treatment approach, the number of MUs could be reduced significantly (up to 52%) without compromising the quality of the treatment plans. The reduction of MUs minimizes the delivered dose by radiation leakage and decreases treatment time, which is advantageous for patient comfort, patient throughput and possibly also for the biological effectiveness of the delivered dose.

1207 poster

RESPIRATORY-GATED EXTRACRANIAL RADIOSURGICAL TARGET LOCALIZATION

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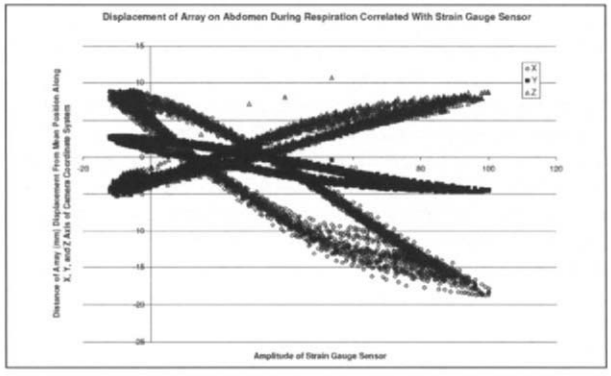
Purpose/Objectif: Stereotactic radiosurgery techniques for intracranial tumors using frames have traditionally been accepted as yielding the most precise tumor targeting available. Lung tumors present a particularly unique challenge due to the effect of respiratory motion. The aim of this project was to characterize an optical guidance system for respiratory-gated extracranial radiosurgical target localization at the time of treatment delivery.
Materials/Methods: Respiratory motion was measured simultaneously with two systems: a strain gauge belt with a pressure sensor (Anzai Medical, Tokyo, Japan)placed at the umbilicus, and two passive-reflection marker arrays visualized by an optical tracking system using infra-red cameras (Northern Digital, Inc.,Ontario, CA) and an in-house developed software. Proof of concept was evaluated for three normal volunteers placed in a supine position mimicking a thoracic treatment. Respiratory motion was simultaneously recorded on both the optical tracking system (15 measurements per second) and the strain gauge belt (40 measurements per second) for approximately 120 complete respiratory cycles (over 10 minutes), providing > 9,000 data points for comparison in each subject. The subjects were instructed to cough near the beginning of the acquisition to allow the three datasets to be temporally synchronized. The stability of the optical tracking system and its setup was verified with a stationary jig revealed at the beginning and end of each study (Z med, Ashland Mass.). The variability in abdominal-array position and thoracic-array position were calculated along each cardinal axis for all phases of the respiratory cycle.
Results: Strain gauge derived respiratory phase was highly predictive of the spatial location of the abdominal-array. For phases of the respiratory cycle determined from the strain gauge system between 80% expiration down to 0% and back up to 60% inspiration, the spatial position of the abdominal-array was within 1 mm for all three axes. In the example below the maximum abdominal motion along any one axis was 25 mm. Strain gauge derived respiratory phase was also predictive of the spatial location of the thoracic-array to within 2 mm in all phases and within 1 mm (95% confidence) between 80% expiration and 60% inspiration. The greatest variability was seen between 60% inspiration and 100% inspiration in all subjects, with all points within 3 mm. The in-house software allowed us to identify three independent arrays, enabling us to fix the third array to the treatment couch for relative couch movement as indicated by the

moving array secured to the subject's thorax.
Conclusions: By gating the measurement of the spatial location of an infra-red reflective array secured to the subject's thorax, we are able to localize the target to within 2 mm throughout the majority of the respiratory cycle for 120 cycles. This appears to be a viable approach for respiratory-gated extracranial radiosurgical target localization at the time of treatment delivery.



1208 poster

SELECTION OF A COLLIMATION TECHNIQUE FOR INTRACRANIAL STEREOTACTIC RADIOSURGERY

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Purpose/Objectif: Comparing 5 different collimation techniques for single fraction high dose intracranial stereotactic radiosurgery. Fysical interpretation of the results.
Materials/Methods: 57 patients were retrospectively re planned (Brainscan 5.31) using the Brainlab M3 (3-5 mm) , Varian 120 MLC (5 mm) in static and dynamic multileaf arc mode and the circular cones in arc mode.
Dose ranging from 10-25 Gy (80% isodose) . Volume ranging from 0.1-30cc.
As a comparison to the original treatment plan, only the collimation technique was changed.
Parameters investigated : target volume coverage (80%,50%), conformity index (80%,50%), irradiated healthy tissue volume (80%/50%), minimal and maximal dose on target volume , dose homogeneity and ellipse factor.
Results: All parameters were analysed with the ANOVA method.
Significant ($p<0.05$) parameters like PTV coverage ,conformity Index, PTV minimal dose and dose on healthy tissue were further investigated. These parameters were better and less variable with MLC than with circular cone. However, for Target Volumes less than 1cc the circular cone is still better due to its smaller penumbra, compared to MLC. There is no significant difference between both MLC's when used in dynamic mode.
Conclusions: 1) In single fraction high dose intracranial stereotactic radiosurgery, MLC seems to be superior to cones in covering irregular lesions above 1 cc. For lesions under 1 cc volume, tissue sparing effect is lost, due to X-ray leakage (larger penumbra).
2) The advantage of smaller leaf size, disappears when using MLC in dynamic mode, due to the fact the MLC reshapes itself around the PTV as the gantry rotates.

1209 poster

SEMI-AUTOMATIC ANALYSIS OF WINSTON-LUTZ FILM IMAGES TO ASSESS ISOCENTRIC ACCURACY

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Purpose/Objectif: The application of stereotactic radiotherapy puts high demands on the accuracy of the mechanical alignment of the linac. For our Novalis system we evaluate this in a weekly scheme by means of a Winston-Lutz test. In this test a tungsten sphere is attached to the couch at the position of the lasers and exposed with a cone shaped beam of 7.5 mm diameter. The entire range of clinically used gantry and couch angles is measured with a film, in a total of 9 combinations. Analysis of the measurement requires assessing the position of the shadow of the sphere with respect to the field edge. Differences in positions can have multiple causes, such as laser misalignment, gantry sag, etc. We developed a method for (1) automatically finding the center of the image of the sphere and of the field edge; and (2) analyzing these values, giving a proposal for adjustment of the lasers. From these, the minimum radius of a sphere containing the mechanical isocenter is determined, after adjustment of the lasers.
Materials/Methods: The film used for 9 consecutive exposures in a standardised setup is developed and scanned in at 300 dpi. The digital image is processed with our own software (Matlab, The Mathworks). The software recognises the areas containing the exposures by thresholding and histogram analysis. These areas are further processed by an edge detection procedure and Hough transformation in order to find the center of the sphere's image and the field edge. The differences between these center positions are used in a geometric model in order to obtain the laser adjustments. The model fit is based on minimisation of the maximum displacement, a formulation that is in agreement with the definition of the mechanical isocentre.
Results: Experimental validation showed that the displacement of the isocentre could be estimated with an accuracy of 0.15±0.05 mm (average ± SD).
Over a period of two years the Winston-Lutz tests were analysed. The minimal radius of a sphere containing the isocentre was 0.51±0.07 mm (average ± SD).
Conclusions: A fast and accurate software tool was developed that facilitates the processing of our weekly Winston-Lutz tests. The tool automatically finds the projection of the applied sphere and the field edge on the film, and deduces values for the offset of the lasers. Using these offset values, a residual error is calculated that reflects the variation of isocentre location for different table and gantry angles, and is an important quality control parameter.

1210 poster

STEREOTACTIC IRRADIATION FOR MENINGIOMAS

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Purpose/Objectif: We evaluated the outcomes of patients who received treatment by stereotactic irradiation (STI) for benign meningiomas at least one year previously.
Materials/Methods: Twenty-seven benign meningiomas in 23 patients were treated with STI between December 1999 and March 2005 and were observed for more than one year. There were four male and 19 female patients. The mean age of these 23 patients was 55.6±13.6 years. Eleven lesions were treated by STI only. Eight lesions were treated by STI for post-operative irradiation, and eight lesions were treated by STI for local recurrence or regrowth after resection. Thirteen patients (14 lesions) had neurological symptoms owing to tumors. Seventeen lesions of 27 were skull base meningiomas. We treated 23 lesions in 19 patients by single fraction stereotactic radiosurgery (SRS) and four lesions in four patients by fractionated

stereotactic radiotherapy (SRT). The mean of the peripheral doses for SRS was 15±2.4 Gy (range: 12-20 Gy). The biologically effective dose (BED) of this value was 94.3±28 Gy_3 (range: 60-153 Gy_3), supposing $\alpha/\beta=3$. On the other hand, the range of the peripheral doses for SRTs was 25-35 Gy / 6-9 Fr and that for the BED was 58.2-80.7 Gy_3. We calculated the reduction rates of the tumors by comparing MR imaging of pre-treatment and post-treatment.

Results: The median observation time was 44 months (range: 12-75 months). The tumor control rate (CR+PR+SD) was 88.9%; the average of the reduction rates was 33.4±55.0%. The reduction rate correlated with BED ($p<0.01$). When we delivered more than 100 Gy3 for the peripheral dose, no tumor expanded after treatment (the reduction rates were over 0%). In four lesions treated by SRT, BEDs were less than 80 Gy_3 and the reduction rates were less than 50%. Six lesions (42.9%) of 14 had an improvement of neurological symptoms, seven lesions (50%) showed no change of symptoms, and one lesion (7.1%) had worsening of symptoms. The reduction rates of all improvement cases were over 50%. Two patients treated by SRT had some neurological symptoms before treatment, and they did not improve the complaints. Four patients had late sequelae. All of them were treated by SRS, and the region of those tumors was the skull base. The patients received various peripheral doses (range: 12-16 Gy), but three of them were treated by the double isocenter technique because of irregular shapes of these tumors.

Conclusions: SRS for benign meningiomas can result in good local control and improvement of symptoms. When one treats skull base meningiomas in which forms are distorted, it is important to choose the cases carefully because there are some risks of increasing the high dose area of brain nerves and brain stem and increased frequency of late sequelae, particularly when using the multi-centric technique. In cases of treatment by SRT for benign meningiomas, there were no late sequelae, but we had neither good local control nor improvement of complaints.

1211 poster

STEREOTACTIC RADIOSURGERY (SRS) FOR INTRACRANIAL LESIONS: CONES OR MLC, WHICH ONE TO CHOOSE?

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Purpose/Objectif: Our centre has used cones as the collimation technique for stereotactic radiosurgery of intracranial lesions since 1995. Since 2003, multileaf collimation (MLC) has also been applied for this indication. In this study, we asked which collimation technique gives the most optimal dose distribution, taking into account the dose delivered on PTV and organs at risk.

Materials/Methods: We selected 60 consecutive patients, suffering from a solitary brain tumour and treated with SRS in the year 2002-2003. These brain tumours included malignant lesions (14 metastases, dose 25 Gy), benign brain tumours (12 vestibular schwannomas (14 Gy), 23 meningiomas (14 Gy) and 7 tumours of the pituitary gland (14-25 Gy)) and non tumoural lesions (4 Arterio-venous Malformations (25-40 Gy)). These doses were prescribed to the 80 % isodose, on the periphery of the lesion. The diameter of the lesions varied between 5.5 and 57.2 mm. Four different treatment plans were made retrospectively: for cone treatments (n=56): using conformal arc with the MLC 120 (5mm leaves), M3 (3mm), both in static and dynamic mode; for MLC 120 treatments in static mode (n=4): cone plan, MLC 120 dynamic, M3 static and dynamic. All 5 plans for each patient (300 in total) were analyzed for conformity, dose delivered to the PTV, organs at risk and the surrounding tissue.

Results: In all types of lesions, a significant difference ($p<0.05$) in minimal dose delivery was observed between planning with cones and MLC techniques. In meningiomas or schwannomas, there was a significant difference ($p<0.05$) in minimal dose delivery between the static and dynamic mode for both MLC types.

However, no significant difference was shown between the dynamic mode of the MLC 120 and the dynamic mode of the M3.

Conclusions: In our series, we observed an advantage in using a multileaf collimator in SRS, particularly in lesions with an irregular shape. Meningiomas or schwannomas benefitted from the use of MLC in dynamic mode. However, there was no significant difference between the MLC 120 and the M3. Based on our study results, for SRS, we actually use the MLC 120 in static mode and we plan to implement the dynamic mode in the nearby future.

1212 poster

STEREOTACTIC RADIOTHERAPY FOR BRAIN LESIONS: ANALYSIS OF TREATMENT OUTCOMES AND TOXICITY FROM A SINGLE CENTER

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Purpose/Objectif: In 1995 we established the first stereotactic unit in Greece and we applied stereotactic radiotherapy (X-knife) in patients with benign or malignant lesions of the brain with a diameter less or equal to 3 cm. The purpose of this study is to describe the epidemiologic (histologic type, sex, age) and treatment related characteristics (total dose, daily dose, number of fractions, arcs per fraction, diameter of the lesion and PTV cover) of all patients treated with this method. Acute and late toxicity as well as overall survival were evaluated.

Materials/Methods: From 1995 until 2006, 61 patients of mean age 45 years were refered to our Department, with the diagnoses: Gliomas 18, metastatic lesions 13, meninigiomas 8, pituitary adenomas 6, AVM 8, acoustic neurinomas 3, ependymomas 2. 3 patients did not finally underwent stereotactic radiotherapy and 3 patients were lost from follow up.

Results:

Results are shown on table 1

Conclusions: Stereotactic radiotherapy (X-Knife) is an effective and safe therapeutic procedure that can be used in patients with a wide variety of brain lesions acquiring radiotherapy. Our home-made immobilization system and the use of a usual linear accelerator makes this method easily available to almost any Radiotherapy Department. Of course, all the necessary medical and physical precautions should be taken into account in order to obtain optimal nervous tissue sparing.

Table 1: Results

Histology	N=58	Survival1 (months)	Survival2 (months)	Current status (alive)	Acute complications	Late complications
Gliomas Grade I	4	121	84.2	3/4	0/4	0/4
Gliomas Grade II	2	57.5	6.5	0/2	0/2	0/2
Gliomas Grade III	4	75.3	57.3	1/3	1/3	1/3
Gliomas Grade IV	8	31.5	17.2	3/8	3/8	2/8
Meningiomas	8	55.7	33.1	8/8	3/8	2/8
Adenomas	6	100	69.3	5/6	0/6	0/6
Ependymomas	1	96	60	1/1	1/1	0/1
Hemanglomas	2	77.8	51.2	2/2	0/2	1/2
Acustic neurinomas	3	83.9	60.8	3/3	1/3	0/3
Metastases	13	23.6	13.5	6/11	1/11	1/11
Arterovenous dysplasia	7	96.2	86.1	7/7	0/7	0/7

1213 poster

STEREOTACTIC RADIOTHERAPY FOR HEAD AND NECK TUMORS

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Purpose/Objectif: To report and analyze outcomes for patients treated with stereotactic radiotherapy for tumors of the head and neck region.

Materials/Methods: Between October 2001 and March 2006, 143 patients with median age of 65 were treated with Stereotactic Radiotherapy (SRT) using the frameless Cyberknife (Accuray, Sunnyvale, CA) system. All patients were immobilized with a noninvasive molded Aquaplast facemask (WRF/Aquaplast Corp., Wyckoff, NJ) that stabilized the head and neck on a radiographically transparent headrest. Using image guidance with the coupling of an orthogonal pair of x-ray cameras, sll lesions were tracked relative to skull bony landmarks within a 1 mm spatial accuracy. 5% of all patients had benign histologies (acoustic neuroma, meningioma, glomus, and neurofibromatosis) which were treated definitively . The remaining 95% patient had malignant primary diagnoses with squamous cell carcinoma as the most common histology (57% of all patients). 76% of all patients had previous external beam radiotherapy to the head and neck region. 92% of all patients received SRT for palliation. The median dose delivered with SRT was 27.5 Gy in 5 fractions (range 1-10). The median tumor volume was 25 cc. 13% of patients did receive IMRT along with SRT. 8% of all patients did receive chemotherapy along with SRT and 1% of all patients received biologic therapies concurrently

Results: The median follow-up is 6 months for the entire cohort. There were no severe acute or late treatment-related toxicities. The 1 and 2 year survival rate for patients with recurrent squamous cell carcinoma was 33% and 20% ,respectively, while the 1 and 2 year survival rate for the benign diseases was 76% and 76%. The 1 and 2 year survival rates for patients with malignant diagnoses other than squamous cell carcinoma are 56 and 40%, respectively. The 1 and 2 year local control rate for patients with recurrent squamous cell carcinoma was 37% and 20%, respectively, as compared to 56% and 45%, respectively, for patients with other malignant diagnoses.

Conclusions: Stereotactic radiotherapy is a safe and efficacious modality for tumor of the head and neck, especially for aggressive tumors which have been previously irradiated. A prospective phase I dose escalation trial is currently nearing completion and will shed greater light on the optimal dose schema in the recurrent head and neck cancer setting.

1214 poster

THE INFLUENCE OF PTV LOCALIZATION ON SPATIAL ORIENTATION AND NUMBER OF BEAMS IN STEREOTACTIC RADIOSURGERY FOR BRAIN TUMORS USING THE CLUSTER ANALYSIS

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Purpose/Objectif: Stereotactic radiosurgery (SRS) is one of the methods used in therapy of brain tumors. However it is difficult to develop standards regulating the geometry (gantry position, table orientation) and number of beams. It appears that recent development in artificial neutral network (ANN) may offer a promising way to solve that issue. To implement ANN in SRS and build a suitable cluster network, it was necessary to analyze and evaluate the main parameters of treatment plans such as gantry and table orientation.

The purpose of this study was to analyze whether the localization of PTV in the brain had an impact on the geometry of beams defined as gantry position, table orientation and number of beams.

Materials/Methods: 218 cases were chosen for retrospective analysis. Treatment plans were prepared using the treatment planning system (BrainLAB). The data describing the geometry for each beam (gantry position and table orientation) were converted from spherical to cartesian notation. These data were divided into four groups: LA - the beam entered from left and anterior direction relative to isocenter of PTV, LP - left, posterior, RA - right, anterior and RP - right posterior. Such defined parameters was normalised as:

$P(LA) + P(LP) + P(RA) + P(RP) = 100\%$

where P(x) is percent of all numbers of beams used in treatment and x was one of the groups. Received percents were analyzed using cluster analysis and this way all cases were divided into subgroups, observer independently.

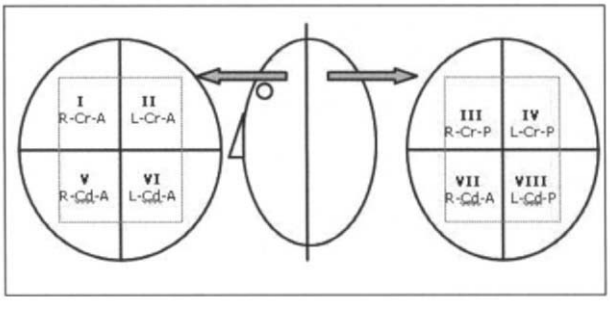
In the second approach, the area of the brain was divided into 8 parts (according figure 1) and each of 218 cases were grouped to one of them - observer dependently. Results of observer's independent (cluster analysis) and those depended (affinity PTV to brain parts) were correlated.

Figure 1. The brain parts defined by observer. R - right, L - left, Cr - cranial, Cd - caudal, A - anterior, P - posterior.

Results: The average number of beams was 8 (from 3 to 11), mean volume PTV was 7,5 cm^3 (from 0,55 cm^3 to 55,9 cm^3). There were no statistically significant differences between number of beams, volume of PTV and affinity PTV to brain parts. It confirmed uniformity of the cases and enabled to grouping PTV using depended method.

The cluster analysis grouped 218 cases in 15 subgroup, which were correlated with affinity PTV to brain parts ($p<0,001$, $R^2=0,367$). Moreover, there were decreasing dependence between number of beams and maximal value of P(x) ($p=0,001$, $R^2= -0,221$).

Conclusions: Obtained results confirmed correlation between spatial orientation of the beams and localization of PTV in one of analyzed brain parts. However, it shows necessity to analyze more parameters related to OAR for reliable implementation of these results in ANN.



1215 poster

THE ROLE OF RADIOSURGERY IN THE MANAGEMENT OF PATIENTS WITH BRAIN METASTASES

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Purpose/Objectif: The aim of the study was to evaluate the effectiveness of radiosurgery with gamma knife, in terms of disease free and overall survival, for pts with brain metastases.

Materials/Methods: Between January 2001 and December 2004, 517 pts were treated in our center for brain metastases with gamma

knife (GK). The primary cancer was lung (NSCLC) in 264 pts (51%), breast in 98 pts (19%), melanoma in 31 pts (6%), kidney in 47 pts (9%), colon in 36 pts (7%), miscellaneous in 41 pts (8%). Inclusion criteria were: less than five metastases; diameter of the lesion ≤ 3 cm (volume 15 cm^3) or total tumor volume in multiple metastases ≤ 20 cm^3; patient in RPA class 1 or 2. The mean tumor volume was 2.47 ml (0.01 - 30.9 ml). Treatment was performed in a single fraction , prescribing 20-25 Gy at isodose 50%. The mean prescription dose to tumor margin was 22.6 ±3.4 Gy (range 9 - 25 Gy).
Survival curves were obtained with Kaplan - Meier method.
Results: The mean follow up was 16 months. Overall median survival rate was 12 months. One and two years survival rate were 51.6 % and 32% respectively. The local control at 1 year is reached in the 89% of cases. Complications are radionecrosis and oedema in the 8.6% of cases. With GK mortality is 0%, while between 2 and 8% with surgery, 0% with with whole brain radiotherapy (WBRT) it is 0% and 2-8% with surgery + WBRT. The one year local recurrence rate is 11% with GK, 46% with surgery, 80-100% with WBRT and 10% with GK followed by WBRT.
Conclusions: This study underlines the effectiveness of GK in the management of brain metastases, but also the importance of high level diagnostic devices, of working as a team (neurosurgeons, radio-oncologists, physicists, neurologists), and of high level quality controls.

1216 poster

TREATMENT OF LUNG LESIONS IS SAFE AND EFFECTIVE WITH CYBERKNIFE STEREOTACTIC RADIOTHERAPY: THE THORACIC EXPERIENCE AT THE UNIVERSITY OF SOUTHERN CALIFORNIA

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Purpose/Objectif: The CyberKnife (CK) is a recently developed image guided robotic stereotactic radiosurgery system with the capability of dynamic targeting of up to 1200 non-coplaner 6 MV photon beams. We conducted a retrospective analysis of our experience in patients treated with CK for either metastatic or primary lung lesions.
Materials/Methods: Between February 2003 and March 2006, a total of 29 lung lesions in 24 patients were treated with the CK for palliation or as part of curative therapy in conjunction with 3-D conformal radiation therapy (3D CRT). The median age of the 24 patients at treatment was 66 years (range 18-83). Fifteen lesions were metastases and the other 14 lesions had originated from a non-small cell lung cancer (NSCLC) primary tumor. Patients underwent either a single dose of irradiation [stereotactic radiosurgery (SRS)] or fractionated stereotactic radiation therapy [SRT] with the CK (Figure 1). Some patients treated with a SRT approach underwent hyperfractionated SRT (H-SRT) during which the first fraction was given in the afternoon while the remaining fractions were given twice a day with at least a 6 hour time interval.
Results: Nine lung lesions were treated using a SRS approach while the remaining 20 lesions were treated with a SRT approach, 9 of which underwent H-SRT (Table 1). None of the patients experienced any acute esophagitis; only 1 patient who was treated with 3-D CRT and then underwent a CK H-SRT boost (2000 cGy in 5 fractions) experienced pneumonitis which resolved with steroids. No late toxicities have been observed. Virtually all patients experienced effective clinical palliation of their symptoms.

Table 1. Summary of CK SRS or SRT Dose Fractionation Scheme

Number of CK Treatment Fractions	Total Dose in cGy (Number of Lesions)
1	1500 (n=2)1600 (n=6)1800 (n=1)
2	1400 (n=2)1600 (n=1)
4	1800 (n=2, 1 treated with H-SRT)2100 (n=1)3000 (n=1)
5	2000 (n=2, 1 treated H-SRT)2100 (n=1 H-SRT)2250 (n=1)2500 (n=5, all treated H-SRT)3000 (n=1 H-SRT)4000 (n=3)

Conclusions: The treatment of lung lesions with Cyberknife using either a SRS or a SRT (once daily or hyperfractionated) approach is safe and effective without any significant acute or late toxicity. Based upon our initial experience, we plan to initiate a phase I/II trial evaluating the safety and efficacy of using CK SRT in the curative treatment of NSCLC.

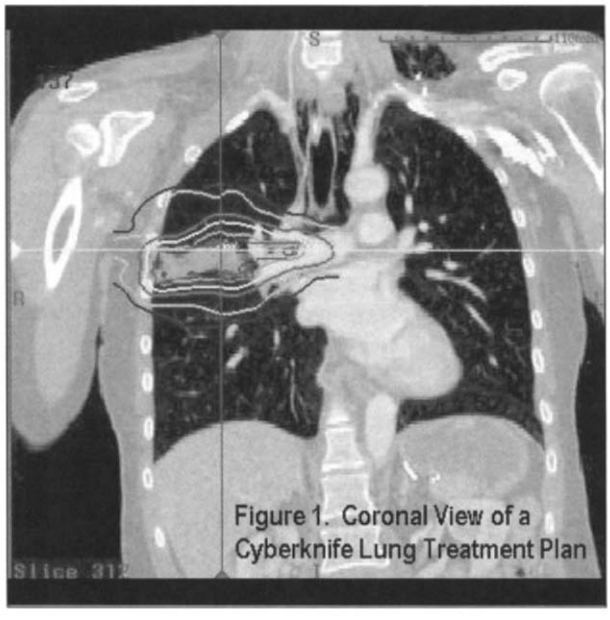

Figure 1. Coronal View of a Cyberknife Lung Treatment Plan

Posters Target Volume Delineation

1217 poster

3D - RECONSTRUCTION OF THE HUMAN VISIBLE LYMPH NODES

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Purpose/Objectif: The dataset from the visible human male was studied. The head and neck, axilla, chest, abdomen, pelvis and inguinal region was investigated. New data on the location of normal size lymph nodes in anatomical optical microtome sections were acquired.

Materials/Methods: The male whose body was used as visible human was 38 years old at the time of death. The cadaver was perfused with 1% formalin and anticoagulant. Optical anatomic microtome produced slices at 1 mm interval and with a resolution of 2.8 pixels per mm were carefully examined. The dataset provided a quality and continuity of data that is superior to any other conventional medical imaging modality. Special attention was devoted to the 3-dimentional topography as well as the number and size of lymph nodes.

Results: "Invisible" nodes were identified, i.e., normal size lymph nodes with diameters of less than 3 mm which remain "invisible" for imaging methods such as CT or MRI. The 3-D reconstruction of the optically identified lymph nodes of the head and neck, axilla, chest, abdomen, pelvis and inguinal region was possible. Around 900 lymph nodes could be identified.

Conclusions:

New data on the location, number and size of lymph nodes based on the VHDS were acquired. A 3D representation of all the identified lymph nodes was performed. These data are of importance for definition of quality of the pathological examination and in training of surgical procedures and the target volume delineation in radiation oncology.

1218 poster

A NEW HYBRID MR METHOD FOR DEFINING CONCOMITANT BOOSTS IN BRAIN IMRT

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Purpose/Objectif: The brain is a good candidate site for the application of simultaneous boosting since both inter- and intra-fractional movements are very small. Although functional imaging has the potential to target regions that would benefit most from boost doses, it is not universally available; moreover, various technical and clinical issues surrounding its implementation in radiotherapy treatment planning remain, one issue being poor resolution. Conventional MR images, such as T_1-weighted (± contrast), T_2-weighted and FLAIR, have long been used in diagnosis and treatment planning and have superior resolution to most functional techniques. We propose that these established techniques be amalgamated to derive anatomical parameter maps of tumour existence probability, denoted TEP, and escalated dose be prescribed to these volumes.

Materials/Methods: In-house software has been developed that reads in multiple images generated via different MR sequences. Here, the user guides an automatic region-based contouring tool to delineate the region of abnormality on both datasets independently. The program then compares the contours slice by slice and fuses them to form a parameter map of TEP derived from set theory analysis of the different contours. Finally, the parameter map is overlaid on the anatomical images and exported in DICOM format to the TPS. Here, escalated dose is prescribed to the TEP volumes plus a planning margin, alongside a conventional dose to the standard PTV.

Results: Data from a patient with a single brain metastasis is presented showing 3 TEP levels defined by amalgamation of T_1-weighted (post contrast) and T_2-weighted images. A treatment plan guided by the TEP parameter map was generated where escalated dose of 60 Gy to the PTV and 75 and 80 Gy to the TEP derived boost volumes was prescribed. This was achieved with negligible effects on normal tissue irradiation when compared with the non-boosted plan.

Conclusions: The hybrid MR method is an effective means of defining concomitant boosts in brain IMRT and the high resolution of the approach results in smaller planning margins on the boost volumes when compared with certain functional techniques.

1219 poster

AUTOMATIC OUTLINING OF STATIC AND MOVING TARGET VOLUMES FOR RADIOTHERAPY TREATMENT PLANNING WITH 18FDG-PET-CT IMAGES

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Purpose/Objectif: Preliminary studies into the use of co-registered ^{18}FDG-PET-CT images for radiotherapy treatment planning have shown that there can be significant differences between the GTV_{PET} and the GTV_{CT}. Clinical outlining using PET images requires significant expertise and experience and the involvement of nuclear medicine physicians and radiologists. Automatic outlining of the PET avid area may aid in the clinical outlining process and could be used in the analysis of gated PET volumes. Thresholding is a standard technique for automatic outlining with nuclear medicine images. The effect of motion on the automatic outlining has not been reported.

Materials/Methods: A PET NEMA IEC body phantom containing six fillable spheres of volumes 0.5ml to 26.5ml, was scanned on a GE Discovery LS PET-CT scanner. The spheres and background were filled with ^{18}F concentrations giving a range of contrasts from 10:1 to 2:1. Images were acquired with different noise levels. To simulate respiration the phantom was placed on a moving platform which simulated movements of different amplitude and frequency. The threshold required to correctly segment the spheres was determined by iteratively adjusting the threshold value until the segmented volume matched the volume of the sphere.

Results: The threshold required was found to depend on the lesion size and image contrast. For lesions with volumes greater than 10ml it is possible to apply a constant threshold value for a set contrast value. The threshold values obtained from a static phantom are not always directly applicable to moving objects.

Conclusions: Thresholding is a standard technique for the segmentation of nuclear medicine images. Its dependence on the size, contrast and motion of an object has been determined using phantom studies. The use and applicability of these data to clinical images will need to be further investigated.

1220 poster

AUTOMATIC SEGMENTATION OF INTRA-THORACIC ORGANS BASED ON BELIEF FUNCTIONS

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Purpose/Objectif: Manual delineation of normal tissues and tumours on planning CT is lengthy and operator-dependent. We applied an algorithm based on the belief functions theory to automatically delineate the lungs, the trachea, the main bronchi and the spinal cord in patients with lung cancers.
Materials/Methods: To identify the structure to which belongs a given voxel V, the information (Hounsfield Unit) contained in that voxel and in its 3D neighbours is collected. As the information provided by neighbouring voxels is less reliable, a 3D filter is applied to modulate the contribution of the neighbouring voxels according to their spatial distance relatively to voxel V. Specific filters are automatically created from the characteristics of each organ, the CT acquisition parameters and the CT images. For instance, the filter for the spinal cord is larger and gives a higher weight to cephalad - caudal neighbours, as opposed to the lung filter where the neighbouring voxels are given the same weight whatever their positions. The contours of each organ is then delineated from the edges of the segmented structures.
Results: The filters parameters were derived from CT images in a learning set of 9 patients, and then used on a validation sample of 12 patients. The quality of the delineation was assessed by an experienced radiation oncologist (OG). Early results show a high concordance between manual and automatic contours, with or without administration of contrast agent.
Conclusions: Belief functions can be applied to automatic segmentation of intra-thoracic organs. Further developments will involve tumour delineation and integration of other imaging modalities.

1221 poster

AUTOMATIC SEGMENTATION OF PELVIC STRUCTURES FROM MRI IMAGES FOR PROSTATE CANCER RADIOTHERAPY

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Purpose/Objectif: Target volumes and organ at risk delineation is a time consuming task in radiotherapy planning. The development of automated segmentation tools is essential but still remains a difficult problem due to pelvic organs shape variability. Thanks to its high soft tissue contrast, MRI is increasingly used in prostate cancer radiotherapy planning.
Materials/Methods: Manual and automatic delineation were compared in 20 patients with stage T1 - T2 N0 M0 prostate cancer, using a sagital T2 weighted Turbo Spin Echo (TSE) and a T1 3D Fast Field Echo (10 patients) or a T1 TSE SENSE (10 patients). A radiotherapist delineated pelvic structures (prostate, bladder and rectum) based on axial (FFE or TSE) and sagital sequences. Clinical Target Volume (CTV) included the prostate from the apex to the base. Rectum was defined from the anal canal to the sigmoid flexure. Manual contouring was considered as the reference for comparison. For prostate automatic delineation, an organ model-based method was used. Prostate model was trained based on manual segmentations from 15 patients MRI images that did not include the targets. Segmentation began with interactive initialisation to position model over the target in the image data using axial and sagital sequences. For bladder and rectum automatic delineation, a growing pattern method was used. The comparison between manual and automatic delineation was made on ARTIview™ software (AQUILAB®SAS). The following parameters were measured for CTV, rectum and bladder: volume ratio (VR) (automatic/manual), volume overlap (Vo) (percent ratio of the volume of intersection to the volume of union, optimal value = 1), correctly delineated volume (Vcd) (percent ratio of the volume of intersection to the manual defined volume, optimal value = 100).
Results: For CTV, the VR, Vo and Vcd were 1.15 (±0.09), 0.78 (±0.05) and 94.42 (±3.3) respectively. For rectum, the VR, Vo and Vcd were 0.98 (±0.11), 0.78 (±0.07) and 86.04 (±6.6) respectively. RV, Vo and Vcd were 0.94 (±0.04), 0.88 (±0.03) and 91.11 (±3.08) for bladder respectively.
Conclusions: Organ model is a promising method concerning automatic prostate delineation. Results show that the method is repeatable and leads to reproducible segmentation with minor interactive corrections. For bladder and rectum automatic delineation MRI soft tissue contrast allows to use region growing methods.

1222 poster

BACKGROUND-SUBTRACTED OPTIMAL THRESHOLD SEGMENTATION ALGORITHM FOR FDG-PET BASED GTV DELINEATION: THEORY AND EXPERIMENTAL VALIDATION

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Purpose/Objectif: An adaptive thresholding method has been proposed for the automatic segmentation of the gross tumor volume on ^{18}F-fluorodeoxyglucose (^{18}F-FDG) positron emission tomography (PET) images [1]. This method is based on a hyperbolic relationship between source-to-background ratio (SBR) and the iso-activity level to be used and claims to be independent of a priori knowledge of the lesion diameter. The purpose is to develop a threshold segmentation algorithm to determine the diameter of radioactive spheres in PET images that is independent of the SBR and allows accurate measurement of diameters down to the resolution of the PET scanner.
Materials/Methods: From image processing theory, a background-subtracted relative threshold level (RTL) method that is optimal for spherical objects of different diameters was derived assuming uniform signals for the object and its surrounding. A correction algorithm was developed for small spheres to increase the measurability. Artificial 2D and 3D PET images were generated by computer simulation using the point spread function (PSF) of the PET-scanner to study the feasibility of the method and to evaluate the effect of the full-width half maximum (FWHM) and the object diameter (D) on the optimal RTL. Validation of the simulations was carried out by using a full-ring dedicated PET-scanner (Siemens ECAT Exact 47) to acquire images of a 6.5 l Jaszczak phantom with six hollow spheres (diameter range 10.2-32.0 mm). Activity concentrations for the background and the spheres were varied to obtain different image contrast ratios (SBR range 1.2-9.8). An ordered subsets expectation-maximization (OSEM) algorithm (4 iterations, 16 subsets) was used for image reconstruction.
Results: The theoretically optimal background-subtracted RTL depends on the diameter-to-FWHM ratio (DFR). For large DFR, it was proven that an asymptotic RTL of 50% of the background-subtracted signal is theoretically optimal. For intermediate DFR, the optimal RTL is ~45% and ~40% for the 2D and 3D case, respectively. For small DFR, the partial volume effect occurs and the optimal RTL is >50%. The optimal RTL was demonstrated to be independent of the SBR. Calibration of the correction algorithm for small diameters was successful. The experimental data endorsed these findings and confirmed the optimal RTL to be independent of the SBR. For the

three largest spheres, optimal mean RTLs of 44% (SD ±1%), 40% (SD ±3%) and 37% (SD ±2%) were emperically found for D = 20.1, 25.1, and 32.0 mm, respectively.
Conclusions: Optimal background-subtracted threshold segmentation of spherical PET volumes is independent of the SBR and has been shown to be applicable in-vitro. The optimal threshold level depends a priori knowledge of the lesion diameter. Calibration of the algorithm using physical characteristics of the specific PET-camera is obligatory.
[1] Daisne JF et al, Radiother Oncol 2003;69:247-250.

1223 poster

COMPARISON OF 4 SEGMENTATION TOOLS FOR FDG-PET BASED TARGET VOLUME DEFINITION IN HEAD AND NECK CANCER

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Purpose/Objectif: To optimize the delineation of gross tumor volume (GTV) in head and neck cancer based on co-registered computed tomography (CT) and 18F-fluorodeoxyglucose (18F-FDG) positron emission tomography (PET) images.
Materials/Methods: 70 patients with a stage II-IV squamous cell carcinoma of the head and neck were prospectively enrolled after informed consent. All patients were eligible for primary curative radiotherapy. The primary tumor was located in the oral cavity (n=3), oropharynx (n=29), hypopharynx (n=7) or larynx (n=31). CT and 18F-FDG-PET were acquired with patients immobilized by custom-made thermoplastic mask, and images were co-registered.
The primary tumor was delineated on CT (GTVct), and four PET-based GTVs were obtained: interpreting the PET-signal visually (GTVvis), applying an isocontour of standardized uptake value (SUV) =2.5 around the tumor (GTV2.5), using a fixed threshold of 40% of the maximum signal intensity (GTV40) and applying an adaptive threshold based on the signal to background ratio as developed by U.C.L. in Brussels (1) (GTVucl). Absolute volumes were compared. Overlap analyses were performed using similarity scores: Dice Similarity Coefficient (DSC), Concordance Index (CI), Confirmation Number (CN) and the overlap fraction of the intersection volume relative to GTVct and the four PET-based GTVs.
Results: The mean GTV volumes were 21.1 (95%CI 15.9-26.3)(GTVct), 19.5 (95%CI 14.9-23.9)(GTVvis), 15.7 (95%CI 12.5-18.8)(GTV40) and 10.3 (95%CI 7.7-12.1)(GTVucl) cm^3. There was a clear decrease in GTV in the following order: GTVct > GTVvis > GTV40 > GTVucl. ($p<0.02$, paired T-test) As the PET-based segmentation tool became more advanced, the overlap analyses demonstrated a decrease of DSC, CI and CN i.e. vis > 40 > ucl ($p<0.03$, paired T-test) due to the aforementioned reduction of GTV volumes. The mean overlap fractions in relation to the PET-based GTVs were 0.66 (95%CI 0.62-0.71) for GTVvis, 0.71 (95%CI 0.66-0.76) for GTV40 and 0.85 (95%CI 0.73-0.97) for GTVucl. An increase in the order vis < 40 < ucl ($p<0.0001$ for ucl relative to vis, paired T-test) was seen. This means that with increasing sophistication of the PET-based segmentation tool the GTVs became smaller and 'moved' into the volume delineated by CT thereby increasing the overlap. In 45% of the patients the GTV2.5 segmentation tool resulted in a completely unsatisfactory volume.
Conclusions: The volumes of PET-based GTVs decreased as the PET segmentation tool became more sophisticated, while the overlap w.r.t. the GTVs delineated on CT increased significantly. This demonstrates that the choice of a segmentation tool for target volume definition based on PET images is not trivial. Depending on the method used, the resulting GTV volume and the PET-CT overlap can differ significantly.
(1) Daisne JF et al, Radiother Oncol. 2003;69:247-250.

1224 poster

DELINEATION OF THE BOOST VOLUME FOR IRRADIATION OF BREAST CANCER: MRI VERSUS CT

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Purpose/Objectif: Accurate delineation of the surgical cavity is required to improve the delivery of the boost dose to the tumor bed for early stage breast cancer. MRI might be a useful tool for delineation due to high contrast between soft tissues. We compared the delineation of the boost volume using MRI and CT scans.
Materials/Methods: Ten patients, with early stage breast cancer underwent a planning CT scan. The patients were positioned supine with their arms placed above the heads in an arm-rest, equivalent to the treatment position. In the same position a 3D T1 MRI scan (1.5 T) was performed. A second 3D T1 MRI scan was performed in prone position using breast coils; this is the position normally used for diagnostic purposes with the best image quality. The boost volume was delineated by a physician in all three scans. In order to analyze the volumes in supine position, the MR images were registered with the CT images using mutual information. Therefore not only the volume but also the location of the boost volume could be analyzed. A similarity coefficient (SC) was determined to quantify the similarity. The SC is the ratio between the total overlapping volume and the total delineated volume in both scans.
Results: The boost volume was delineated for eight patients; the image quality of MRI scans in supine position of two patients was poor and could therefore not be used. The average volume of the boost volume was 10.3 ±5.2, 10.7±6.4 and 15.1±10.0 cm^3 for the MRI in prone position, the MRI in supine position and the CT respectively. On average the MRI volumes were 20 % smaller relative to the CT volumes. The difference between the volumes in the two MRI scans was not significantly different. Registration between the MRI and CT in supine position was possible. The similarity analysis resulted in an average SC of 0.6 ± 0.1.
Conclusions: The volume delineated using MRI scans instead of the clinically used CT scans was smaller compared with the CT volumes. There was no difference observed in volumes between the two different patient positions on MRI. The images in supine position could be registered, further analysis of the similarity is however, needed.

1225 poster

DIFFERENCES IN VOLUME DEFINITION BETWEEN CONVENTIONAL AND CT-BASED PLANNING FOR INVOLVED-FIELD RADIOTHERAPY OF SUPRA-DIAPHRAGMATIC MALIGNANT LYMPHOMA

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Purpose/Objectif: To assess differences between conventional and CT-based treatment volume and field definition in patients undergoing involved-field supradiaphragmatic radiotherapy lymphoma.
Materials/Methods: All supra-diaphragmatic lymphoma patients CT-planned over the last 2 years were reviewed. Twenty patients were included, ten having treatment to the cervical region and ten to the mediastinal nodes, of whom 13 had Hodgkin's and 7 had non-Hodgkin's lymphoma. Four of the mediastinal patients also had hilar node involvement. A CTV was delineated on CT. This was grown using the three dimensional algorithm in the planning system by

5mm to create a PTV. This was further grown by 6mm to account for penumbra, thus directly comparing it to the conventionally placed fields. These were defined on digitally reconstructed radiographs from the CT data and shielding of critical organs was drawn onto these fields. 2D and 3D irradiated volumes were thus identified and compared two-dimensionally from the anterior field of view. Any discrepancies were further analysed three-dimensionally slice by slice on the CT data. The comparison was made in terms of target volume coverage and shielding of critical organs. All critical organ doses were kept within tolerance when planning in 3D.

Results: Comparing conventional with CT planning in the mediastinum, part of the hilum was missed in 3/4 and 4/4 patients on the right and left, respectively; sections of the lower mediastinum were missed in 5/10 and 9/10 cases on the right and left sides, respectively; the upper mediastinum and lower supra-clavicular fossa (SCF) were not adequately covered in 3/10 and 5/10 patients on the right and left, respectively. A shorter field was defined conventionally in 3/10 cases. The inferior tumour coverage by conventional planning was compensated by better lung and heart shielding in most patients. Conventional planning of the cervical region undertreated the medial part of the volume in 8/10 cases in the lower SCF and in 7/10 patients in the upper SCF and neck. However, as a result there was a lower spinal cord dose. Laterally, the conventionally planned field was too wide in the upper SCF in 8/10 patients. In the lower SCF this was seen in 4/10 cases, but compared to CT 3/10 fields were too narrow. 9/10 patients had shorter fields superiorly and half the cases had longer fields inferiorly with conventional planning.

Conclusions: Using CT-based volume definition as the standard for volume definition, conventional treatment fields result in inadequate coverage of the hilum and lower mediastinum in the thorax and medially in the neck and SCF in the cervical region. Conventional fields also tend to extend too far laterally in the upper SCF. CT-based planning allows more precise coverage of the target volumes and accurate shielding of the critical organs.

1226 poster

DIFFERENT APPLICATIONS OF MATCHING TOOLS IN 3D-CRT PLANNING FOR LUNG CANCER PATIENTS

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Purpose/Objectif: An accurate delineation of the GTV in patients with lung cancer requires several changes of the CT slices in the lung and mediastinum L/W settings. On the other hand, if pre-chemotherapy GTV are to be treated, the use of co-registered pre-treatment and planning CT scans enable a more precise reconstruction of prechemotherapy target volumes and a better response evaluation.

Materials/Methods: Since June 2005, we have an Oncentra Master Plan treatment planning system available and we developed different ways of use of matching tools.

a) CT-CT with lung and mediastinum L/W settings: Two identical series of CT images, for each patient, were subsequently transferred to a workstation. The main window showed the CT slices in the lung W/L settings (window 1600 Hounsfield units (HU), level -600 HU). The right upper side window showed the corresponding CT slices in mediastinum W/L settings (window 400 HU, level 40 HU). Thereafter both image sets were automatically matched using identity fusion algorithm. The user can draw and edit contours on either CT with lung settings or CT with mediastinum settings images without changing the CT slice in the main window. Thus, depending on the tumor location, the corresponding window could be viewed, only moving a scroll bar.

b) Pre and post treatment CT scans: CT images after treatment were transferred to a treatment planning system and were coregistered with initial CT images pre-treatment using mutual information algorithm, the paired studies were prospectively evaluated for therapeutic response at known sites of disease.

Results: Since November 2005, all lung cancer patients underwent the first CT-CT fusion type. This method allows a better treatment volume definition and a shorter delineation time. As well as, in January 2006 we started the second CT-CT fusion type, performing 10 coregistrations that provided an easy and more accurate delineation of pretreatment volume. To incorporate the findings of FDG-PET scans into CT-based radiotherapy planning, a second coregistration of one series of CT images and PET images is needed, because the software does not allow a coregistration of more than two images series at the same time.

Conclusions: In summary, we performed a simple procedure, which can be used routinely, to superimpose CT images, to optimize the delineation process, because this tool facilitates the use of an appropriate L/W setting by radiation oncologist and reducing the observer variation in the delineation of lung cancer after induction treatment. It seems necessary work on these matching tools, to allow coregistration of more than two images series for patient, at the same time, for example: CT-CT-PET; CT-CT-MRI...

1227 poster

DOES THE PRESENCE OF INTRAVENOUS CONTRAST HAVE A SIGNIFICANT DOSIMETRIC IMPACT IN HEAD & NECK RADIOTHERAPY PLANNING?

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Purpose/Objectif: In several anatomical sites including head and neck, acquisition of contrast enhanced CT is one of many strategies used to improve the accuracy of target volume and organ at risk delineation. The presence of contrast can enhance the primary tumor, but also aids in the accuracy of nodal station contouring in line with consensus guidelines for treatment of prophylactic nodal stations. Contrast alters the electron density information and may introduce clinically significant changes in dosimetry when used for treatment planning. To avoid this complication, many centres utilize additional non-contrast CT datasets for the dosimetric calculation. A dosimetric study was conducted to determine whether a non-contrast CT studyset is necessary for planning purposes in the treatment of head and neck cancers. The objectives of this study are to: 1. Determine the magnitude of change in electron density information with administration of intravenous contrast at CT simulation in head and neck cases using departmental image acquisition and contrast administration protocol. 2. Establish the dosimetric differences between a treatment plan calculated on a contrast study set versus a non-contrast study set. 3. Assess the clinical significance of the differences observed (if any).

Materials/Methods: Ten (10) head and neck patients on study were sampled for electron density information from vessels with and without contrast Major vessels in the Head and Neck region were then contoured. Varying electron density were assigned to these vessels and dosimetry assessed. Forced density values ranged from 1 to 3. Treatment plans of varying complexity were overlaid to assess the dosimetric impact in order to test the study hypothesis and assess dosimetric impact. The analysis using dose and volume 2 dimensional and 3 dimensional assessments for varying forced density values will be presented.

Results: Results will be presented in graphical and tabular forms demonstrating the impact of contrast on CT based dosimetry.

Conclusions: Results indicate that alteration in the electron density information due to the presence of contrast does not alter the

generated dosimetry, using forced densities of 1.2 , 2 and 3. This is independent of choice of techniques (3d CRT or IMRT). Contrast enhanced simulation CT study sets can be used for both contouring and for plan generation without dosimetric consequences.

1228 poster

HELICAL TOMOTHERAPY PLANNING OF MALIGNANT GLIOMAS USING (11) C-METHIONINE PET/CT/MRI IMAGE FUSION

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Purpose/Objectif: Using computed tomography (CT) or magnetic resonance imaging (MRI), it is difficult to differentiate residual tumors from nonspecific postoperative changes in patients who undergo resection for malignant gliomas. The higher specificity and sensitivity of 11(C)-methionine positron emission tomography (MET-PET) in brain tumors has been demonstrated in previous studies and may be useful for delineation of gross tumor volume. We developed a technique that incorporates routine integration of MET-PET in intensity-modulated radiotherapy (IMRT) with helical tomotherapy (HT). In this study we examined the combined use of MET-PET and CT/MRI to quantify the effect of MET-PET in gross tumor volume definition for HT planning of malignant gliomas.

Materials/Methods: We postoperatively examined 5 patients who had undergone resection of malignant gliomas. The CT, MRI and MET-PET data sets were fused utilizing the Pinnacle System. The gross tumor volume (GTV)-1 was defined as the area of severe MET uptake. GTV-2 was defined as the area of mild MET uptake. The planning target volume (PTV)-1 encompassed the GTV-1 plus 5mm margin, and PTV-2 encompassed the GTV-2 plus 2mm margin. Stereotactic radiotherapy was performed by HT in 8 fractions, keeping the dose for GTV-1 68 Gy (BED 126 Gy), PTV-1 56 Gy (BED 95Gy) and PTV-2 40Gy (BED 60 Gy). This dose was prescribed to the 95 % isodose line, which covered the GTV-1, PTV-1 and PTV-2, respectively. We compared the GTV-1 on MET-PET and the volume of contrast-enhancement on CT/MRI using fusion images. The homogeneity index and conformity index were assessed using our target planning method.

Results: In 3 patients the GTV-1 was bigger than the volume of contrast-enhancement in the CT/MR fusion image. In one patient the GTV-1 corresponded to the volume of contrast-enhancement. In one patient the volume of contrast-enhancement was bigger than the GTV-1 and was believed to be due to radiation necrosis. Our target planning demonstrated that the conformity index was 95% and the homogeneity index was 107%. There was no acute toxicity in any of the patients.

Conclusions: In most postoperative cases of resected malignant gliomas the size and location of residual MET uptake differs considerably from the abnormalities found with CT/MRI. Since postoperative changes cannot be differentiated from residual tumors by CT/MRI, the use of MET-PET, which has a greater specificity for tumor tissue, helps to outline the gross tumor volume with greater accuracy. Our clinical study demonstrates that HT planning using MET-PET offers excellent target coverage, homogeneity and organ sparing. This provides the opportunity for dose escalation studies and retreatment of previously treated tumors. To more clearly define the impact of MET-PET with HT planning, subsequent experimental and clinical analyses are required.

1229 poster

HYPOFRACTIONIATED (HF) RT OF LOCALLY ADVANCED PANCREATIC CANCER: A PLANNING DESIGN

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Purpose/Objectif: The majority of PTs affected by pancreatic cancer have advanced disease at the time of diagnosis and vessel invasion prevents the possibility of surgical resection. HF RT may provide a benefit in local control. 4D-TC_PET procedure allows an optimised target volume definition. On-board MV_CT reduces set-up errors. The evaluation of tumour mobility during free breathing condition. The comparison of "conventional" vs 4D definition of PTV. The analysis of dose distribution obtained with HT TPS for a central dose of 48-50 Gy in 15 fractions.

Materials/Methods: 7 PTs, immobilised by a vacuum pillow, underwent both standard whole-body PET_CT and a 4D-PET_CT limited to the region of interest. The scans were acquired during free breathing monitored by the RPM: each reconstructed image was assigned to a specific respiratory phase and 3D bins at 10 selected phases were generated. A software tool combined the ten 3D-PET_CT scans into a single "integral" set applying the maximum-intensity-level algorithm. Tumour motion was estimated comparing the centre-of-mass position at extreme phases. Three different PTVs were analysed: 1) PTVstd obtained from CTV outlined on standard CT/PET scan and adding 10-15 mm (motion+set-up errors) 2) PTV3bin is the encompassing volume of CTVs at three phases with the addition of 5mm margin 3) PTVint is the CTV outlined on the "integral" data set with the addition of 5mm margin. Considering only PTV3bin as target volume, treatment planning was obtained by HT TPS with highest priority PTV coverage. Inside PTV3bin, a sub-volume was defined around the region of vessel infiltration: the prescribed dose was 45 Gy at PTV3bin periphery and 48-50 Gy at internal sub-volume.

Results: The average amplitude of target motion was 6.8±1 mm in 3D space. The three PTVs were: 298±135 cc (PTVstd), 209±115 cc (PTV3bin) 194±110 cc (PTVint). Dose distribution was uniform both in PTV3bin (Dmean=45±0.3 Gy, SD=1.1±0.4 Gy) and sub-volume (Dmean=49±1.0 Gy, SD=0.5.±0.2 Gy). All OARs received very low dose levels. Dmax and Dmean were 47±2 Gy and 16±3 Gy for duodenum, 46±8 Gy and 14±10 Gy for stomach. Spinal cord Dmax was 9±6 Gy. Kidney and liver received a Dmean equal to 4±2 Gy and 7±6 Gy respectively.

Conclusions: The 4D-CT_PET procedure permits a patient-specific evaluation of tumour mobility, thus avoiding the use of standard margins that determine unnecessary normal tissue irradiation. The (moderate) HF irradiation approach is feasible with the possibility of dose escalation to PTV or its sub-volume.

1230 poster

IMPACT OF 18F-FDG-PET/CT ON TARGET VOLUME DELINEATION IN LUNG CANCER PATIENTS WITH ATELECTASIS

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Purpose/Objectif: Conformal radiotherapy in lung cancer depends on GTV definition and a reliable imaging modality is an essential prerequisite. We compared shape and size of CT- and FDG-PET-based gross tumor volume (GTV) delineations for combined chemo-radiotherapy in patients (pts) with locally advanced lung cancer (stage III) and tumor-associated atelectasis.
Materials/Methods: Patients with locally advanced lung cancer were planned for induction chemotherapy (cisplatin 50 mg/m^2, d1+8, and paclitaxel 175 mg/m^2 d1, qd 21) followed by concurrent chemo-radiotherapy (cisplatin 50 mg/m^2, d2+9 of RT, and vinorelbine 20 mg/m^2, d 2+9). PET/CT scans for radiotherapy planning were performed after induction chemotherapy. The GTV was at first delineated on the basis of the CT scan alone (GTV_CT) followed by contouring the GTV using the PET information (GTV_PET). The relative mutual volume of the GTV representing the 3-dimensional overlap of both volumes was calculated as Boolean operation: concordance index (CI) = (GTV_CT ç GTV_PET) / (GTV_CT è GTV_PET).
Results: Between January 2004 and March 2006, 36 pts (m/f: 26/10, median age 59 (34-73) years, T 2/3/4: 7/7/22, N 0/2/3: 11/16/9, IIIA/IIIB: 8/28), with locally advanced tumors and consecutive atelectasis have completed induction chemotherapy and were planned for radiotherapy. The mean GTV_CT volume was 94.6 (SD +64.1) ccm, mean GTV_PET was 99.1 (SD +74.8) ccm (p=n.s.). A volume reduction of the GTV was possible in only 36% of the cases by delineation based on PET information due to exclusion of atelectasis. Though nearly equivalent in volume size, the concordance index of both volumes accounted only for 0.41 (SD +0.18, p=0.002), i. e. there are significant differences in the geometric location of the GTV.
Conclusions: Target volume definition in lung cancer patients with atelectasis based on functional imaging may vary significantly from the CT-based contour but leads to volume reduction in only one third of the patients.

1231 poster

IMPROVING THE ACCURACY OF PROSTATE DELINEATION BY REGISTRATION OF FIDUCIAL MARKERS ON PLANNING CT AND ULTRASOUND

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Purpose/Objectif: Delineation of the prostate on ultrasound (US) is considered superior to the use of CT images. In our institute fiducial markers are inserted in the prostate guided by US routinely and used for daily position verification and online correction. During the implantation US images of the prostate are made. It was investigated how this information could be helpful in the delineation of the prostate by registration of the US- and CT-images, making use of the fiducial markers as reference points.
The purpose of this study is to assess the benefit of the US-CT registration, on the accuracy of prostate delineation.
Materials/Methods: Four prostatic fiducial markers are inserted by the radiation oncologist, prior to conformal therapy for localized prostate cancer, using the Variseed system with B&K ultrasound equipment. During the implantation procedure the fiducial markers and the prostate are delineated in Variseed, after which a CT scan is acquired. In a group of eighteen patients the prostate was initially delineated on CT by a physician who was unaware of the US images and contours. Next US- and CT-images were registered by matching the implanted fiducial markers. After registration, the CT-US registered studies were presented to the physician accompanied by the US-delineation of the prostate. The prostate was CT-delineated again on the registered images. The discrepancies between the CT- and CT-US defined prostate contours with respect to the US-delineation were recorded in a coronal, sagittal and axial plane through the centre of the prostate.
Results: In the axial plane, the greatest systematic discrepancy was in posterior-lateral direction. On CT-only it was on average 3.5 mm (SD = 0.6 mm) which decreased to 1.8 mm (SD = 0.2 mm) in CT-US delineation. In the coronal plane the greatest discrepancy was found in cranial direction and averaged 2.8 mm (SD= 0.2 mm) in CT-only which reduced to 1.4 mm (SD= 0.4 mm) in CT-US. In the sagittal plane the posterior cranial direction showed the greatest discrepancy, on average 5.0 mm (SD= 1.7 mm) in CT and 1.6 mm (SD= 0.7mm) CT-US respectively. The volume of the CT-only studies exceeded the US studies by 30 % (SD= 28 %). In the CT-US studies no significant deviation of the volume (0.6 %, SD= 10 %) was observed.
Conclusions:
Delineation of prostate contours can improve considerably by registering CT with US data that is routinely available in our institute as part of the fiducial marker implantation procedure.

1232 poster

INTER-OBSERVER VARIABILITY IN SEROMA CONTOURING FOR PARTIAL BREAST RADIOTHERAPY: IMPACT OF GUIDELINES

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Purpose/Objectif: Inconsistencies in contouring target structures can undermine the precision of conformal radiation therapy (RT) planning and compromise the validity of clinical trial results. This study evaluated the impact of guidelines on consistency in target volume contouring for partial breast RT (PBRT) planning.
Materials/Methods: Guidelines for target volume definition for PBRT planning were developed by members of the steering committee for a pilot trial of PBRT using conformal external beam planning. In phase 1, delineation of the breast seroma in five early-stage breast cancer patients was independently performed by a "trained" cohort of four radiation oncologists who were provided with these guidelines and an "untrained" cohort of four radiation oncologists who contoured without guidelines. Using automated planning software, the seroma target volume (STV) was expanded into a clinical target volume (CTV) and planning target volume (PTV) for each oncologist. Means and standard deviations were calculated, and two-tailed t-tests were used to assess differences between the "trained" and "untrained" cohorts. In phase 2, all eight radiation oncologists were provided with the same contouring guidelines, and were asked to delineate the seroma in five new cases. Data were again analyzed to evaluate consistency between the two cohorts.
Results: The 'untrained' cohort contoured larger seroma volumes and had larger CTVs and PTVs compared to the 'trained' cohort in 3 of 5 cases. When seroma contouring was performed after review of contouring guidelines, the differences in the STVs, CTVs, and PTVs were no longer statistically significant.
Conclusions: Guidelines can improve consistency among radiation oncologists performing target volume delineation for PBRT planning.

1233 poster

IPSILATERAL IRRADIATION FOR OROPHARYNX AND ORAL CAVITY CANCER: A PROPOSAL FOR CASE SELECTION AND PRELIMINARY RESULTS

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Purpose/Objectif: In head and neck cancer (H&N) bilateral elective neck irradiation is the prevailing treatment for many tumor subsites and stages. The better knowledge of the pattern of nodal invasion and recent innovations in radiotherapy techniques offer the opportunity for more precise targeting and sparing of normal tissue, specially the contralateral parotid gland. We present guidelines for patient selection, target determination, and our preliminary results.
Materials/Methods: Between February 2000 and December 2003, 15 H&N patients were treated using ipsilateral 3DCRT techniques. Primary tumor was located at the tonsillar region in 6 patients, retromolar trigone in 3, mobile tongue in 2, and bucal mucosa in 4. Seven patients received definitive RT: 5 stage I and 2 stage II disease. Eight patients received postoperative RT: 3 with stage II (positive surgical margin) and 5 with stage III (2 T1N1, 3 T2N1). Using 3D planning, CTV1 encompasses the gross tumor or the resection bed with 10-15 mm margin. CTV2 includes the elective ipsilateral nodal levels with 5-10 mm margin. Nodal levels were included if the risk of subclinical disease was estimated >10%. Guidelines used for the selection of ipsilateral nodal target volume (CTV2), according to primary site and stage were as follows:

Tonsillar region	T1-2N0	Levels II-III, RP
	T1-2N1	Levels II-IV, RP
Retromolar trigone	T1-2N0	levels Ib, II, III
	T1-2N1	levels Ib, II-IV
Mobile tongue	T1-2N0	levels Ib, II, III
	T1-2N1	levels Ib, II-IV
Bucal mucosa	T1-2N0	levels Ib, II, III
& alveolar ring	T1-2N1	levels Ib, II-IV

Prescribed dose to PTV1 was 64-70 Gy for definitive RT and 50-64 Gy for postoperative RT. Dose to PTV2 was 50 Gy.
Results: Two to four 6 MV portals with customized blocks ± wedges have been used for each patient. Target coverage varied from 95% to 105% for both PTV1 and PTV2. Maximum dose to spinal cord was ≤ 48 Gy. Contralateral parotid gland received <20 Gy in all cases (mean dose 10-12 Gy). With a minimum follow-up of two years, no contralateral neck failures have been found in any of these patients. No patient experience grade 2+ xerostomia.
Conclusions: Symptomatic xerostomia may be avoided in selected patients with lateralized H&N carcinoma without an increased risk of contralateral nodal failure. Derived from H&N literature information and our own preliminary results, we present guidelines for the use of ipsilateral radiotherapy, including patient selection and nodal target determination.

1234 poster

OPTIMIZING MRI FOR THE DELINEATION OF GTV FOR HYPOPHARYNGEAL AND LARYNGEAL CARCINOMA

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Purpose/Objectif: To optimize and test a MRI protocol for delineation of the gross tumor volume (GTV) for treatment planning purposes of hypopharyngeal and laryngeal carcinoma.
Materials/Methods: MR images (T1w, T2w (turbo) SE) of a healthy volunteer were acquired using a 1.5T and 3.0T MR scanner. Various receiver coils were investigated that could be used in combination with the immobilization mask needed for reliable co-registration. Signal-to-noise ratios (SNR) of the vocal cords were determined. For the optimal receiver coil the influence of resolution, slice thickness and magnetic field strength were studied. Special attention was paid to obtain an acceptable scan time and to reduce motion artefacts. Finally the protocol was used for 28 patients with hypopharyngeal and laryngeal carcinoma.
Results: Large differences in SNR were obtained for the various coils. SNR obtained using flexible 2 element circular coils (d=11 cm) was three times higher than was obtained using a standard head-neck coil used for diagnostic purposes and five times higher compared to a body coil (figure 1). The flexible 2 element circular coils were applicable in combination with the immobilization mask. Images with a resolution of 0.4x0.4x4 mm^3 showed superior anatomical detail and resulted in a scan time of 4 minutes. Reducing slice thickness resulted in unacceptable scan times what could not be compensated for by using scan time reduction techniques (for example parallel imaging, SENSE) while maintaining an acceptable SNR. A 3.0T magnetic field resulted in a longer scan time because of an increased specific absorption rate (SAR) beyond safety margins that could not be compensated for by SENSE. 28 patients (20 laryngeal carcinoma, 8 hypopharyngeal carcinoma) were scanned with this protocol. 3 patients (11%) were not able to complete the whole examination. Motion artefacts did not substantially degrade image quality as only in 2 patients (7%) GTV delineation was not possible because of motion artefacts.
Conclusions: Scanning at 1.5T with a 0.4x0.4x4 mm^3 resolution and flexible 2 element circular coils provides superior images of the larynx that are not substantially degraded by motion artefacts. This protocol facilitated tumor delineation in patients with hypopharyngeal and laryngeal carcinoma treated with radiotherapy.

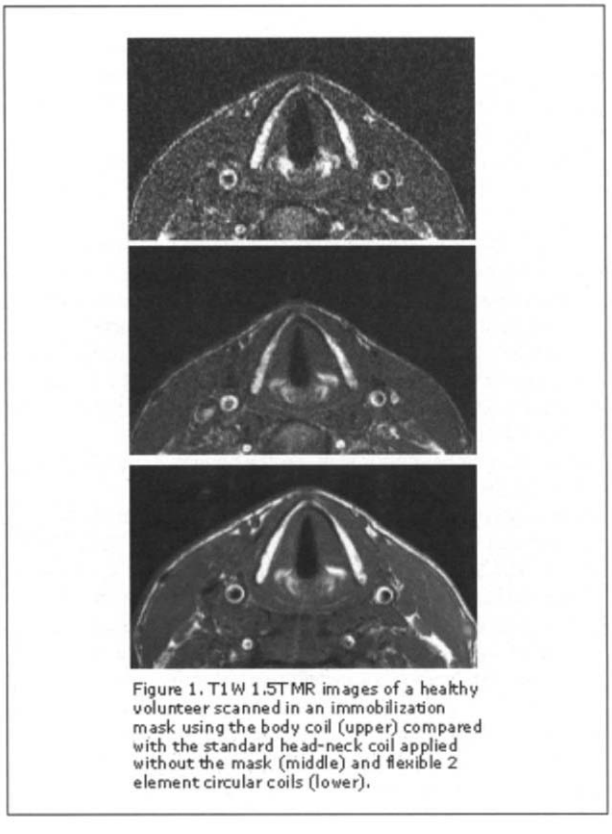

Figure 1. T1W 1.5T MR images of a healthy volunteer scanned in an immobilization mask using the body coil (upper) compared with the standard head-neck coil applied without the mask (middle) and flexible 2 element circular coils (lower).

1235 poster

PELVIC VESSELS UNCERTAINTIES DURING A COURSE OF PELVIC EXTERNAL BEAM RADIATION FOR PATIENTS WITH CERVICAL CANCER: IMPLICATION AS SURROGATE NODAL CLINICAL TARGET VOLUMES

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Purpose/Objectif: Expansion of the contours of pelvic vessels has been proposed as a surrogate of nodal CTV (nCTV) for precision radiotherapy of pelvic tumors. The uncertainty of these vessels is assumed to be small although this has never been demonstrated during a course of treatment where motion and deformation of both tumor and surrounding organs exist. We reviewed the contours of the major pelvic vessels in a group of cervical cancer patients who underwent a course of radiotherapy to assess the error and impact of a uniform expansion on the nCTV.

Materials/Methods: Patients undergoing radical radiotherapy (RT) for cervical cancers were eligible for this study. Axial volumetric T2w MR images were obtained from the sacral promontory to the ischial tuberosity at time of radiation planning and repeated weekly over the 5-weeks of external beam treatment. The 6 MRI images sets were fused to the patient's planning CT scan based on the bony pelvis. Major pelvic vessels (common, external and internal iliac veins and arteries) were outlined manually using Pinnacle^{3TM} (Philips Medical Systems, Bothwell, N.A.) from the level of the sacral promontory superiorly. The inferior extent of the external iliac was defined by the crossing of the inguinal ligament while the most posterior recognizable branch of the internal iliac was contoured to the level of the acetabulum. The combined artery and vein contours of each scan were then expanded 2-dimensionally by 5, 10 and 15-mm and delimited by the adjacent normal tissue contours (bladder, rectum, sigmoid and bowel) to form nCTV5, nCTV10 and nCTV15, respectively. A uniformity index (UI) was calculated by dividing the overlapped volume of the repeated scan and baseline scan by the union of the volume of these 2 scans. No overlap is 0 while complete match is 1. This is repeated for each repeat scan.

Results: Scans of 10 patients with FIGO stage 1B to 4A cervix cancer were accrued. They received 45 to 50 Gy of conventional CRT in 25 fractions. Analyses have been performed on the first 5 patients with a total of 28 scans. The mean vessel volume was 46.30 cm^3 (SD 14.14). The mean nCTV5, nCTV10 and nCTV15 were 175.61, 334.15, and 506.00 cm^3, respectively. The mean UI of the contoured vessel was 0.45 (range 0.41-0.49). The mean UI for 5, 10 and 15-mm expansion for the nCTV were 0.68, 0.73 and 0.74.

Conclusions: A number of errors can contribute to the apparent uncertainties of the pelvic vessels. The process of image fusion and delineation error due to image artifacts and observer error may compound the results. This resulted in poor UI of the vessels of only 0.45. With a modest increase of margin of just 5-mm, it was improved to 0.68 of the nCTV of the baseline scan. This suggests an expansion of nCTV based on published literature is sufficient to account for nCTV errors. Future study with contrast enhanced angiography and improved fusion technique will result in better identification of true motion error.

1236 poster

POST-OPERATIVE RADIOTHERAPY OF SOFT TISSUE SARCOMA: IMPACT OF DIGITAL FUSION OF PRE-OPERATIVE WITH POST-OPERATIVE CT IMAGES ON TARGET VOLUME DELINEATION

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Purpose/Objectif: To compare the conventional delineation of the CTV based on the visual correlation of pre-operative images with post-operative treatment-planning CT (CTVcnv) versus the CTV delineation based on digital fusion of post-operative treatment-planning CT with pre-operative images (CTVfsd), and, subsequently, to evaluate the coverage of the fusion-based PTV (PTVfsd) by the 3D plan originally aimed at encompassing the conventional, visual correlation-based PTV (PTVcnv).

Materials/Methods: We revised the RT charts of 10 soft tissue sarcoma patients referred to our department for adjuvant irradiation for whom pre-operative CT and/or MRI scans were available. For each patient, CTVcnv and CTVfsd were outlined and the corresponding PTVs (PTVcnv and PTVfsd) were automatically generated by uniform expansion of CTVs by 1 cm. A 3D-Conformal treatment plan was created to encompass the PTVcnv according to the ICRU-62 recommendations. We compared the absolute volumes obtained with both approaches and we evaluated the CTVcnv relative to the CTVfsd in terms of: overlapping, missing and/or unnecessarily delineated volumes. We then evaluated the coverage of the PTVfsd by the 3D plan originally aimed at encompassing PTVcnv.

Results: As expected, the CTVfsd and PTVfsd were found to be larger than the CTVcnv and PTVcnv (781 and 1254 vs. 496 cc and 953 cc respectively). The mean ratios of CTVfsd and PTVfsd to CTVcnv and PTVcnv were 2 and 1.5 respectively. The volumes of the overlapping CTVs and PTVs for the two delineation policies were 419 and 836 cc respectively. On average,using conventional CTV delineation approach, we unnecessarily included a volume of 77 cc and missed 362 cc of the CTVfsd (117 cc and 418 cc respectively in terms of PTVfsd) although this could be partially explained by the centripetal collapse of the surrounding tissues following the excision of GTV (mean volume of 234 cc). This translates in 34 % of PTVfsd (range 22-60 %) not covered by PTVcnv but, surprisingly, only 16% (4-34.8%) of PTVfsd was not adequately enclosed by the 95% isodose probably because of the incidental improvement of the PTVfsd coverage when 2-fields setup with relative high conformity index (1.64) were employed.

Conclusions: In the adjuvant irradiation of soft tissue sarcoma, 16 %, on average, of the PTV can be under-dosed by conventional contouring technique: digital fusion of pre- with post-operative CT images improves CTV (and PTV) delineation.

1237 poster

POTENTIAL ADVANTAGE OF STUDYING THE LYMPHATIC DRAINAGE BY SENTINEL NODE TECHNIQUE AND SPECT-CT IMAGE FUSION FOR PELVIC IRRADIATION OF PROSTATE CANCER

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Purpose/Objectif: This study aims to investigate the "in vivo" drainage of lymphatic spread by using the sentinel node (SN) technique and SPECT-CT image fusion and to analyze the impact of such infor-

mation on conformal pelvic irradiation.
Materials/Methods: Twenty-three prostate cancer patients candidates for radical prostatectomy already included in a trial studying the SN technique were enrolled. Computed tomography (CT) and single-photon emission computed tomography (SPECT) images were obtained after intra-prostate injection of 115 MBq of ^{99}Tc-nanocolloid allowing identifying the SN representing the first echelon of lymphatic drainage and, after an interval of 90-180 minutes, other pelvic lymph nodes. Target and non-target structures including lymph nodes identified by SPECT were drawn on SPECT-CT fusion images. CTV_1 included the prostate and seminal vesicles and CTV_2 included prostate, seminal vesicles, obturator, internal, and external iliac lymph nodes. A 3-dimension conformal treatment plan was performed for each patient.
Results: The SN technique was well tolerated by all patients and no case of relevant toxicity related to trans-rectal injection was observed. SPECT lymph nodal uptake was detected in 20/23 cases (87%). The SN was inside the pelvic clinical target volume (CTV_2) in 16/20 cases (80%) being the most frequent location (8/20, 40%) in the external iliac nodes. It received no less than the prescribed dose in 17/20 cases (85%). The most frequent locations of SN outside the CTV_2 were the common iliac and presacral lymph nodes. In addition to the SN, SPECT images were able to identify other 32 lymph nodes in 20 examined patients with an average of 1.6 per patient (range 0 - 6). Sixteen of them (50%) were found outside the CTV_2. Overall, the SN and the other intra-pelvic lymph nodes identified by SPECT were not included in the CTV_2 in 5/20 (25.0%) patients.
Conclusions: The study of lymphatic drainage can contribute to a better knowledge of the "in vivo" potential pattern of lymph node metastasis in prostate cancer. The characterization on an individual basis of the lymphatic pathway by sentinel node technique and SPECT-CT image fusion would have changed the CTV in at least 25% of our patients. This fact shows that such approach can allow avoiding the geographic missing of potentially involved lymph nodes.

1238 poster

PROBABILITY VOLUME HISTOGRAMS: QUANTIFYING SYSTEMATIC AND RANDOM PROSTATE DELINEATION ERROR

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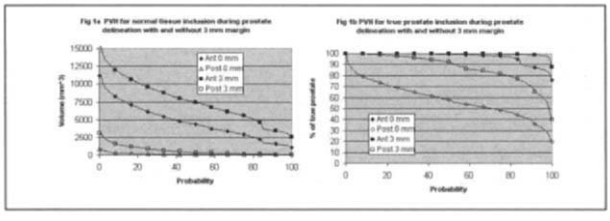
Purpose/Objectif: To measure the systematic and random error in prostate (CTV) delineation
Materials/Methods: Inter & intra observer variation in CTV definition have been well studied, but few studies report systematic errors, since most use the observer mean as the gold standard. In this work data from the Visible Human Project® provided indexed CT and cross sectional photographic images of the frozen human male cadaver. A multi disciplinary group of experts defined prostate on each cross sectional photo through to create a gold standard volume. On the corresponding CT images, six radiation oncologists (RO) each delineated the prostate 20 times, with at least 3 days between each targeting session, for a total of 120 CTV delineations. We introduce the concept of Probability Volume Histogram (PVH), similar to the DVH, and being the integral histogram of the frequency of inclusion and applied to target and normal tissue
Results: In the population of radiation oncologists in this study, the systematic and random delineation errors are directionally dependent. Our results show that every radiation oncologist in the study underestimated the extent of the posterior border of the prostate by a mean of 2.8 mm (standard deviation of 1.8 mm), thus systematically missing prostate. Conversely all observers over estimated the extent of the anterior border by an average of 5.8 mm (standard deviation of 3.9 mm), thus systematically including normal tissue such as bladder in the clinical target volume. The data was also analysed for trends in the superior inferior direction. The over estimate of prostate was shown to be significantly larger (average 9 mm) in the superior third of the prostate than the inferior third (3 mm). Posteriorly the maximum error in delineation occurred in the middle slices (4 mm). The PVH for prostate and normal tissue are shown in fig 1a and 1b respectively, showing the probability of including true target or normal tissue in the delineation of the CTV. The effect of adding a 3 mm margin the radiation oncologists target definition is shown.
Conclusions: At our centre we find systematic error in prostate delineation. The target is systematically missed posteriorly, while anteriorly there is systematic inclusion of normal tissue. This likely reflects significant concern about causing normal tissue complications in the rectum. We have found the concept of PVH to be a useful tool in assessing contouring and the effect margins around the CTV.



Posters Technology

1239 poster

BREATHING ADAPTED RADIOTHERAPY (BART) OF BREAST CANCER USING A MANUALLY CONTROLLED CT SCANNER FOR DOSE-PLANNING: A TECHNICAL REPORT

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Breathing adapted radiotherapy (BART) of breast cancer has been shown to reduce irradiation to the heart and ipsilateral lung when the radiation is given during deep inspiration. Several radiotherapy equipment suppliers have developed systems to deal with BART. However, many CT scanners are not, or only partly, compatible to these systems. Particularly, deep inspiration breath-hold is a challenge to some systems or combination of systems.
Our institution installed the Varian Real-time Position Management system (RPM™) in September 2005. However, our CT-scanner (General Electric HiSpeed CTi) did not have an interface port for the RPM-system to use as a scan trigger. We therefore had to use an alternative strategy to scan the patients to utilize BART.
This technical report describes how we carried out a manually controlled breathing adapted CT scanning. The RPM™-system was used to monitor and log the respiratory motion and to visually guide the manual starting and stopping of the CT scanner repeatedly to make a complete patient scan.

1240 poster

ELECTRON MLC (EMLC) MAY REPLACE TRADITIONAL BOLUS IN ELECTRON BEAM RADIOTHERAPY

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Purpose/Objectif: Traditional water-equivalent boluses are widely applied in low-energy (4 to 9 MeV) electron beam treatments to increase absorbed dose close to skin surface. Their use has problems with curved anatomical sites (nose, eye, ear, vulva, pubic and anal regions), skin with hair and daily hygiene. Since very small electron beams have no build-up, we investigated the potential of narrow sliding window of the electron multileaf collimator (eMLC) to replace traditional bolus.
Materials/Methods: An eMLC prototype consisting of non-focusing 2 cm thick and 5 mm wide steel leafs coupled with Varian 2100 C/D linac 20x20 electron applicator was constructed. Isodoses and depth doses of eMLC-shaped electron beams with beam width from 2 to 10 mm and length 10 cm were measured in a water phantom and calculated using Voxel Monte Carlo (VMC++) code of the Oncentra MasterPlan treatment planning system of Nucletron.
Results: For electron energies 6-9 MeV and beam widths less than 5 mm both phantom measurements and calculations confirmed the non-existence of build-up region, i.e. the maximum dose was at the surface. For each energy the therapeutic range R85 was dependent on the beam width. R85 was also much shorter than R85 of large open beams. For example, the R85 for 6 MeV eMLC field (5 mm x 10 cm) was 0.8 cm compared with 2.0 cm for 10 x 10 cm field. The energy of an electron beam used to generate an eMLC field without build-up region must then be higher than with the large open beam to ensure adequate therapeutic range.
Conclusions: In addition to offering many advantages in electron beam shaping, beam matching and intensity modulation, an eMLC offers an attractive alternative for traditional bolus. As soon as eMLC's will be commercially available, the clinical problems with the present bolus could be avoided.

1241 poster

IS A FREE BREATHING CYCLE DURING IRRADIATION REPRODUCIBLE SO THAT PATIENTS IRRADIATED FOR BREASTCANCER MIGHT BENEFIT FROM GATED IRRADIATION?

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Purpose/Objectif: Respiration changes position of target and critical organs during irradiation (IR). Planning margins need to account for this variability. More natural tissue is IR. The use of gated IR can reduce normal tissue damage. To use this technique, breathing movement has to be significanty pronounced, stable and reproducible from one cycle to the next.
Materials/Methods: 1/06 - 4/06 : 32 pts irradiated for breastcancer were evaluated. During free breathing a baseline respiration pattern was recorded during simulation and 3 weeks later. We used the Varian Real-time position management (RPM) connected to the Acuity simulator. At least 7 cycles were recorded. Amplitude, regularity and reproducibility and benefit of gated IR was evaluated.
Results: In 11/32 of all free breathing curves, the amplitude of the baseline patterns, caused by chest wall movement, was large enough to be detected separately. Movement ranged from 3.6 to 5.5 mm. For 7 pts the range was 2 - 3mm, with reproducible acceptable breathing cycle. For 14 pts free breathing was too flat, so the RPM system could not be used. 87.5 % of pts had a stable, regular pattern during their free respiration. Also 87.5 % of pts had a reproducible breathing pattern when reevaluated after 3 weeks.
Conclusions: In 30 % of all cases movement of chest wall is that large that pts can benefit from gated IR. The technique is possible since most pts have a stable and reproducible free breathing respiration cycle.
The % of duty cycle to be used for gating during a free breathing pattern must and will be optimized.
More pts will be included.

Posters Treatment Planning and Dosimetry

1242 poster

A DOSIMETRIC TEST FOR INHOMOGENEITY CORRECTIONS IN TREATMENT PLANNING SYSTEMS

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Purpose/Objectif: The aim of this work was the development of a systematic dosimetric test under reference conditions for the inhomogeneity correction calculations of treatment planning systems. This test should replace the inhomogeneity test recommended by the AAPM and complement the dosimetric test set developed within the NCS for quality control of treatment planning systems (TPS's).
Materials/Methods: An inhomogeneity consisting of balsa wood (relative electron density 0.23) with dimensions of 5x5x10 cm^3 was positioned in a water phantom at a depth of 2 cm. Measurements in water were performed at the central axis and various off-axis positions using a small ionisation chamber (0.03 cm^3). Measurements inside the balsa wood were performed at the central axis and off-axis positions using thermoluminescence dosimeters (TLDs). Measurements were performed for 6-, 10- and 18-MV photon beams for field size of 5x5, 10x10 and 20x20 cm^2. Calculations for the same geometry were performed using our clinical TPS (PLATO RTS 2.6.3) which uses an equivalent tissue-air-ratio (ETAR) inhomogeneity correction.
Results: The reproducibiltiy of the absolute dose measurement using the TLDs amounted to 2% (1 SD). At the central axis behind the inhomogeneity, the calculations and measurements agreed to within 3% of the local dose at all positions. For off-axis positions differences of 2% were observed in water. Within the inhomogeneity, the measurements and calculations agreed within 4% for 20x20 cm^2 and 10x10 cm^2 field sizes. The largest differences were observed for the 5x5 cm^2 field at the most distal position in the inhomogeneity where a difference of approximately 10% between measurements and calculations was observed.
Conclusions: A dosimetric test set for inhomogeneity corrections has been developed that can be used to validate treatment planning calculations and for QA purposes.
For the ETAR corrections of our clinical TPS satisfactory agreement between measurement and calcualtions was observed except for the relatively small field sizes (5x5 cm^2) where differences of 10% were observed.

1243 poster

A STUDY ON VOLUME COMPUTATION IN ONCENTRA MASTERPLAN V. 1.4 SP3

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Purpose/Objectif: Dose response curves and overall treatment outcome are strongly dependent on an accurate definition of volumes in radiotherapy. Recent developments, namely the introduction of IMRT in clinical routine, are based on dose-volume constraints and criteria. Quality assurance recommendations on treatment planning systems include tests on the calculation of volumes and manipulation of contours for anatomical structures. These were the main reasons for having carried out the present study on the calculation of volumes in Oncentra MasterPlan (OMP), Nucletron TPS (version 1.4SP3).
Materials/Methods: The study involved a first phase with two physical phantoms (one geometrical and other with different density materials) that have been scanned in order to verify the computation

of distances and volumes in OMP (both in Anatomy Modelling and Evaluation modules). In this phase also a study on automatic margin expansion has been done. Both axial images (directly imported from CT scanner) and reconstructed images (sagittal, coronal and oblique plans) were analysed. Different voxel sizes and matrix calculation grid sizes have been used. In the second phase we have used clinical cases in order to assess both anatomical structure volumes and dose values extracted either from DVH tables directly accessible in the plan printout or from an exported DVH file. Also different voxel and matrix calculation grid sizes have been used.

Results: Given the quite large scope of the study concerning structure manipulation and volume computation in OMP, different kind of results can be reported: i)concerning margins we have concluded that automatic expansion works quite well with deviations from the nominal margin width of less than 0.8 mm, both for axial and reconstructed images; ii) differences of up to 10%, depending on the volume, have been found for volumes calculated in different TPS modules; iii) significant differences have also been found between information reported in DVH table (plan printout) and DVH exported file. These differences can reach up to 30% in minimum dose and 15% in mean dose. This can be explained by the way the DVH table is constructed from the DVH file information.

Conclusions: This quite comprehensive study have aware all clinical staff involved in treatment planning - dosimetrists, physicians and physicists on the importance of knowing how volumes are manipulated in OMP and its influence on DVH evaluation. It has also enabled the establishment of the best choice for calculation settings (voxel and matrix grid sizes) in order to minimize discrepancies.

1244 poster

A USEFUL SOLUTION TO IMPROVE THE ACCURACY OF IN-VIVO DOSIMETRY WITH A MICROMOSFET SYSTEM IN IORT TREATMENT WITH MOBILE LINAC

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Purpose/Objectif: Intra-Operative Radiation Therapy (IORT) is usually carried out with electron beams produced by a dedicated LINAC (LINear ACcelerator) that can be employed directly into an operating room. IORT refers to the application of radiation during a surgical intervention, after the removal of a neoplastic mass.

IORT foresees a single session only; it is therefore necessary to verify in real-time the accuracy of the prescribed dose in order to define an action level if needed. For this aim, micromosfet detectors are recommended. One of the main problems in the use of these detectors is the correctness of their positioning that can bias the dosimetric measure. A useful simple solution is here proposed to improve the accuracy of in-vivo dosimetry with a micromosfet system.

Materials/Methods: A mobile LINAC (NOVAC7 Hitesys , Italy) has been installed at Ospedali Riuniti di Bergamo (Bergamo, Italy). It produces electron beams in the nominal energy range 4-9 MeV and currently it is employed for the treatment of early breast cancer patients. Beam collimation is performed with perspex cylindrical applicators (diameter between 40 and 100 mm), mounted on exit window head.

The purpose is reached by the use of a plex disk (diameter 2 cm larger of the applicator) that lightly compresses the detector towards the target surface in a stable position. To guarantee the sterility, the micromosfet is inserted in a sterile thin transparent covering, available in the operating room; the surgeon puts the micromosfet in the covering and fixes it to the disk with sterile strips. In practice, the mosfet is sandwiched between the disk and the target surface.

Furthermore, the use of the disk has also two advantages: (1) to compress lightly the target volume (1-2 mm), making it more uniform and compact and (2) to give a more uniform dose to the target volume (build-up effect).

Usually, the thickness of the target volume determines the energy choice; differently, if the treatment energy is fixed, the thickness of the target volume determines the choice of the thickness of the disk to use.

Results: Using only the maximum energy available for NOVAC7 (most probable energy $E_{p,0}$ of 7 MeV), the optimisation process brought to the following treatment set-up: for target thickness up to 15 mm, a 5 mm plex disk; for target thickness between 16 and 20 mm, a 2 mm plex disk. For target volume thickness greater than 21 mm no disk should be used.

This procedure is clinically in use and the in-vivo dosimetric data for the first 40 patients confirm the reliability of the proposed method. The ratio between the measured and the expected dose ranges 0,9539-1,0397, with the mean value of 1,003± 0,021 (1 SD).

Conclusions: The use of the plex disk not only improves the accuracy of in-vivo dosimetry system with micromosfets, but guarantees better accuracy of the whole IORT treatment.

1245 poster

CALIBRATION OF SEMICONDUCTOR DETECTORS FOR IMPLEMENTATION OF AN IN VIVO DOSIMETRY PROTOCOL

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Purpose/Objectif: In vivo dosimetry provides an overall check of the entire dosimetry procedure and patient set-up being a powerful tool for tracing dosimetric errors during radiotherapy treatments. In this method, the dosimeters are placed on the patient's skin or in natural cavities, in order to verify that the correct dose has been delivered. The aim of this study is to characterise an in vivo diode dosimetry system for clinical use during photon irradiation.

Materials/Methods: Before calibration acceptance tests were performed to check the diodes behaviour during irradiation and for each parameter that influences their response. The perturbation of radiation field behind the diode was estimated based on film. The calibration procedure was performed in two main steps. The first was the calibration in reference conditions to establish the diode calibration factor and the second was the determination of a series of correction factors to account for differences when measurements are performed under non reference conditions. During calibration, dose measurements were performed in strategic points located on the central axis of the beam, using a water phantom and an ionisation chamber.

Results: The measured attenuation of the radiation field by the diode is significant. The results showed that the majority of the tested diodes is in good working conditions, e.g., the signal is stable, the measurements are reproducible and sensibility is good. Only one detector did not show an acceptable performance and was discarded.

Conclusions: The main advantages of diodes are: a high sensitivity to radiation, small size, good mechanical stability, absence of external voltage and immediate available of the measured dose. On-line dose verification has the advantage that reasons for large deviations can be investigated with the patient still in the treatment position.

1246 poster

CAN WE PREDICT FINAL DOSE DISTRIBUTION IN REAL TIME PROSTATE HDR BRACHYTHERAPY?

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Purpose/Objectif: The ultrasound-guided real-time HDR brachytherapy has become more and more popular technique in prostate cancer treatment. It offers real time visualization of the needle placement followed by calculation of a conformal treatment plan during the surgical implantation. The aim of the study is to determine how needle displacement in relation to virtual plan might influence final dose distribution in prostate gland.
Materials/Methods: In our study we analyzed dosimetric data of HDR prostate treatment plans calculated by Nucletron SWIFT™ and realized in the Center of Oncology-Institute in Gliwice, since 2003. Needle displacement was determined by measuring the distance between virtual and real positions of respective needles in three axial images acquired at the base and the apex of the gland and in the reference image. In our Department the placement of needles always begins with upper right horizontally and ends with lower left.
Results: The value of mean needle displacement affects V100 parameter however such relation depends on prostate volume. The bigger prostate the final dose distribution is less dependant on needle displacement. For prostate volume above 25 cc even major needle displacement may be corrected by optimization procedure. The needle displacement is the smallest for the apex and the biggest for the base. Mean values of needle displacement decrease with the consecutive number of needles in all analyzed axial images.
Conclusions: From our analysis can be concluded that in smaller prostate glands the improvement in final dose distribution could be achieved better by needle relocation than by optimization. The way of needle placement and their sequence may affect optimal implant geometry thus influences final dose distribution.

1247 poster

CHARACTERIZATION OF ADVANCED MARKUS CHAMBER, EBT RADIOCHROMIC FILMS AND "SKIN MOSFETS" FOR SURFACE, INTERFACES AND PATIENT-SKIN DOSIMETRY

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Purpose/Objectif: The dose released to the patient skin during a radiotherapy treatment is important when the skin is an organ at risk, or on the contrary is included in the target volume. Since most treatment planning programs do not predict dose within several millimeters of the body surface, in the past years different dosimeters were investigated. Recently new types of detectors were introduced in Radiotherapy: Advanced Markus chamber, "skin MOSFETs" and EBT radiochromic films. The aim of this study is to evaluate these detectors for surface and patient skin dosimetry.
Materials/Methods: Water-equivalent depth (WED) was first investigated. Ideally, surface dosimeters should have WED@0, while for detectors suitable for patient skin dosimetry this value should be in the range of 0.04 to 0.1 mm; the latter should also be robust, yield reproducible findings and show no temperature dependence. WEDs relevant to the studied detectors were verified by matching experimental 6-MV PDDs (relevant to 3 radiation fields) and reference PDD data relevant to the buildup region (obtained from Monte Carlo calculations). Reproducibility was verified along with angular dependence for the skin-MOSFETs (utilized in vivo during total body irradiations (TBI)).
Results: The table below reports the results concerning the smallest field size (5x5 cm^2):

	Surface PDD (%)	WED (mm)
Advanced Markus chamber	13.0	0.100
EBT radiochromic films	14.6	0.136
Skin MOSFETs	10.6 ¸ 11.6	0.053 ¸ 0.073

Reproducibility, skin-MOSFET angular dependence and *in vivo* TBI results are also reported.

Conclusions: The Advanced Markus chamber was more reliable in yielding reproducible results. Due to its chamber design, the WED is lower with respect to older models as in surface over-response. WED of EBT radiochromic films is consinstent with the degree of thickness. Considering water-equivalence properties and improved sensitivity, they could be used for in vivo dosimetry; additional investigations concerning temperature dependence are however required for definitive confirmation. Skin MOSFETs have the WED closest to the epidermis, and due to the small dimensions and the depth spatial resolution, along with the immediate readout, they are suitable for both patient-skin and tissue-interface dosimetry. In vivo measurements have proven the importance of skin dosimetry in TBI.

1248 poster

CLINICAL APPLICATION OF ONEDOSE™ MOSFET FOR SKIN DOSE MEASUREMENTS DURING INTERNAL MAMMARY CHAIN IRRADIATION WITH HIGH DOSE RATE BRACHYTHERAPY IN CARCINOMA OF BREAST

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Purpose/Objectif: Skin dose measurements are important to monitor the reactions or cosmesis and ensure the accurate dose delivery to the patients. Several detectors are used for in-vivo patient dosimetry. Thermoluminescent dosimeters (TLDs) and silicon diodes are most commonly used. A newly designed Metal Oxide Semiconductors Field Effect Transistor (MOSFET) OneDose™ was used during high dose rate brachytherapy (HDRBT) of internal mammary chain (IMC) irradiation in Carcinoma of breast. This dosimeter has been evaluated at our centre for use at Iridium-192 (380 keV) as an in-vivo dosimeter and also provides the required characteristics for in-vivo dosimeters similar to TLD's. The aim of this study was to investigate whether this system could be used in the place of TLD for routine skin dose measurements in HDRBT. In addition, the aim was to assess its value as an effective quality assurance tool in HDRBT. Comparisons of skin dose measurements obtained by the MOSFET and TLD are also discussed.
Materials/Methods: Skin dose was measured for ten patients. All the patients were planned on PLATO treatment planning system. Average treatment length was 7.0 cm [range 5 to 9 cm]. A dose of 340 cGy was prescribed at 1.0 cm treating a 2.0 cm diameter sphere in 10 fractions twice a day with 6 hours apart. TLD measurements were performed to compare the accuracy of measured results from MOSFET.
Results: Mean dose measured with MOSFET was 53.91 cGy (15.85% of the prescribed dose, SD 8.47) while it was 53.92 cGy (15.85% of the prescribed dose, SD 8.70) with TLD. Mean dose was overestimated by TPS and was 59.23 cGy (17.42% of the prescribed dose, SD 9.25). Mean deviation between measured dose with MOSFET and calculated by TPS was found -8.99% (SD 0.55). Overall, TPS overestimated the skin dose by 9% and hence this was actually verified by MOSFET and TLD. There was no difference between skin dose measured with MOSFET and TLD. MOSFET measurements showed that the mean skin dose of 53.91 cGy has been received by the patient for a single fraction during HDRBT for IMC irradiation. For 10 fractions, patient has received total skin dose of 539 cGy from 3400 cGy. This dose is unlikely to cause any skin reactions to the patient.

Conclusions: Skin dose measurements with MOSFET compared with TLD has shown that the MOSFET system is an acceptable alternative to the use of TLD dosimeters. The system is linear and can be calibrated at the correct energy for clinical use. The immediate readout of the entrance surface dose is the major advantage of this system. The dosimeter is easy to use and cableless. This MOSFET system shows promise as a dosimeter for routine clinical use. The small size, instant readout, permanent storage of dose and ease of use make the MOSFET a viable alternative, in certain radiotherapy treatments, to the labor demanding and time consuming TLDs.

1249 poster

CLINICAL APPLICATION USING TARGET APPROXIMATION BY SELF-DEVELOPED METHODS IN STEREOTACTIC RADIOSURGERY

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Purpose/Objectif: Stereotactic radiosurgery (SRS) is a technique to deliver a high dose to a particular target region and a low dose to the critical organ using only one or a few irradiations while the patient is fixed with a stereotactic frame. It is tedious to find a specific condition to satisfy this object. In this study, the treatment planning techniques were developed both the cubic and cylindrical methods for reconstruction of irregularly shaped target. These methods for arrangement of multi-isocenters must be used to obtain a conformal dose distribution for radiosurgery.

Materials/Methods:

1.1 Cylindrical approximation

The previous study approximated the tumor volume using a cylinder, and automatically packed the isocenters inside the cylinders1. In this study, following three methods were used mainly, one step, create new target coordinates using the target characteristic, two step, development of a cylinder piling method for reconstruction the target, three step, development of sphere packing in each cylinder with the object of including each cylinder within a 40% isodose level.

The frame coordinates system was used in the conventional planning. The planning results may be different even though targets have the same shape. To settle this problem, a virtual axis was created within the target, and the cylinders were piled up around this axis. If the length of the longest line is L, then the target is located between z=L/2 and z=-(L/2) after a coordinate translation from the frame coordinates to new target coordinates. The cylinders were positioned to reconstruct the target according the following methods.

1.2 Cubic approximation

Another study approximated the tumor volume using a cube, and automated multi-isocenter arrangement was determined mainly using the following methods.

(¥i) A rectangular parallelepiped was used to create cubes surrounding the tumor volume.

(¥¢) For an array isotropy spheres, the rectangular parallelepiped is divided into cubic regions.

(¥£) The regions of the cube and tumor were composed of voxel units in three dimensional space, each cubes contained tumor fragments with different voxel counts. The voxel size was defined as 1×1×1 mm^3, and a voxel ratio was determined as the voxel counts in the tumor area by the voxel counts in the cube area. The optimal locations of the isocenters were determined to deliver a high dose in the tumor, while a low dose was delivered in the tissue outside tumor, was selected by a specific voxel ratio that was calculated automatically. Here, the multi-isocenter arrangement depends on the cubic structure and a voxel on space. The cubic structure does not allow a superposition of the spheres.

1.3 Clinical target and dose evaluation

The clinical target utilized meningioma with 8.1 cc volume and has approximately x-28mm, y- 27mm, z-26.5mm of the longest lines on axis. The figure 1 is showed spatially reconstructed volume of target. Moreover, an isodose surface covering at least 95% of the target volume (as determined by target volume DVH) was selected as the prescription isodose. Ideally, the prescription dose represents the minimum dose to the target. However, choosing a dose based on 100% target coverage by DVH usually results in a rather low dose level. This plan evaluation was based upon the dose volume data from the DVHs. The dose distribution for each sphere arrangement within the targets was evaluated with the conformity and homogeneity referred by the Radiation Therapy Oncology Group (RTOG) stereotactic radiosurgery criteria.

Results: Clinical target was arrayed automatically into multi-isocenters by cylindrical and cubic structures considering 6mm and 10mm collimator sizes. These planning methods by a cylindrical and cubic approximation conformed to the arrangement of the isocenters satisfying the tumor shapes. Then, 95% target volume was covered above 50% (of the normalized dose) of the isodose shell. Furthermore, the conformity and homogeneity to target volume is less than 2.0.

Conclusions: These planning methods using target reconstruction and sphere packing were not fully satisfied due to the limits of the target reconstruction using cylinders and cubes. However, the proposed techniques are a feasible approach for radiosurgery planning.

1250 poster

COMPARISON OF IMAGE QUALITY BETWEEN TWO KV CBCT AND CT MODALITIES.

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Purpose/Objectif: The aim of the study was to compare the volume density and geometry of image reconstruction on simulator and accelerator Cone-Beam Computed Tomography (CBCT) with diagnostic/planning Computed Tomography (CT) scans.

Materials/Methods: We evaluated the CBCT system consisting of simulator or linear accelerator equipped with an amorphous silicon electronic portal imaging device (aSi EPID).

An anthropomorphic head and neck phantom and a calibration phantom (Catphan) were taken under consideration. For both phantoms three sets of images with scan distance 1mm and 1.5mm were taken: CBCT on simulator Acuity-Varian; CBCT on linear accelerator CL23EXS-Varian and diagnostic CT Somatom Sensation Open-Siemens. An automatic CT and CBCT image registration in Eclipse Treatment Planning System (TPS) was provided.

For the first anatomical phantom the density of bone, air and soft tissues volumes were compared. For the second one the density of the air, PMP, LDPE, polystyrene and acrylic volumes were checked. Additionally distances between chosen circular markers for all three image sets were measured and compared.

Results: We demonstrated that sufficient image quality is provided by both CBCT systems mounted on simulator and linear accelerator. Good image geometry and correct volume densities were achieved by both modalities.

Conclusions: The investigated devices are useful and efficient in treatment planning procedures and patients positioning verification on linear accelerator. Their clinical implementation was confirmed.

1251 poster

COMPARISON OF IMRT AND 3D-CRT TREATMENT TECHNIQUES FOR LOW-GRADE GLIOMA

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Purpose/Objectif: To compare target volume coverage and normal tissue sparing of intensity-modulated radiation therapy (IMRT) and three-dimensional conformal radiotherapy (3D-CRT) treatment techniques for low-grade glioma.

Materials/Methods: Ten patients with supratentorial low-grade glioma were planned and treated with 3D-CRT using a common technique of two lateral opposed fields and one vertex field. Two types of IMRT treatment plans were then created for the planning study: a 3-field plan with the same beam arrangements (3F-IMRT), and a 5-field plan with two lateral oblique fields on each side and one vertex field (5F-IMRT). The planning target volume (PTV) consisted of the gross tumor volume (GTV) plus a margin of 20 mm. A dose of 54 Gy was prescribed to the isocenter. The dose-volume histograms (DVH) were generated for both the PTV and brain tissue. Only the normal brain tissue was considered for the DVH calculation as the PTV was subtracted from the brain volume. Dose conformity for the PTV was assessed using the conformity index (CI). Normal tissue-sparing index (NTSI) (Miften MM, et al. J Appl Clin Med Phys 2004;5:1-13) was generated to analyze the level of brain sparing. Finally, the Lyman-Kutcher-Burman normal tissue complication probability model (NTCP) was used to project the risks of brain damage.

Results: Both 3D-CRT and IMRT plans showed an excellent coverage of the PTV. As much as 99.9%, 100%, and 100% of the PTV was covered by the 95% isodose for the 3D-CRT, 3F-IMRT, and 5F-IMRT plans, respectively. However, the corresponding rates of CI (0.59, 0.67, 0.71) suggested higher degree of PTV dose conformity for the IMRT techniques. The volume of normal brain tissue irradiated to 50 Gy was significantly lower for the 3F-IMRT and 5F-IMRT plans compared to the 3D-CRT plan (17.5% vs. 24.0%, $p<0.001$; 14.2% vs. 24.0%, $p<0.001$). Brain sparing associated with both IMRT techniques was still significant at the level of 25 Gy. The NTSI values of 0.78, 0.84, and 0.88 for the 3D-CRT, 3F-IMRT, and 5F-IMRT plans reflected the evidence of reduced brain volume irradiated with intensity modulation. According to the NTCP model, the predicted hazard of brain necrosis was approximately 2% after 3D-CRT treatment. By contrast, this was only 1% and 0.6% for the 3F-IMRT and 5F-IMRT techniques, respectively.

Conclusions: IMRT is able to provide significant brain sparing which may be beneficial for the long-term survivors with low-grade gliomas.

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1252 poster

COMPARISON OF PHOTON DOSE MEASUREMENTS WITH CALCULATIONS FOR INHOMOGENEOUS MEDIA

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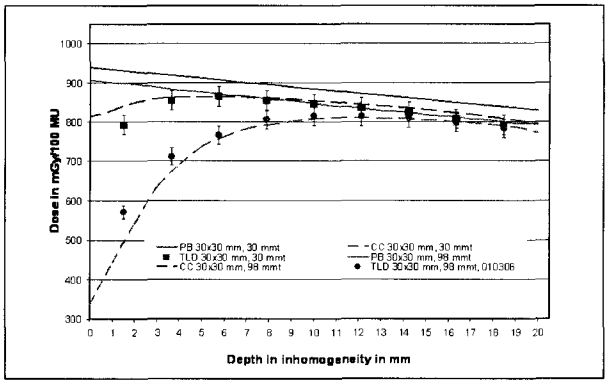
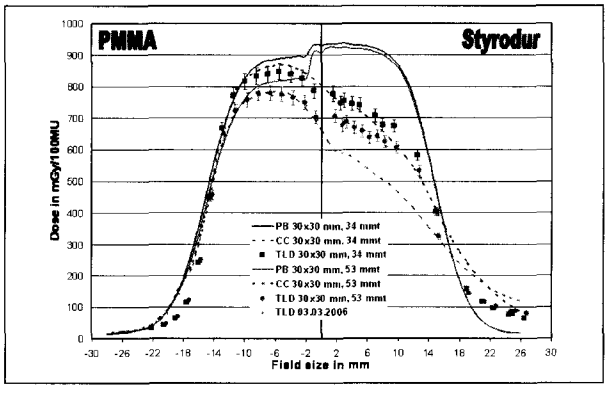
Purpose/Objectif: Calculations of photon dose distributions by pencil beam algorithms fail for regions with adjoining materials of different densities. Therefore superposition algorithms should be used for these situations. The purpose of this work was to compare results by pencil beam (PB) and by collapsed cone (CC) calculations with measured values for two typical geometric configurations.

Materials/Methods: The investigations were performed with a self made cuboid phantom consisting of PMMA with a styrofoam core. Dose was measured at different distances from the PMMA - styrofoam interface (PSIF) for several field sizes of a 6 MV photon beam incident parallel to the interface simulating tangential breast irradiations. The second scenario included dose measurements within a cylindrical PMMA inhomogeneity (CIH) with a diameter of 2 cm inside the styrofoam modelling the irradiation of solid lung lesions. Measurements were done with TLD detectors and the calculated dose values were extracted from the TMS treatment planning system by the line dose utility.

Results: The agreement between calculated and measured dose values is better for the CC calculation for all cases. For the PSIF modelling PB calculations overestimate the dose to the low density inhomogeneity by 20 - 70 % for all field sizes whereas the deviations of the CC results increase from about 3 % for the 5 x 5 cm^2 field up to 20 % for 1 x 1 cm^2. PB overestimates dose in the CIH model by about 5 % for field sizes above 5 x 5 cm^2 and underestimates it by more than 10 % for the 1 x 1 cm^2 field. CC gives dose values which agree with measurements within about 3 - 8 % respectively. In general deviations between calculated and measured values increase with decreasing beam dimensions.

Conclusions: Despite describing a worst case scenario (the density of the styrofoam was only 0.05 g/cm^3) the results suggest that for dose calculations in areas of electronic disequilibrium the use of more elaborate dose calculation algorithms like the CC should be mandatory.





1253 poster

DOSIMETRIC STUDY OF THE IMPACT OF BREATHING USING A DYNAMIC PROTOTYPE SIMULATING THE RESPIRATORY MOTION

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Purpose/Objectif: The radiotherapy treatments aim to conform the target volume whose shape is often based on nongated computed tomography (CT). Dosimetry is then carried out on dilated volumes, what could bring an additional dose on the surrounding organs and prevent a dose increase to target volume. It is then important to create a tool, in the absence of recommendations of approved organization, to study the dosimetric impact of respiration-induced organ motion. The aim of our work was to design a dynamic prototype simulating respiratory motion.
Materials/Methods: The experimental prototype consists of a 20x20 cm^2 motorized plate, able to carry out about from 15 to 20 respiratory cycles/min. Moreover, this model takes the constraints related to a radiotherapeutic treatment into account. In particular, its limits the presence of metal parts. The platform of the prototype can support various phantoms (homogeneous or with heterogeneities) with different measurements techniques : films, thermoluminescent dosimeters, ionisation chambers. The movement amplitude as well as the frequency are scalable thanks to the engine, controlled with a program implemented in C.
Conclusions: The flexibility prototype allows to simulate the various cranio - caudal movements from each thoracic organ. An amplitude and a given frequency could represent the motion of a precise organ. The study of the motion effect on the dosimetric distribution could then install as well as quality control of the devices 4D (respiration-gated radiotherapy, 4D CT scanner). The first results will be presented and in prospect, the prototype will be improved with an additional anterior - posterior movement in order to move in 2 dimensions.

1254 poster

DOSIMETRICAL VEIFICATION OF TREATMENT PLANNING SYSTEMS IN RADIOTHERAPY DEPARTMENTS OF BALTIC STATES

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Purpose/Objectif: A group of participants of the IAEA coordinated research project "Development of procedures for quality assurance for dosimetry calculation in radiotherapy" designed a number of clinical test cases for photon beams to verify the treatment planning systems (TPS) dose calculations as part of its commissioning procedure. This set of test cases was evaluated on different beam-TPS combinations in radiotherapy departments of Baltic States.
Materials/Methods: Verification measurements were carried out in 5 major radiotherapy departments of the region. CIRS thorax phantom (Model 002LFC, CIRS inc., Norfolk, VA) has been used to verify the dose calculated by TPS with measurements. In each hospital the phantom was scanned twice on CT used locally for the treatment planning. The first scan was performed to derive the relative electron densities to CT numbers conversion. The second scan was used for treatment planning. Proposed clinical test cases were designed to check the wide range of conditions. The doses were measured both on axis and off axis with ionisation chamber placed inside the CIRS phantom. More detailed information about the tests will be presented in the poster. Altogether, there are 28 different combinations of photon beams and TPS algorithms/inhomogeneity correction methods tested.
Results: All TPS tested had a satisfactory performance with deviations less than 3% in the majority of clinical test cases, except those dose measurements points, which were situated in the lung equivalent material. The deviations of up to 16.5% between measured and calculated doses were discovered for these points. A number of small discrepancies related to the beam data fitting were discovered as well. The time required for the whole chain of activities in the hospital: setting up the phantom, CT scanning, planning and measuring were in the range of 10-15h for dual photon energy machine and TPS with three different photon algorithms/inhomogeneity correction methods. It was dependent on the following factors: availability of record and verify system, TPS and logistics.
Conclusions: The verification measurements for TPS dose calculations of photon beams in the Baltic States showed acceptable results with few exceptions related to TPS algorithm limitations. The proposed clinical tests are useful tool to verify the TPS calculations with the measurements and to help the user to appreciate the possibilities of their system and understand its limitations.

1255 poster

DOSIMETRY QUALITY ASSURANCE OF HELICAL TOMOTHERAPY TREATMENTS, EFFECT OF DENSITY INHOMOGENEITIES

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St-Luc University Hospital in Brussels recently acquired a helical tomotherapy treatment unit (Hi ART II, TomoTherapy, Inc, Madison, WI) and clinical treatments have begun since december 2005. Tomotherapy is a new modality of radiation treatment that combines very sophisticated beam collimation with an on-board computed tomography scanner to image the region of interest prior to treatment. It provides highly accurate beam delivery allowing for tumor dose escalation while also reducing the dose to healthy tissue. There are a number of different malignancies that could potentially benefit from the unique characteristics of tomotherapy. It integrates treatment planning, patient positioning and treatment delivery with one machine.The convolution/superposition method, a model-based dose computation method is well suited for tomotherapy. The incident energy fluence issuing from the MLC and interacting in the patient is first modeled. Kernels, pre-calculated using the Monte Carlo method, are used to a take into account the scatter and charged particle transport in a heterogeneous patient. The treatment planning of tomotherapy is unique, specific to the machine and is an integrated system. It is therefore extremely important and essential to concentrate on dosimetry and accuracy of treatment planning with the use of in particular very high dose gradients. Consequently, an independent dosimetry check has been performed verifying all steps starting from the treatment planning until treatment delivery, this could be done thanks to some specific dosimetry audits. In addition to these complexities, the effect of density tissue inhomogeneities (present in many of our cases) has to be ensured, in particular into air cavities.Specific inhomogeneous phantoms have been studied, designed and built, and have been used to try to quantify the quality of the convolution superposition algorithm present in tomotherapy treatment planning. Results of this dosimetry quality assurance study will be presented and discussed and a comparison will be made with Monte Carlo.

1256 poster

EFFECT OF GATROINTESTINAL GAS ON DOSE CALCULATION ACCURACY FOR LUNG CANCER PATIENTS

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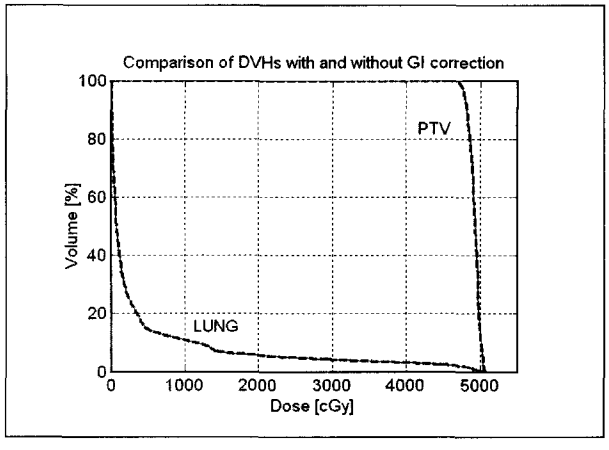
Purpose/Objectif: Previously we had reported that heterogeneous dose calculation using only 4 levels of electron densities corresponding to air, lung, soft tissue and bone provides an accurate method of dose calculation with the exception of patients with bullous emphysema. However, besides the trachea, the air region also includes gastrointestinal (GI) gas which could enlarge, shrink, or disappear during fractionated treatment depending on the patient's condition. The aim of this study was to investigate the influence of GI gas on the dose calculation accuracy of lung cancer patients.
Materials/Methods: Treatment plans with 4 levels of bulk electron densities were generated for 15 lung cancer patients with 16 tumors and no bullous emphysema using a commercial treatment planning system with an adaptive convolution algorithm with tissue heterogeneity correction (Pinnacle^3, Philips Medicals Systems, Shelton, Connecticut,). For each case, 2 plans were generated. The first was a bulk density plan with the population averaged densities of 0.15, 0.32, 0.98, and 1.11 g/cc assigned to air, lung, soft tissue, and bone, respectively, for the entire set of patients as used in our previous studyÅ@(Plan with GI correction); the areas were identified by an isodensity segmentation tool. The second plan was a bulk density plan using the same parameters except for the GI gas, and we applied the soft tissue density of 0.98 g/cc instead of the air density of 0.15 g/cc. Monitor units were kept constant and no normalizations were employed (Plan without GI correction). Dose volume histograms (DVH) and dose difference distributions for the two plans were compared for all cases.
Results: The median target volume of the 16 tumors was 99.9 cm^3 (range, 4.2 - 821.4 cm^3). The median volume of the GI gas of all of the slices and slices the same as the target were 33.1 cm^3 and 0.3 cm^3, respectively. In all cases, the target volume and the normal tissue DVH agreed to better than 1%. There was no difference in the dose to the target volume, even in the 4 patients for whom the relative volume of GI gas to the tumor at the same slices where the tumor was located was larger than 1% (1.9%, 4.1%, 4.4%, and 11.9%). Figure 1 shows a comparison of the DVHs (PTV and lung) between the 2 plans (with and without GI correction) for the patient with the largest relative volume of GI gas to the tumor at the same slices where the tumor was located (11.9%). The thin solid line is for the plan with GI correction and the thick dotted line is for the plan without GI correction. The DVHs are undistinguishable.
Conclusions: GI gas showed little influence on normal tissue and target dose calculation in all examined patients for whom the relative GI gas volume to the target at the same slices as the tumor was up to 11.9%. Therefore, while GI gas size may change depending on the patient's condition, no special correction would be needed.



1257 poster

ELECTRON BACKSCATTER MEASUREMENTS FROM LOW-DENSITY MATERIALS

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Purpose/Objectif: As part of the process to establish an independent monitor unit secondary check for electron beam calculations a project was set up to examine the effect on the dose to tissue due to an underlying low density medium e.g. lung or air. A number of papers appear within the literature regarding the effect of backscattered of high-energy electrons from underlying inhomogeneities. However, the majority of these deal with backscatter from high-density materials. When compared to dose measured in the tissue phantom alone, a decrease in dose for a maximum of 2 cm around the tissue phantom/lung phantom interface, for the range of energies in question, was expected from the previous studies within the literature.
Materials/Methods: Measurements were taken with a Markus and Roos PTW ionisation chambers, both were inverted with the chamber window at the distal side of the beam and placed in water equivalent plastic holders, w.e.p. The backscattering media used were cork slabs and a foam block. For comparison measurements were also made in w.e.p. only and in w.e.p. and air. The detectors were placed at the depth of the 90% point beyond dose maximum for each energy, or as close as would be allowed by the thickness of the w.e.p. slabs. The front face of the detector was placed at the interface. The Markus chamber was used without its protective cover to examine the change in dose at the interface. The Roos chamber has a 1mm thick entrance window and so measured the variation within the w.e.p. The backscattering materials were CT scanned in order to determine the Hounsfield numbers.
Results: Table 1 summarises the results obtained using the Markus chamber, for two electron energies. The electron backscatter factor, EBF, is the ratio of the measured ionisation with low-density backscatter material to ionisation with full we.p. backscatter. These measurements were taken at the interface.
Table 1: Variation of EBF with backscattering material for two electron energies

Material	6 MeV EBF	15 MeV EBF
w.e.p.	*1*	*1*
Cork slabs	1.016	0.996
Foam block	0.958	0.952
Air	0.907	0.923

No significant effect was found at the cork/w.e.p. interface for a 15 MeV beam, a small effect, 1.5%, was seen for a 6 MeV beam. A large effect was found for both energies at the w.e.p./foam interface and w.e.p./air interface. For measurements taken with the Roos chamber in the w.e.p. phantom no significant change in EBF was found with cork slabs as the backscattering material, for electron energies ranging from 4 to 18 MeV. The Hounsfield number for the cork slabs was measured as -780 HU ± 6%, 1 standard deviation, the Hounsfield number for lung tissue was found to be approximately -783 HU ± 1.3%.
Conclusions: It was found that the effect on the dose to tissue above underlying lung is negligible for electron energies from 4 to 18 MeV. A measurable effect was found, 3.2% and 2.6% with air and foam as the backscattering material. The focus of the work was to account for any variation in dose due to underlying lung for the monitor unit checker. As a result, no correction was applied.

1258 poster

ENERGY DEPOSITIONS ON THE NANOMETER SCALE FROM LOW ENERGY ELECTRONS

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Purpose/Objectif: To investigate the track structure and spatial dose distribution from low energy electron pencil beams in water.

Materials/Methods: Low energy delta-electrons have a considerable capacity to induce complex clustered damage in DNA. The knowledge of their energy depositions is therefore of great importance for radiation therapy. This is especially true for light-ion therapy where most of the biological effect comes from spatially correlated low-energy electrons. The energy depositions can be calculated with detailed MC techniques, but since fast calculations are needed for treatment plan optimization, exact and computational efficient analytical expressions are valuable. The Pencil Beam concept was developed for higher energies in the MeV range and may therefore be less accurate at the low energies around a few keV or lower, since the electron can loose a large fraction of energy in a single collision. The aim of this work was to investigate the lateral energy deposition of mono-energetic electron pencil beams. Of special interest is to decide weather there are discrepancies from the Gaussian distribution commonly seen at higher energies with many individual collisions. The Monte Carlo code PENELOPE was used for the transport of the electrons.

Results: When calculating the total number of interactions it is seen that so few interactions take place that the central limit theorem is not fulfilled. Even by the end of their range, electrons with energies as low as 100 eV will not have gone through enough number of interactions. Higher energies around 1000-10000 eV does not even fulfil the conditions in the beginning of their track. The lateral dose distribution for 1000 eV shows a prominent peak at the central axis at depth less than the range of the electrons. This peak represents the electrons that deposit most of their energy in a single event. Beneath this strong peak a close to Gaussian energy deposition distribution is seen. An attempt has been made to fit this peak by a analytical expression. The total energy imparted from the narrow peak is however much less than from the wide and low level Gaussian shaped part of the pencil beam and thus accurate modelling of the Gaussian part is more vital.

Conclusions: It might be possible to combine the Gaussian and another analytical expression for the central peak in order to more accurately describe the lateral energy deposition.

1259 poster

EVALUATION OF DOSE TO UTERUS IN ELECTRON BEAM IORT FOR EARLY-STAGE BREAST CANCER

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Purpose/Objectif: To determine the absorbed dose to uterus during intraoperative electron beam radiotherapy (IOERT) for early-stage breast cancer (EBC). At our Institute, IOERT using mobile linear accelerators is the most commonly used technique for exclusive partial breast irradiation (21 Gy dose, prescribed at 90% isodose) in a selected pt population.

Materials/Methods: Treatment was simulated on an Alderson anthropomorphic phantom, using electron beams produced by Novac7 (5-9 MeV) and Liac (4-10 MeV) dedicated mobile linacs in the operating room. The largest applicator usually used in clinical practice for EBC pts, that is 6 cm diameter, was selected. Absorbed dose to the uterus was measured by means of calibrated (±20% uncertainty) thermoluminescence dosimeters (TLDs), inserted in the abdomen at several depths and distances from the applicator. Additional TLDs were put on phantom ventral surface. Measurements were made with and without a shielding apron (2 mm lead equivalent) draped above the abdomen. In vivo dosimetry was also performed on three non-pregnant pts up to now, using TLDs (unshielded or under a 2 mm lead cap) taped on the abdomen skin at different levels. In such cases, dose at depth was then estimated using the ratio of depth to surface readings obtained on phantom.

Results: For unshielded TLDs, doses measured on pt and phantom surface ranged between 10 and 170 mGy, mainly depending on beam energy and distance from treatment area. In contrast, surface dose in the midsagittal plane under lead protection was never higher than approximately 2 mGy, so showing that peripheral dose at the skin level is mostly due to scattered electrons rather than brehmsstrahlung X-rays. Consistently, doses measured at different depths in the phantom were found to be in the range 0.2-4 mGy without any shielding and lower than 2.5 mGy using the abdominal apron.

Conclusions: Our data showed that dose to uterus during exclusive IOERT for EBC delivered with mobile dedicated linacs can be kept approximately below 3 mGy, using an abdominal shielding. Based on results of this study, next step will be addressed to carefully evaluate risks and benefits of IOERT for pregnant women affected by EBC.

1260 poster

FORWARD PLANNED IMRT IN BREAST CANCER: A DOSIMETRIC EVALUATION ON 100 CONSECUTIVE PATIENTS

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Purpose/Objectif: Simplified techniques of IMRT in postoperative irradiation of conservatively resected breast carcinoma have been proposed. The aim of this analysis was to compare the dosimetric results obtained in 50 consecutive patients treated with postoperative conformal radiotherapy (group A: 2 tangential wedged 3D-shaped beams) with those of 50 consecutive patients treated with forward planned IMRT (group B).

Materials/Methods: One-hundred patients were included in the analysis (median age: 59, range: 32-90). In group A, two wedged tangential beams (energy: 6-10 MV) were used. In group B, two tangential fields were used, and the dose was divided into a larger segment, including the whole irradiated breast (energy: 6-10 MV), and a smaller segment (10-15 MV), directed to the larger and deeper part of the gland, to improve dose homogeneity. Unpaired T-test was used for statistical comparisons between the two groups. Treatment plans and DVHs were calculated using the PLATO system (Nucletron, The Netherlands).

Results: No significant differences between the two groups (A vs B) of patients were recorded, in terms of patients age, body weight, PTV (in cm^3), and separation bridge (in cm). After a learning curve, time required to plan a forward IMRT treatment was not significantly longer than that for standard treatment. A forward IMRT treatment is normally performed during a standard 15' treatment time. A significant reduction of mean VPTV (cc) receiving more than 107% of the prescribed dose was observed: A: 7.1 ± 8.7, B: 4.5 ± 8.7 ($p=0.038$); similarly, a significant reduction of mean D_{max} (in % of prescribed dose) to the body was recorded: A: 111.2 ± 2.8, B: 108.2 ± 2.8; ($p<0.001$). Mean lung dose (%) was also reduced (average: A: 9.7 ± 7.1, B: 6.5 ±7.1; $p=0.003$) and D_{max} (%) to the heart (in left breast

affected pts) was significantly lowered (mean: A: 73.2 ± 45.2, B: 52.4 ± 45.2; p=0.043).
Conclusions: Electronic compensation achieved using a simplified step and shoot IMRT technique improves dose homogeneity and reduces the dose to the OAR (lung and heart) as compared to standard treatment based on tangential wedged beams.

1261 poster

GAFCHROMIC XR TYPE-R FILM FOR BREAST SKIN DOSE DETERMINATION DURING LOW KV INTRAOPERATIVE RADIOTHERAPY

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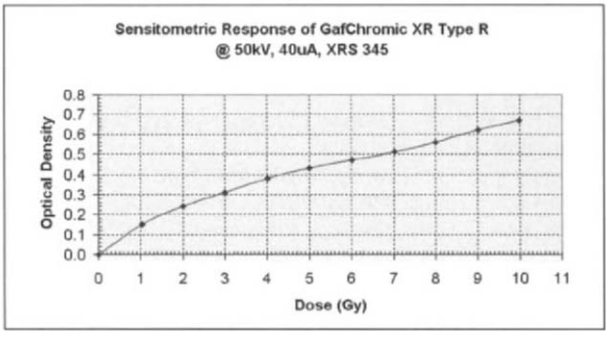
Purpose/Objectif: Intraoperative radiotherapy (IORT) using a low kV, miniature X-ray source (XRS) has the potential to impart the same clinical benefit as several weeks of post-operative external beam radiotherapy (EBRT), in a high dose single fraction. IORT facilitates partial breast irradiation by delivering a radiation dose in a spherical pattern to a clinically relevant margin of the tumour bed. It is important to quantify the skin dose because of the larger dose fraction and smaller target volume compared to whole breast irradiation. Gafchromic XR Type-R film (GC-XRR) (International Specialty Products, Wayne, NJ) has been specially developed for the measurement of absorbed dose of low energy photons and has the added advantage that dose readout is a simple procedure. The use of other methods of in-vivo dose determination such as TLDs, MOSFETs and diodes is more complex.
Materials/Methods: GC-XRR radiochromic film (Lot no. L04A50XRR) was used for this study. It consists of three layers with a 100 µm top layer of translucent yellow dye which acts as a protective barrier, a 15 µm active middle layer and a 100 µm white, opaque base layer providing image reflection. The top layer enhances the contrast of the radiation induced chromatic changes that occur in the film. A miniature XRS (Carl Zeiss AG, Oberkochen, Germany) operating at 50 kV and 40 µA with a measured half-value layer of 0.11 mm Al was used to obtain a plot of the film response in terms of net reflection density versus absorbed dose from 1 to 10 Gy in increments of 1 Gy (Fig. 1). A transmission densitometer (X-Rite Inc., Grandville, MI) was used to read the optical density at each exposure. Three readings were taken and the average value was used. To obtain the breast skin dose, four pieces of the calibrated film each 1.5 cm x 1.5 cm were wrapped in sterile film in the operating room before being placed by the surgeon concentrically around the wound site prior to irradiation. The spacing of the films was intended to give an indicative value of the average skin surface dose. After treatment, the optical density of the films was measured and the absorbed dose interpolated from the sensitometric response curve.
Results: We used GC-XRR film on five patients (on going) in order to quantify breast skin dose during low kV IORT. The prescribed dose was 5 Gy to a uniform 1 cm margin in tumour cavity after excision. Treatment times ranged from 18.46 to 29.79 minutes and the applicator sizes were 4.5 cm in four cases and 3.5 cm in one. The absorbed doses ranged from 1.30 to 5.35 Gy with a mean of 3.25 Gy. This is comparable with TLD doses determined at an earlier stage of the Targit trial.
Conclusions: Initial results indicate that GC-XRR film is a valid alternative to TLD for the determination of breast skin surface dose during low kV IORT. It is easy to use in the operating room, requires no prior preparation, provides a direct read-out and has the potential to provide dose distribution information.



1262 poster

HOW MUCH MARGIN IS ACCEPTABLE WITHIN A TOLERABLE V20 LEVEL IN RADIOTHERAPY TREATMENT PLANNING FOR NON-SMALL CELL LUNG CANCER?

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Purpose/Objectif: The purpose of this study was to assess the acceptable margin size within a tolerable V20 level in radiotherapy treatment planning for non-small cell lung cancer.
Materials/Methods: We studied randomly selected computed tomography data sets of 30 patients with primary lung cancer. We prospectively simulated chemoradiotherapy treatment planning. Primary tumors and enlarged lymph nodes were contoured and defined as gross tumor volume (GTV). Elective nodal irradiation was omitted. A prescribed dose of 60Gy in 30 fractions was used in this simulation. An anterior-posterior portal was used for 40Gy and an off-cord oblique portal was used for 20Gy. Margin size was defined as the distance between the GTV and the block edge. The margin size was automatically opened out in a 5-mm interval from 5 mm to 30 mm around the GTV. On the assumption that a tolerable V20 value is 25%, an acceptable margin size was assessed in all patients.
Results: If the margin size is fixed for all patients, a 15-mm or smaller margin size would be acceptable. However, the acceptable margin size differed from patient to patient and it tended to be smaller in patients with positive lymph nodes than that in patients with negative lymph nodes.
Conclusions: Considering set-up error, internal organ motion, and leaf margin, a margin size of 15 mm would not be enough for good dose distribution. On the other hand, patients with negative lymph nodes could safely tolerate a larger margin size. A new concept for target definition that includes variability of margin size is needed from the perspective of dose-volume-histogram parameters such as V20.

Table 1: Percentage of patients over 25% in V20 value

	Margin size (mm)					
	5	10	15	20	25	30
All patients (n=30)	0%	3%	7%	33%	47%	60%
Positive lymph node patients (n=19)	0%	5%	11%	53%	68%	84%
Negative lymph node patients (n=11)	0%	0%	0%	9%	9%	18%

1263 poster

IMAGE NETWORKS FOR RADIOTHERAPY PLANNING IN A DEVOLVED RADIOTHERAPY SERVICE: METHODOLOGY AND QUALITY ASSURANCE

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Purpose/Objectif: In 2004 the Royal College of Radiologists published a document which outlined the possible use of multi-site centres to increase radiotherapy capacity in the [1]. It was recognised that for such facilities to function it would be necessary to make full use of modern information technology so that parts of the planning and treatment process may be shared between the sites.

The Kent Oncology Centre is part of the Kent and Medway Cancer Network and operates on 2 sites at Maidstone (West Kent) and Canterbury (East Kent). These two sites are separated by 56 km. Oncologists based at Maidstone hold clinics throughout Kent and Medway. In order to reduce travel time for the clinician a network was set up which would allow the patient to be imaged at either Maidstone or Canterbury, planned by the clinician at their home base and then treated at either site.

Materials/Methods: The software applications involved in the treatment process are ProSoma™ virtual simulation, Pinnacle™ treatment planning, VISIR record and verify and PortalVision. A semi-bespoke DICOM RT server was used to facilitate transfer and storage of DICOM RT objects (Plans, Images and Structures) at each site and between sites. The DICOM server was based upon CTN software (Central Test Node) from Mallinckrodt Institute of Radiology. This software was modified to accommodate DICOM RT objects in addition to the usual diagnostic medical imaging modalities. A web-based front-end was developed based upon Apache, PHP and MySql, running under a Linux operating system. The DICOM RT services have been configured on a high availability cluster by using "Heartbeat" in conjunction with mirrored network block devices to provide automatic failover and limited load balancing of the services. It was necessary to perform quality assurance on the transferred data prior to use of the system, after changes to the server code and at 3 month intervals. An anatomical phantom was CT scanned in 4 orientations on each site. Plans were created using realistic clinical protocols. The images, plans and structures were transferred between the applications by all possible routes and the parameters received by each application were collated in an MS Excel spreadsheet.

Results: The quality assurance using the anatomical phantom showed that the parameters,structures and images that were transferred between sites both pre- and post-planning showed no defects or abberations. However although all manufacturers claim DICOM RT compliance they may not all handle the data in the same way and a thorough understanding of how each application behaves and clear import/export procedures for users are required.

Conclusions: This system has now been in operation for 6 months and its use will continue to grow as the number of oncologists based at Maidstone and working across grows.

[1] Guidance on the Development and Management of Devolved Radiotherapy Services, Royal College of Radiologists 2004

1264 poster

IMPACT OF ORGAN-AT-RISK DELINEATION DESIGN ON THE DOSIMETRIC EVALUATION OF LOCALISED CONFORMAL RADIOTHERAPY PLAN FOR PROSTATE CANCER

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Purpose/Objectif: Physical dosimetric parameters or Dose-Volume-Constraints are used to evaluate the quality and safety of Conformal Radiation Therapy (CRT) plans. The study objective was to determine the impact of organ-at-risk delineation design on the dosimetric evaluation of CRT plans for prostate cancer.

Materials/Methods: The plans of 205 patients treated by localised 3-Dimensional CRT (Prostate + Seminal Vesicles) were used to compare 2 delineation designs for bladder and rectum: Institutional whole organ delineation vs. entire wall delineation, excluding the lumen (EORTC 22991 protocol). For each delineation design, dose-volume-histograms were compared for the following pre-determined dosimetric end-points (dose expressed as % of prescribed dose): minimum, maximum, mean and median dose, and for a series of relative dose volume parameters expressed both as a % of organ volume and in absolute terms (cc). Non-parametric Sign-test was applied.

Results: For the specified dose end-points, no significant difference between the 2 delineation designs was observed. However, a statistically significant impact of delineation design was found for the dose volume parameters (expressed in both cc and % of organ volume) for dose levels between 55% and 101% (V55% to V101%) for bladder and between 70 % and 101% (V70% to V101%) for rectum. A regular pattern was seen, with a statistically significantly higher estimation of the irradiated volume for whole organ if expressed in cc and for organ entire wall if expressed in %. The table below illustrates the results for V100%.

Whole Organ	Entire Wall	95%CI for individual difference	Rectum V100%	Bladder V100%
10.5% (*)	5.5% - 14.7% (**)	14.8% (*)	10.1% - 19% (**)	- 4.6% to - 3.8%
9.4 cc (*)	4.3 cc - 15.7 cc (**)	2.9 cc (*)	1.8 cc - 4.8 cc (**)	4.8 cc to 8.2 cc
4.7% (*)	1.9% - 9.3% (**)	10.8% (*)	5.2% - 15.7% (**)	-5.4% to -4%
13.9 cc (*)	6.4 cc - 26 cc (**)	4.2 cc (*)	2.5 cc - 6.2 cc (**)	8.4 cc to 12.1 cc

(*) Median value, (**) first - third quartile

The delineation design significantly modified the plan acceptance rate if a 5% and/or 5cc volume maximum limit was applied for organ-at-risk volume receiving ≥ 100% of the dose.

Conclusions: This large planning study demonstrates the significant impact of organ-at-risk delineation design on the evaluation and acceptance of prostate CRT plans. When applying published Dose-Volume-Constraints in clinical practice, attention should be given to the used delineation design.

1265 poster

IMPLEMENTATION OF ENHANCED DYNAMIC WEDGES INTO XIO TREATMENT PLANNING SYSTEM

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Purpose/Objectif: The XIO system implementation of Varian's enhanced dynamic wedges (EDW) is presented. Calculations of both dose distributions and effective wedge attenuation factors are based on a segment treatment tables (STTs). Calculation dose requires a "transmission matrix" derived from an STT (segment treatment table) to model the modified fluence from the source. The dose calculation is then performed using either the Clarkson or con-

volution/superposition algorithms.
Materials/Methods: For the implementation of EDW into XIO the only required data are the measured of the effective attenuation factors (EWAF's) for 60 degree EDW for five square field sizes (4, 10, 15, 20, 30 cm^2). For this measured we use an ionization chamber, Farmer PTW 31002, in a water-phantom. We also obtained wedge profiles for computational evaluation with a linear array, PTW-Freiburg LA48. We have taken profiles for a sufficient number of wedge angles (15, 30, 45, 60 degrees) and field sizes (5, 10, 20 cm^2) in order to optimize the STT table for production of the best results through the range of clinical setups.
Results: We have taken profiles for a sufficient number of wedge angles (15, 30, 45, 60 degrees) and field sizes (5, 10, 20 cm^2) in order to optimize the STT table for production of the best results through the range of clinical setups. Calculated and measured EWAF's and dose comparisons with measured distributions showed good agreement.
Conclusions: The implementation of EDW in XIO Treatment Planning System provides clinics with an additional effective tool for conformal radiotherapy treatment planning.

1266 poster

IMPROVED PHOTON DOSE CALCULATION IN THE LUNG WITH THE ANALYTICAL ANISOTROPIC ALGORITHM (AAA)

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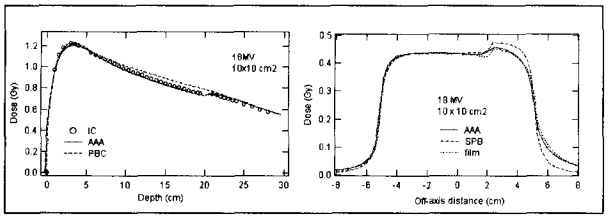
2 - Oncology Department, University Hospital, Helsinki, Finland,
3 - Varian Medical Systems, dept, Helsinki, Finland

Purpose/Objectif: A new dose calculation algorithm AAA (Analytical Anisotropic Algorithm) has been implemented in the TPS Eclipse (Varian Medical Systems, Palo Alto) to replace the single pencil beam (SPB) algorithm for photon dose distributions and to improve the dose calculation accuracy in heterogeneous media. The AAA algorithm consists of two modules: the configuration module constructs the phase space of the treatment unit (a primary photon source, a secondary finite-size photon source and an electron contamination source); the dose calculation module calculates the dose as the superposition of the dose deposited by the two photon sources and by the electron contamination source. The photon dose is calculated by a 3D convolution of Monte-Carlo pre-calculated scatter kernels. The interacting scatter kernels are scaled using the electron density matrix.
Materials/Methods: We have focused on testing the accuracy of the heterogeneity correction with AAA in lung equivalent material. Ion chamber point dose measurements were performed at different depths to monitor the depth dose behavior in cork slabs with different thicknesses, sandwiched between solid water plates. Data were acquired for a series of symmetric and asymmetric field sizes. To analyze the modeling of the dose deposited at the lung/tumor interface, films were irradiated and analyzed at different depths and with different combinations of cork slabs and solid water. Point dose measurements were performed in a thoracic phantom.
Results: Depth dose curves as well as profiles acquired in heterogeneous cork/solid water phantom setups are substantially better with AAA than with the single pencil beam. Point dose measurements in the thoracic phantom are mostly within 5 %. As an illustration, calculated (AAA and SPB) and measured depth dose curves and profiles for a 15 cm cork slab are shown in the figure (field size: 10 x 10, 18 MV)
Conclusions: Dose to the lung and dose profiles at the lung/tumor interface are better modeled with the AAA algorithm implemented in the Eclipse TPS. The improved modeling changes significantly the shape of dose volume histograms and isodose distributions and will have its impact on clinical decisions in lung treatments.



1267 poster

LARGE INTERINDIVIDUAL VARIABILITY OF UPPER ABDOMINAL LYMPHATIC ANATOMY IS THE BASIS FOR INDIVIDUALISED RADIATION TREATMENT PLANNING.

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Purpose/Objectif: Radiation of upper GI malignancies often requires inclusion of regional lymph nodes which run alongside the major abdominal vessels. But standard demarcations in radiotherapy are still defined by vertebrae. Vascular anatomic variability was analysed in this study to estimate its influence on PTV variability.
Materials/Methods: CT measurements of abdominal vessel anatomy in 104 individuals in three dimensions served to estimate target PTV variability. Volumes were calculated separately for each patient adding a 15 mm margin to the right, to the left, ventrally and dorsally. To confirm these calculations, 3-D conformal treatment planning was performed for patients with pancreatic adenocarcinoma (PDAC). Different vascular landmarks were used to define PTV margins and volume variability was compared.
Results: Vascular distance measurements in all directions in the CT scans of 109 patients showed variations for every orientation. Variation was most pronounced craniocaudally (e.g.: distance between the celiac trunk and the IMA ranged between 6 and 13 cm (median 9.5 cm)). Consequently, only this direction was further assessed for its influence on treatment volume variability. There are two possible inferior borders for elective para-aortic nodal treatment in PDAC: (1) the IMA; (2) the most caudal renal vessel or the level 2 cm caudal to the inferior edge of the pancreatic head whichever level is situated more caudally. The latter is thought to be sufficient for PDAC < 3 cm without enlarged para-aortic lymph nodes. Mathematical calculations based upon distance measurements aimed to estimate the amount of additional volume to treat the lower para-aortic nodes in PDAC. In most of the calculated cases the additional volume was < 100 ccm but ranged up to 350 ccm. To confirm the results of the CT based model, 3D-treatment planning for 31 PDAC patients ± the lower para-aortic nodes was performed: in good correspondence with the CT based calculations the differential volume was < 100 ccm in 16/30 patients, and 100 - 199 ccm in 11/30 patients. But of note, this difference was >200 ccm in 3/31 patients with a maximum at 259 ccm.
Conclusions: (1) there is considerable interindividual vascular and hence lymphatic anatomical variability. Thus, planning for these nodal areas should be based on the individual vascular anatomy. (2) Patients with PDAC > 3cm should be treated including the lower para-aortic nodes. Exceptions should be made if the PTV would exceed 850 ccm to avoid hematotoxicity from concomitant gemcitabine which is proportional with PTV size (Crane et al. 2001).

1268 poster

NORMAL TISSUE COMPLICATION PROBABILITIES (NTCP) FOR MODIFIED REVERSE HOCKEY STICK TECHNIQUE.

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Purpose/Objectif: To evaluate the risk of heart and lung injury in patients treated with the Modified Reverse Hockey Sick technique (MRHS technique). To compare the risk of injuries for MRHS and tangential field technique.

Materials/Methods: The MRHS technique differs from Reverse Hockey Stick technique by implementing individually designed bolus for electron beam in order to decrease the dose delivered to lung and for left sided patients for heart. The 3D CT based dose distributions for 25 left sided and 25 right sided patients consecutively irradiated in the Hplycross Cancer Centre with the MRHS were calculated. For the same group of patients the 3D dose distributions were calculated for tangential technique For each patient before the NTCP was calculated all physical doses were converted into biological doses according to α/β model with a/b vale of 3 Gy. The NTCP for lung for each patient was calculated with generalized Lyman model with two parameters: the biological mean dose and the volume above a biological threshold dose of 13 Gy (V13). For heart the NTCP was calculated using seriality model. The parameters of the models were taken from literature. For heart, for each patient the partial volume of heart receiving more than 30 Gy (V30) was also calculated. The correlation between the NTCP and V30 for heart and between the mean physical dose and the mean biological dose for lungs was obtained.

Results: Heart For the MRHS technique for all left sided patients but two the NTCP for heart is smaller than 0,01. For tangential technique the calculated risk of heart injury was much higher - in some cases it exceed 0,05. A very good correlation between the V30 and the NTCP was obtained for both techniques. Mathematical formulae has been established. Lung For lung larger NTCPs were obtained for both techniques for patients treated on the right side. About two times higher values of the NTCP were obtained if calculated with the V13 parameter than with the mean dose. Based on the mean dose on the left side the NTCP is always smaller than 0,05. For some patients treated on the right side the NTCP exceeded 0,1 for both techniques. There is a very good correlation between the mean physical and mean biological dose. There are two different formulas for left and right side describing these relationships.

Conclusions: For the left sided patients the MRHS technique is fully safe for heart and is superior to the tangential technique. The risk of lung injury is higher for patients treated on the right side. Regarding the risk of lung injury there is no difference between both techniques. There is a very good correlation between the NTCP and V30 for heart and between the mean physical and biological doses for lung.

1269 poster

NOVEL BRACHYTHERAPY DOSIMETRY USING LUMINESCENCE FROM SMALL CRYSTALS ATTACHED TO OPTICAL FIBER CABLES

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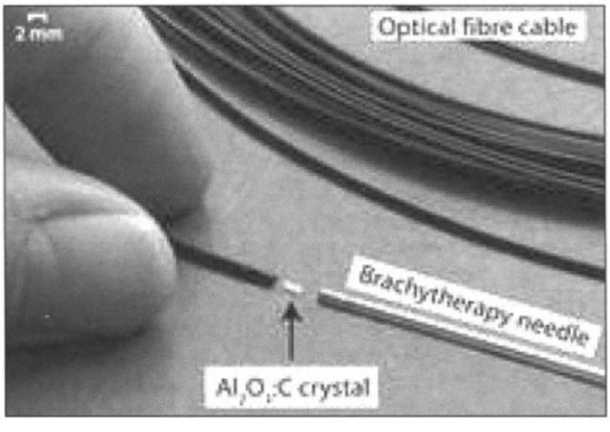
2 - Risø National Laboratory, Radiation Research Department, Roskilde, Denmark

Purpose/Objectif: The rationale for using brachytherapy is the highly localized delivery of dose. This makes it possible to deliver a significant dose to the tumor while maintaining a tolerable dose to normal tissues. However, this strong dose gradient constitutes the very challenge of establishing an optimal and safe dose delivery as the source positioning has to be very accurate to avoid misadministration. Additionally, traditional detectors are too large for dose measurements in the strongly varying radiation field of brachytherapy.

Materials/Methods: We have developed a new dosimetry system for in vivo measurements during brachytherapy. The system uses radioluminescence (RL) and optically stimulated luminescence (OSL) from small (0.5 by 2 mm^2) carbon-doped aluminum oxide crystals (Al_2O_3:C) attached to 15 m long optical fiber cables. Each cable has one crystal, small enough to fit inside a brachy needle (see figure). The crystals can be read out remotely using special instrumentation and during the treatment, the RL signal provides a real-time measurement of the dose rate at the position of the crystal. Immediately after the treatment, the OSL signal then gives the absorbed dose. The RL signal resembles the output from a conventional scintillator whereas the OSL is an all-optical equivalent of thermoluminescence. A small laser (20 mW) is used as stimulation source during the OSL readouts. Measurements were carried out using an Ir-192 source in a GammaMed 12i afterloading unit (Varian).

Results: Two luminescence probes were placed in a 30 by 25 by 25 cm^3 water phantom. The effective atomic number of Al_2O_3:C is 10.2 (cf. 7.5 for tissue) and to quantify the energy dependence of the detector material, depth dose profiles were acquired. The measured profiles 5 to 80 mm away from the source were found to be in good agreement with values from the treatment planning system and with independent measurements carried out using GAF-film. The positioning uncertainty close to the source is, however, considerable (at 5 mm distance, the dose rate changes about 10% per 0.3 mm). The reproducibility of the luminescence measurement results is close to 0.5 %.

Conclusions: We provide a detailed account of the data and demonstrate how the system can be applied for in-vivo dosimetry as well as for improved dose-verification tests of optimized treatment plans prior to the treatment. Next step will be to utilize the system for dosimetry in patients.



1270 poster

POST MASTECTOMY RADIATION WITH TANGENTIAL FIELDS: HOW MUCH BOLUS IS REQUIRED?

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Purpose/Objectif: There is a wide variation in the use of bolus for post mastectomy radiation. An international survey showed significant regional differences in the use of a bolus as well as in the schedule of application and thickness used (Radiother. Oncol. 76 suppl. 1(2005) S2). One of the widely used techniques for post mastectomy chest wall irradiation is two opposed tangential fields. In the current study, the dose close to the chest wall surface has been measured in a phantom as a function of bolus thickness and chest wall thickness.

Furthermore, the dose versus depth in the chest wall has been determined to investigate if a bolus covering the total chest wall area is required for patients with a very thin chest wall.
Materials/Methods: To simulate the chest wall, a hemicylindrical cork phantom covered with a varying number of 3 mm thick plastic sheets was used. In the cork and plastic, a hole was drilled allowing a diode photon field detector with an effective depth of measurement of 0.5 mm to be mounted. The phantom was irradiated with opposing tangential fields of 6 MV x-ray. Gantry angles were chosen to obtain angles between the normal of the diode and the beam direction in the range 50°-80°. This corresponds to the typical angles between the beam direction and the normal to the chest wall for a patient. Measurements were carried out for chest walls with water equivalent thicknesses of 7.5 mm, 11 mm, and 29 mm. The dose 0.5 mm below the phantom surface was measured for different bolus thicknesses and also without a bolus. Furthermore, the dose versus depth in the chest wall phantom was determined for a chest wall thickness of 7.5 mm and 11 mm, to investigate if a bolus is required to obtain the prescribed dose in very a thin chest wall.
Results: The dose 0.5 mm below the surface of the chest wall without bolus was in the range 73%-87% of the prescribed dose. The lowest value was obtained for an angle of 50° and the highest value for an angle of 80°. No dependence on the chest wall thickness was found for the surface dose. When a 1.4 mm bolus was covering the chest wall, the dose was found to be 87-99% of the prescribed dose. For bolus thicknesses of 3 mm, 5 mm, and 8 mm the measured dose was larger than 95% of the prescribed dose for all angles. The measurements of dose versus depth in the chest wall showed that at least 95% of the prescribed dose is obtained for all depths greater than 3 mm independent of chest wall thickness.
Conclusions: In conclusion, for all chest wall thicknesses studied a bolus with a thickness of 2 mm is sufficient to obtain a surface dose of at least 85% of the prescribed dose whereas a bolus thickness of 3 mm will result in a surface dose of more than 95% of the prescribed dose.

1271 poster

RADIOTHERAPY DOSE VERIFICATION USING IN-VIVO DOSIMETRY SYSTEMS

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Purpose/Objectif: Characterization of an In-vivo dosimetry systems which include, PTW semiconductor diodes, for 6MV energy, TLD-100H Thermoluminescent detectors. Evaluation of an In-vivo dosimetry system, OneDose™ MOSFET disposable detectors. Verification of the prescribed target dose due to different therapy conditions to be as recommended (5%). Implementation of the In-vivo dosimetry systems at King Abdulaziz University Hospital (KAAUH), Department of Radiation Therapy.
Materials/Methods: Calibration of the diodes and TLDs at reference conditions: Open Field, from 6MV x-ray from VARIAN 600C, 100 cm SSD, 10x10 Field size. Diodes at the surface of the slab phantom, TLDs, Markus chamber at Depth of dose maximum (as a reference). OneDose™ MOSFETs, Pre-calibrated by the manufacturer, "Evaluation", Placed at depth of dose maximum. Determination of correction factors of diodes and TLDs under various parameters:SSD, Field size, Wedge, Incident photon angle, temperature of the skin, Linearity with Dose. Evaluation of the pre-set correction factors of OneDose™ MOSFET under various parameters: SSD, Field size, Wedge, Incident photon angle, temperature of the skin, Linearity with Dose.
Conclusions: Diodes and TLD-100H were characterized, but implementing diodes for In-vivo dosimetry required a few modification on the design of the treatment room (cables problem).OneDose™ MOSFETs were evaluated, its calibration and correction factors were agreed with the manufacturer accuracy (5%). Angular dependence for diodes and MOSFET was large, to eliminate this factor, the incident photon beam should be perpendicular to the sensitive area of the detector. To eliminate the need of such correction factors, calibrate the detector on a phantom for each treatment case. (prefared for complex cases,e.g., Head and Neck). Using a calibration factor of a group of TLDs show better reproducibility (<2% vs. 16%) than using individual calibration factor for each chip which agreed with (C. Furetta, et. al., Med. Phys.,v.21,n.10). Separating TLD chips according to its individual reproducibility (not according to its responses) gave a very good reproducibility for the average of the group (<2%)., the whole group assumed to be single chip. The results of using MOSFETs and TLDs without buildup material show good agreement compared to that with buildup material.

Patient/Phantom	Patient	Patient	Patient	Patient
Case	Pelvis	Pelvis	Pelvis	Pelvis
Buildup	Yes	Yes	Yes	No
TLD	97.9	300	111.7	114.5
MOSFET	96.88	298.7	113.5	102
Diode	NA	NA	NA	NA
TPS	97.11	308.35	109.65	98.04
Max. Discrepancies TLD	-0.81	2.71	-1.87	-16.79
Max. Discrepancies MOS	0.24	3.13	-3.51	-4.04

1272 poster

RESPONSE OF THERMOLUMINESCENT (TL) MATERIALS TO KILOVOLTAGE RADIATION AND ITS APPLICATION IN PATIENT AND PERSONAL DOSIMETRY.

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2 - Sydney University, Faculty of Health Sciences, Sydney, Australia,
3 - Liverpool Cancer Therapy Centre, Medical Physics, Liverpool, Australia

Purpose/Objectif: The purpose of this work was to measure the response of LiF:Mg, Cu,P (TLD100H), CaF_2:Mn (TLD400) and CaF_2:Dy (TLD200) to kilovoltage radiation and apply this information to correct dose estimation used in patient and personal dosimetry.
Materials/Methods: Four TL chips of each type of above mentioned materials were irradiated to x-ray beams of varying tube potential from 75 kVp to 300 kVp and Co60 gamma radiation. Effective energy of kilovoltage beams was calculated from half value thickness of each beam. The responses were normalized to 1 mGy dose of Co60 radiation. Using Sigma plot software, polynomial fits were obtained to the TL response vs effective energy. The ratio of responses of TLD200 & TLD100H and TLD400 & TLD100H were plotted against the effective energy. To estimate the accuracy of this method a set of TLD100H, TLD200 and TLD400 was exposed to x-ray beam of unknown energy. The responses of all materials were measured and from the ratio of TL responses, the effective energy of the beam was estimated. This is compared to the energy measured by HVL measurements using an ionisation chamber.
Results: The responses of all the TL materials used show a maximum at approximately 30 keV. The ratios of TLD200 & TLD100H showed the highest sensitivity to variation in energy of the incident beam. The measured accuracy of method described above was better than 10 %.
Conclusions: Thermoluminescent (TL) dosimetry, especially using LiF, is widely used for both personal monitoring and patient dose measurement. However, the evaluation of dose may be hampered by the energy dependence of the TL materials, which provides the highest contribution to the total uncertainty in TL dosimetry. For ac-

curate assessment of dose, information on the spectrum of radiation and knowledge of TL response at commonly encountered photon energies is essential. The method described above can be used to estimate the effective energy of radiation a TL monitor has been exposed by including TLD100H and TLD200 or TLD400 materials with LiF. This will improve the dose estimation by applying appropriate energy correction to the response of LiF TL monitors which are known to exhibit energy dependency in the kilovoltage region.

1273 poster

SIMULTANEOUS INTEGRATED BOOST FOR LOCALIZED PROSTATE CANCER WITH HELICAL TOMOTHERAPY: PLANNING AND PRELIMINARY EARLY TOXICITY REPORT

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2 - H. San Raffaele, *Radiotherapy, Milano, Italy,*

3 - Istituto Nazionale per lo Studio e la Cura dei Tumori, *Prostate Programme, Milano, Italy,*

4 - H. San Raffaele, *Radiotherapy and Nuclear Medicine, Milano, Italy*

Purpose/Objectif: To report planning data and preliminary early toxicity results of a phase I-II study using a moderately hypofractionated simultaneous integrated boost (SIB) approach delivered with Helical Tomotherapy (HT).

Materials/Methods: Different CTVs were defined: CTV1: Pelvic nodes (N); CTV2: most cranial 2/3 of seminal vesicles (SV); CTV3: most caudal 1/3 of SV; CTV4: prostate; OP: overlap region between PTV4 and rectum. For PTV1-4 definition, the same margins used in our Institution for 3DCRT were applied (LR: 0.8 cm; PA: 0.8 cm; CC: 1 cm; 1cm in all directions for N), although daily MVCT image-guide was used to take prostate motion into account. Different doses to each PTV, according to a grouping risk based on NCCN criteria, were delivered in 28 fractions: low risk: 56 Gy, 61.6 Gy and 71.4 Gy for PTV2-4, respectively; intermediate risk: 51.8 Gy, 61.6 Gy, 65.5 Gy and 74.2 Gy for PTV1-4, respectively; high risk: 51.8 Gy, 65.5 Gy for PTV1-2 and 74.2 Gy for both PTV3 and PTV4. The dose to OP was always limited to 65.5 Gy. Up to now, 11 patients entered the protocol (9 low risk; 2 intermediate risk). Inverse planning optimisation was performed on the HT planning station; rectum, bladder, femoral heads + femurs (FH), penile bulb (for 5 selected pts with MRI-based contouring) and intestinal cavity (in case of N irradiation) were considered as OARs. Dose statistics and DVHs for PTVs and OARs were recovered for all pts. For Eight out of 11 pts who completed the treatment acute gastro-intestinal (GI) and genito-urinary (GU) toxicity data were available (RTOG/EORTC scoring system).

Results: Rectum sparing was excellent: D_mean was 38.2 Gy (median value; range 31 - 45 Gy), median V50 was 33 % (range: 20-44 %) and median V65 was 11.5% (range: 2-19 %). The median value of bladder D_mean was 37.5 Gy (range 32-50 Gy) for "full" bladder patients. D_max of FH ranged between 32 and 48 Gy with small values of V20 (range: 8-32 %), if N were not irradiated. The penile bulb D_mean was 30.5 Gy and the intestinal cavity D_mean was around 18-20 Gy with median V30 Gy of 14 %. PTV coverage was also excellent: V95 % for PTV1-4 ranged between 93 % and 99.5 %; D_max of PTV4 was less than 76.5 and 78.5 Gy for low and intermediate risk pts respectively. Acute toxicities were as follows: GU: 5 G0 and 3 G1; upper GI: 8 G0; proctitis 5 G0 and 3 G1.

Conclusions: Dosimetrical findings and preliminary data of acute toxicity support the possibility to safely deliver high-dose SIB for prostate cancer with Tomotherapy.

1274 poster

THE COMMISSIONING OF AN IORT DEVICE

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Purpose/Objectif: During the last years intraoperative radiotherapy (IORT) with electron beams has been re-introduced in the clinic. This technique that was abandoned by radiotherapists in the past is now being used as an alternative modality for partial breast irradiation. The purpose of this work was to commission a device for IORT.

Materials/Methods: The new IORT device (Arplay Medical) is to be used connected to an Elekta Precise (Elekta Oncology Systems) accelerator. The device includes an adapter that connects to the linac head, and a set of Perspex tubes with circular cross sections. The inner diameters of the available tubes are 30, 40, 50, 60, 80 and 100 mm. All measurements were performed for 6, 9, 12 and 18 MeV electron energies. Jaw settings were kept constant at 14 x 14 cm^2. PDDs and profiles at depths of 0.2 cm, D_{max}, D90, D80 and D50 were measured in a water phantom using a Markus plane-parallel ion chamber. The dependence of PDD and profile shapes on SSD was checked for the applicators with the smallest and the biggest diameters. Output factors for all applicators were measured in a solid water phantom using a Roos plane-parallel ion chamber. SSD dependence of the output factors was measured.

Results: PDD and profile shifts due to SSD changes from 100 cm to 110 cm were less than 0.5 mm for the smallest and the biggest applicator diameters, for all measured energies. Therefore PDD and profile dependence on SSD changes may be neglected. Hardcopies of PDD and beam profile curves were prepared to help the team during the procedure, on the decision making of the applicator size and energy to be chosen. SSD corrections of output factors were calculated and found to be applicator size independent and the energy dependence was weak (about 3% difference between 6 MeV and 18 MeV). Based on the presented measurements and results, an EXCEL data sheet was prepared to allow for quick MU calculations during the procedure.

Conclusions: The IORT device has been fully commissioned and has been already used in our clinic for breast irradiation.

1275 poster

THE CONTRIBUTION OF VIRTUAL SIMULATION TO IMPROVED DOSE HOMOGENEITY IN BREAST AND LYMPH NODE IRRADIATION

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Purpose/Objectif: A method of breast cancer treatment planning using the virtual simulator implemented at the Radiation Oncology Department of Athens Medical Center is described. When irradiating the breast or chest wall as well as the regional lymph nodes, dose inhomogeneity problems arise at the matching interface of the involved fields. Improved dose distributions at the match-line are produced by implementation of the virtual simulator features.

Materials/Methods: Patients for breast cancer radiotherapy treatment are placed supine on the CT couch with both arms up using an in-built immobilizing system. 5mm CT slices of the thorax and the neck are aqcuired and sent via Dicom software to the Exomio virtual simulation system. The algorithm generates reconstructed slices in all planes, digitally reconstructed radiographs and 3D representations of the patient. A pair of tangential fields at conventional angles and an anterior supraclavicular field are set, based on PTV contouring. The couch, gantry and collimator angles are adjusted to achieve a complete geometrical match in all planes at the junction of the three fields. CT data and fields are transferred to a treat-

ment planning system for three-dimensional dose calculation. The wedges and relative weights of the beams are optimized to provide the best dose uniformity throughout the target volume. Sagittal and coronal multiplanar reconstruction images are generated in a few planes. Further adjustments to the gantry, couch and collimator inclinations are made to improve dose uniformity at the match line. Three dimensional dose distributions and dose volume histogram data are used to evaluate plans.

Results: Thirty consecutive patients with breast cancer entered the study. The geometrical accuracy at the junction of the three fields is within 1mm in all planes. In 93% of the patients the dose at the match plane was within the range 95%-107%, as recommended by ICRU 62. 7% of the patients received doses no more than 110% at the match line.

Conclusions: Our data indicate that the use of virtual simulation is a simple, fast and accurate method to optimize field matching and dose homogeneity in the treatment of the breast and lymph nodes.

1276 poster

THE IMPACT OF BLADDER VOLUME ON DOSE DISTRIBUTION IN THE BLADDER AND SURROUNDING CRITICAL ORGANS

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Purpose/Objectif: The aim of the study was to measure the differences in dose distribution within the bladder and surrounding critical tissues in relation to bladder volume in patients with bladder cancer treated with radiotherapy.

Materials/Methods: The study is based on the evaluation of treatment plans constructed for 16 patients with bladder cancer. CT-based, conformal treatment planning was performed in each patient with bladder filled with 80cc of saline and after this subsequent CT-scans were taken with bladder filled to 150cc. In all treatment plans the PTV enclosed bladder with a 2 cm margin in all directions. Critical tissues were delineated, as follows: whole rectum and pelvic part of bowels. The field margins were shaped with a MLC. The same 3-field technique (0^0,90^0,270^0) has been applied. The typical total radiation dose was 70 Gy with dose per fraction of 2 Gy, but in analysis it was presented as a percentage values (%). The data for calculations were taken from DVHs. The comparison was performed between dose distribution for treatment plan with bladder volume of 80cc or 150cc.

Results: There were no significant differences in dose distribution within the PTV in treatment plans with different bladder volumes. In cases with larger bladder volume (150cc) there was significantly more absorbed dose by bowels and rectum. The volume of rectum which receives more than 90%, 80% and 70% of the prescribed dose (i.e., V90%,V80%,V70%) were 15%, 20% and 23% for smaller bladder volume and 18%, 24%, 28% for larger bladder volume. With respect to bowels; V90%, V80% and V70% were 123 cc, 144 cc and 162 cc for smaller bladder volume and 136 cc, 158 cc and 180 cc for larger bladder volume, respectively.

Conclusions: Dose distribution in rectum and bowels is slightly but significantly worse if radiotherapy is performed with larger bladder volume, which suggests that bladder should be emptied during radiotherapy for bladder cancer.

1277 poster

THE VALUE OF HAPTIC FEEDBACK IN MEDICAL IMAGING AND TREATMENT PLANNING

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Purpose/Objectif: The purpose was to investigate if haptic feedback can help users to interact with medical imaging and treatment planning systems.

Materials/Methods: Everyday we use our senses to get information of all kinds. Touch is an important means of feedback. Haptics is the science of incorporating the sense of touch and control into computer applications. The project began with a field study where three physicians were observed in their regular working environment. Then a haptic application was implemented in OpenDX imaging software. Finally, the haptic application was evaluated via a controlled experiment with twelve physicians.

Results: Even though the sample size was small, and the application only a prototype, results show that haptic feedback can increase the speed of outlining target volumes and organs at risk significantly. No significant effects were found for increased precision or perceived usability.

Conclusions: In the very graphics intensive work environment of radiation therapy planning significant advantages can be gained with haptic interfaces when it comes to outlining efficiency (speed). The promising results show that it should be of interest to further develop the application.

1278 poster

TREATMENT PLANNING STUDIES AND DOSE MEASUREMENTS FOR BEAMS PASSING METAL HIP PROSTHESIS

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Purpose/Objectif: An increasing number of patients undergoing radiotherapy have metal hip prosthesis. The treatment planning process and the precise dose calculation is difficult for patients with prostate carcinoma due to different reasons which were investigated in this study.

Materials/Methods: The CT images of patients with metal implants such as hip prosthesis include great artefacts so that the image is distorted and no reliable outlining is possible. Furthermore the artefacts influence the CT values which are converted into relative electron densities and thus influence the dose calculation. The attenuation is underestimated which leads to an overestimation of the target dose behind the metal implant. To investigate this influence a phantom including titanium inserts was used. Planning studies with CMS XiO 4.2.0 were performed using a single field that passes the artefact area in the image. Dose verifications were made with ionisation chambers. Another impact on the dose calculation is due to the limited capability of the dose calculation algorithms to handle such high Z structures. Here also planning studies and dose verifications with ionisation chambers and GafChromic films were performed. Particularly the regions directly in front and behind the metal implant were of big interest.

Results: The influence due to the artefacts in the image does not influence the dose calculation as much as expected. The TPS can not handle the high Z materials in the dose calculation very well when the beam passes the prosthesis. The increased dose in front of the

prosthesis of approx. 12% and the decreased dose behind of approx. 15% can not be considered. A manually inserted relative electron density for the prosthesis improves the results behind the prosthesis. The dose deviation between calculated and measured dose in the isocenter was decreased from 7.5% to 1.8%.
Conclusions: The study shows that a TPS can not consider the prosthesis very well so that beams passing through the hip should be prevented. In cases where the rectal dose has to be minimized and the beams passing through the prosthesis are indispensable a manually inserted relative electron density can lead to more precise dose calculations.

1279 poster

ULTRASOUND-BASED TREATMENT PLANNING IN ELECTRON BEAM IORT: A PILOT STUDY

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Purpose/Objectif: To investigate the feasibility and reliability of treatment planning based on peri-operative US images during intraoperative electron beam radiotherapy (IOERT).
Materials/Methods: The project was structured in three successive phases. In the first step, a sterile intraoperative linear probe connected to an US device was used to acquire transaxial and midsagittal scans of the irradiated volume, in the context of IOERT as an anticipated boost (12 Gy) for locally advanced prostate cancer, immediately followed by radical prostatectomy. Prostate dimensions and rectum depth were measured to properly select the electron beam energy (8-10 MeV) and applicator size (5-7 cm diameter), based on a dosimetry atlas previously determined in a water phantom. In the second phase, the role of in vivo dosimetry by means of calibrated MD-55 radiochromic films is currently under evaluation, to verify the consistency of dose values determined using US images. Film strips were put in sterile envelopes below the prostate and around a cylindrical brachytherapy applicator in the rectum. Films were analysed 48 hrs after the irradiation using a scanner and a dedicated software. The third step in progress will consist of the implementation of an intraoperative, US-guided treatment planning system (TPS) to calculate dose distribution in the irradiated volume more accurately and in more details.
Results: Twelve pts treated between June 2005 and April 2006 using a Liac mobile linear accelerator in the operating room have been investigated. Mean prostate thickness, width and length were 3.4, 4.6 and 4.9 cm, respectively, while the minimum depth of the rectum lied in the range 2.5-4.4 cm. The following average doses were evaluated: 4.6-11.3 Gy to the margins around the prostate capsule, while 4.9 Gy to the anterior rectal wall. Up to now, in vivo dosimetry was performed in one case, appearing feasible, however more data will be collected to assess the consistency between measured and calculated doses to rectum and posterior margin of prostate gland.
Conclusions: Peri-operative US scanning clearly appeared as a feasible and valid procedure for the determination of absorbed dose to the target and organs at risk in IOERT, especially in combination with in vivo dosimetry. We also expect of the future availability of a dedicated TPS to achieve a useful tool, mainly in terms of treatment documentation.

1280 poster

VALIDATING MAGICA NORMOXIC POLYMER GEL FOR BRACHYTHERAPY DOSIMETRY WITH MRI

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Purpose/Objectif: polymer gels are an emerging new class of dosimeters which are being applied to the challenges of modern radiotherapy modalities. Since the beginning of the modern gel dosimetry researches in 1984, several gel generations have been proposed, the last of which are the normoxic polymer gels with capability of being easily manufactured under normal atmospheric conditions on the bench-top of a small laboratory. An optimum amount of agarose had already been added to a previously proposed normoxic gel (named MAGIC) in order to obtain a stiffer gel which is more resistant against environmental changes. The energy dependence and dose response chracteristics of the gel are investigated in our recent study, for clinical brachytherapy treatments performed at our site.
Materials/Methods: The gel was irradiated with three different brachytherapy sources with energies ranging from 380KeV to 1.25MeV. Four dosimeters were irradiated with Cesium-137 sources, Cobalt-60 HDR BT sources and Iridium-192 interstial wires. The data of our TPS for a single Cesium source was used for calibration of the other three dosimeters.
Results: With MRI measurements, a maximum distance-to-agreement of 1.5 mm in high dose gradient regions and a maximum dose difference of 0.4Gy in plateaus were observed for all experiment.
Conclusions: The gel does not show energy dependences as the discrepancies observed are the same for all experiments and are not indicative of any energy dependence. The dynamic range of the gel was also increased compared to that previously reported for MAGIC which is due to the presence of agarose in the gel. Yet the dose rate dependence of the gel needs more quantiative investigations as significant dose rate dependence of MAGIC gels have been reported by other investigators. We expect that this dependence by very smaller for our formulation due to presence of agarose.

1281 poster

WHAT PRECAUTIONS SHOULD WE USE WITH A FLATBED SCANNER FOR RADIOCHROMIC FILM DOSIMETRY

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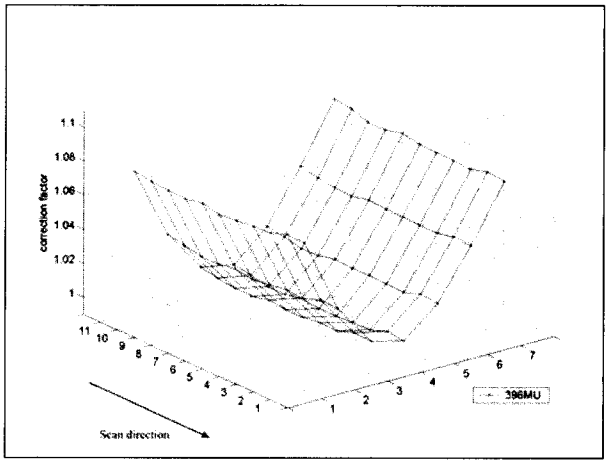
Purpose/Objectif: In this study we investigate the use of the EPSON Pro 1680 Expression scanner as densitometer for 2-D film dosimetry with Gafchromic EBT film. This type of radiochromic film has superior properties compared to other types of both radiochromic and radiographic film.
Materials/Methods: An accurate and efficient scanning procedure was established. Drift and warm-up effects of the scanner lamp were investigated and the influence of the white fluorescent light of the scanner lamp on the radiochromic film itself was assessed. Next, the uniformity of the response over the scanning field was investigated. Therefore, we defined 11 × 7 equally distributed points over the scanner field in which the ratio of the optical density to that at the center of the scanner field was determined. Furthermore, it was examined if the accuracy of the radiochromic film was improved by subtracting the optical density of the unirradiated blank film from the optical density of the irradiated film. To validate EBT film dosimetry using the EPSON scanner, the depth dose of a 2 × 15 cm^2 field and the in-plane and cross-plane profiles of a 15 × 15 cm^2 field were measured and compared with diamond detector measurements which were considered as reference.
Results: When taken several scans after each other in a short time span, it was found that the optical density taken from the first scan was about 1 % higher than the optical density taken from the subsequent scans. This is due to the warming up of the scanner lamp. Longer-term drift of the scanner was found to be absent. The use of a correction matrix was found to be necessary to correct for the non-uniform response over the scanning field. Especially in the direction

perpendicular to the scan direction, substantial deviations up to 8% were observed (fig 1). Subtracting the optical density of the unirradiated blank film from the irradiated film further improves the accuracy of the EBT film dosimetry. Depth dose and profile measurements with EBT film and the diamond detector were in agreement within 2 % when previous precaution taken into account.
Conclusions: The EPSON Pro 1680 Expression scanner is an excellent scanner for accurate 2-D film dosimetry with EBT film if some precautions and corrections have to be taken into account.



1282 poster

WHOLE BREAST IRRADIATION: A COMPARISON OF PLANNING TECHNIQUES

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Purpose/Objectif: To compare the quality of 4 tangential whole breast planning techniques: 2D conventional plan (CP), forward-plan (FP), surface-compensated (SC) and hybrid IMRT (hIMRT); using dose volume parameters and equivalent uniform dose (EUD) for the PTV and organs at risk.
Materials/Methods: The heart, lung and whole breast PTV were contoured on 10 CT-simulated patients (6 left, 4 right). 4 treatments plans were designed for each on Eclipse 6.5, using tangential half-blocked beams. The CP employed dynamically-wedged fields with angles chosen for homogeneity on a single axial slice. The FP technique used 2-3 static MLC-defined apertures to shield volumes of dose >105% within the PTV. For the SC technique, external patient contours were compensated for with dynamic MLC fields, optimized to produce a uniform dose on a plane at a patient-specific depth. The hIMRT technique combined 2 open with 2 dynamic-MLC tangential fields, optimized for uniformity to the PTV. Manual fluence editing was allowed. 3D plans were normalized so the mean PTV dose was 100% of the prescription. The CP was normalized to a point 1.5cm anterior to the lung interface along the field bisector. The homogeneity index (HI = %PTV >95% & < 105%), whole lung V20, heart V30 (left breasts only), and EUD (Gy) for the PTV (a=-7.2), heart (a=5) and lung (a=2) were calculated. Paired t-tests were performed to detect differences between plans.
Results: The mean separation was 23 cm and mean PTV was 1207cc. Results are shown below. Normalization to a point on the central slice rather than the volume resulted in an average increase of 1.4% in 3D PTV dose for CP, as seen in the CP's higher PTV-EUD.

Mean dosimetric parameters (1sd; * $p < 0.05$)

	CP	FP	SC	hIMRT	PTV
	HI	0.83 (0.07) *	0.95 (0.02)	0.94 (0.1)	0.96 (0.01)
	EUD	42.5 (0.7) *	41.8 (0.6)	40.0 (2.2) *	41.5 (1.0
Lung	V20	5.2 (1.9)	5.1 (1.9)	4.8 (1.8)	5.0 (1.9)
	EUD	9.0 (1.9)	8.7 (1.8)	8.6 (1.8)	8.7 (1.7)
Heart	V30	3.7 (1.5)	3.5 (1.5)	3.4 (1.4)	3.5 (1.5)
	EUD	19.8 (2.5)	19.1 (2.6)	19.6 (2.6)	19.3 (2.8)
Planning Time (min)		20	60-90	20-30	30-45

Conclusion: 3D planning techniques significantly improved PTV homogeneity compared with conventional plans, however, no difference in homogeneity was detected between the three investigated 3D planning techniques. The lower EUD for the surface-compensated plans may be attributed to observed cooler regions (<95%) in the posterior PTV. Heart and lung doses were similar for all 4 techniques. Given these results, resource issues and efficiencies will have an important impact on the 3D planning technique chosen.

Posters Treatment Techniques/Technology

1283 poster

CRANIOSPINAL IRRADIATION WITH INTEGRATED SIMULTANEOUS BOOST DELIVERED WITH HELICAL TOMOTHERAPY IN A PATIENT WITH MENINGEAL MELANOCYTOMA

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Purpose/Objectif: To evaluate the feasibility of radiation treatment with integrated simultaneous boost delivered by helical Tomotherapy for craniospinal irradiation in a patient with meningeal melanocytoma.
Materials/Methods: A male, 36 years old, blind since three years for pseudotumor cerebri, affected by meningeal melanocytoma with para vertebral localization since 2000, was treated with laminectomy of C2/C3 and C6/C7, and then, for progression of disease, with temozolamide for two cycles of 12 months. A neuraxis RM images revealed PD both of intradural and paravertebral lesions. Biological Target Volume (BTV) was defined with a PET/CT. A CTV, including BTV, was defined on CT and RM imaging. PTV was obtained from CVT with a margin of 10 mm. We defined neuraxis as PTV1, a boost on BTV in neuraxis as PTV2 and para vertebral lesions as PTV3. Critical structures (OAR) were also contoured: eyes, heart, lungs, kidneys. The planned dose was 40 Gy (2 Gy/fr) for PTV1, of 43 Gy (2,15 Gy/fr) for PTV2 and 47 Gy (2,35 Gy/fr) for PTV3. An inverse planning optimisation process was implemented for dose calculation. The patient was set supine with a thermoplastic mask (Head Fix, MedTec). Daily MVCT images were acquired and fused with planning CT for set up verification before treatment delivery.
Results: A good coverage of PTV was obtained: 98-100% of PTVs were covered by the prescribed dose. The maximum dose and the average dose were respectively: 47.82 and 40.58 Gy for PTV1, 47.28 and 43.62 Gy for PTV2; 52.63 and 47 Gy for PTV3. A satisfactory OAR sparing was also reached. The average dose to OAR was: 10.96 for right eye, 10.77 for left eye, 26.31 Gy for heart, 19 Gy for lungs, 10.35

Gy for right kidney and 9.62 Gy for left kidney. Radiation induced early side effects were mild.
Conclusions: Craniospinal irradiation with integrated simultaneous boost delivered by helical Tomotherapy shows advantages relative to standard external beam radiotherapy. Firstly, the simultaneous integrate boost allows us to deliver a different dose to diverse PTV and to decrease length of radiation treatment. Secondarily, the set up is more comfortable for the patient that lies in supine position instead prone. Acute toxicity was very low, but it is necessary a longer follow up to evaluate later toxicity.

1284 poster

HELICAL TOMOTHERAPY IN RADIATION RETREATMENT

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Purpose/Objectif: It is difficult to successfully deliver a second course of radiation therapy for patients with overlapping treatment volumes. There are few data regarding retreatment and the most are related to brain and spinal cord metastases, and to the head and neck cancer recurrence. The aim of this study is the evaluation of an image-guided helical Tomotherapy system for the radiation retreatment of cancer recurrences in various anatomical sites.
Materials/Methods: From January 2005 to March 2006 12 patients underwent radiation retreatment. The sites of second irradiation were: 7/12 metastatic lymph nodes (primitive neoplasm: 4/7 breast;1/7 prostate; 1/7 limphoma; 1/7 kidney), 2/12 bone metastasis; 1/12 lung cancer recurrence, 2/12 head and neck recurrences. The total delivered dose ranges from 30 to 60 Gy with daily fraction from 2 to 2.5 Gy. In 9/12 cases the target volumes were totally included in previously irradiated volume but in 3/12 the overlapping treated volume was only partially. For every patient a full dose is delivered taking into account the disease being treated. Every patient had a treatment planning including PET/TC. Slice by slice BTV (Biological Target Volume) and GTV are identified. The expansion from GTV to CTV and from CTV to PTV were driven by: the biology of the disease being treated, the dose distribution at organ at risk (OAR), the total dose received by the OAR and the interval time from previous irradiation.
Results: The acute toxicity of the entire group of patients was very low: G0 in 8/12 patients, G1 (cutaneous or mucosae) in 4/12. All patients are in complete response with a median follow up of 8 months (range 3-14 months). The response evaluation was carried out with PET/TC at 1-3-6-9-12 months after radiation retreatment. 5/12 patients reached 12 months after radiation retreatment without adverse late effects.
Conclusions: In our preliminary experience radiation retreatment performed with image guided helical Tomotherapy is a safe and effective treatment modality in selected cases of recurring cancer disease. Treatment planning based on PET/TC is useful to define the real extension of the disease in order to decrease the irradiation of the OAR. However further investigation is warranted to consolidate these results and to extend these indications to other clinical situations.

1285 poster

HYPOFRACTIONATED 4D-PET/CT-BASED HELICAL TOMOTHERAPY FOR THE TREATMENT OF LIVER METASTASES: A FEASIBILITY STUDY.

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Purpose/Objectif: The aim of this study is to verify the feasibility of hypofractionated 4D-PET/CT-based Helical Tomotherapy for the treatment of patients affected by liver metastases
Materials/Methods: Three patients (pts) with 1 and two patients with 2 unresectable liver metastases were studied. A PET/CT scanner was used to acquire PET/CT images in 4D-mode on the region of interest in the abdomen. PET and CT images were acquired during free breathing, digitally reconstructed and coregistered. All CT images were contrast enhanced . "Integral" PET/CT images representing the entire respiratory cycle were obtained. An "Integral" Gross Tumor Volume (GTVint) was contoured considering all respiratory phases, expanded to an "integral" Clinical Target Volume (CTVint : +5 mm) for microscopic infiltration and to an "integral" Planning Target Volume (PTVint : +5,5,7 mm) for set-up errors. Three pts received a dose of 40 Gy on PTVint in 5 consecutive fractions (Frs), two additional pts a dose of 40Gy in 8 Frs and 44 Gy in 9 Frs respectively. Treatments were delivered by Helical Tomotherapy . Before each fraction a MV-CT was acquired and co-registered both automatically and manually with reference images to accurately reposition the patient.
Results: The dosimetric parameters were as follows :

PTVint (cc)	229,04±158,86
PTVint , D95% (Gy)	37,30±2,59
Liver , Dav (Gy)	11,16±3,11
Duodenum/Stomach , Dmax (Gy)	19,35±10.43
Duodenum/Stomach , Dav (Gy)	4,68±1,97
Spinal cord , Dmax (Gy)	11,35±2.46
Right Kidney , Dav (Gy)	5,93±5,77
Left Kidney , Dav (Gy)	1,62±2.03

Acute toxicity: nausea G1 in 3/5 patients. Responce: two pts reached a PET/CT-confirmed complete response, 1 pt a CT-confirmed stable disease, 2 pts have not been evaluated (too early). Median follow-up period 3,9 (0,6-12,9) months.
Conclusions: Treatment of liver metastases with 40-44Gy in 5-9 fractions and with 4D-PET/CT-based Helical Tomotherapy is feasible. A phase I trial to determine the maximum tolerated dose has been initiated.

1286 poster

HYPOFRACTIONATED 4D-PET/CT-BASED HELICAL TOMOTHERAPY FOR THE TREATMENT OF LUNG METASTASES : A FEASIBILITY STUDY

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Purpose/Objectif: The aim of this study is to verify the feasibility of hypofractionated 4D-PET/CT-based Helical Tomotherapy for the treatment of patients affected by lung metastases.
Materials/Methods: Seven patients affected by isolated lung metastases were studied. A PET/CT scanner was used to acquire PET/CT images in 4D-mode on the region of interest. All images were acquired during free breathing. "Integral" PET/CT images representing all the phases of the respiratory cycle were obtained. An "Integral" Gross Tumor Volume (GTVint) was contoured considering all the respiratory phases, expanded to an "integral" Clinical Target Volume (CTVint : +2 mm) for microscopic infiltration and to an "integral" Planning Target Volume (PTVint : +3,3,5 mm) for set-up errors. Furthermore a "standard" Gross Target Volume (GTVst) was contoured on "standard" PET/CT; GTVst was expanded (+2 mm) for microscopic infiltration to a "standard" Clinical Target Volume (CTVst), to a "standard" Internal Target Volume (ITVst, +5-15 mm, according to GTV location) for organ motion and to a "standard" Planning Target Volume (PTVst , +3,3,5 mm) for set-up errors. A dose of 36 Gy / 6 fractions / 2 weeks was prescribed to be delivered on PTVint by Helical Tomotherapy. Before each fraction a MV-CT was acquired and co-registered both automatically and manually with reference images to accurately reposition the patient.
Results: The dosimetric parameters were as follows :
PTVint = 36.09±23.89 cc
PTVint/PTVst = 0.14 - 0.46
PTVint , D95% = 35.71±0.56 Gy
Lung , V20 = 6.07±2.42 %
Lung , Dav = 5.07±1.38 Gy
Oesophagus , Dmax = 10.96±2.27 Gy
Oesophagus , Dav = 3.32±1.01 Gy
Heart , Dav = 2.07
Conclusions: Hypofractionated 4D-PET/CT-based Helical Tomotherapy for the treatment of lung metastases is feasible. Lack of toxicity could be due to a "personalized"-4D-PET/CT-PTV definition , an accurate patient set-up verification and a highly conformal dose distribution of Helical Tomotherapy . For further evaluation of this treatment modality a phase I trial of dose escalation has been initiated .

1287 poster

PET/CT WITH [18F]FDG TO EVALUATE THE RESPONSE TO HELICAL TOMOTHERAPY IN NSCLC AND LUNG METASTASES

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Purpose: To evaluate with PET/CT and [^{18}F]FDG the metabolic response to tomotherapy in patients with surgically unresectable NSCLC and lung metastases.
Materials/Methods: 5 pts (group A) with surgically unresectable NSCLC (stageIIIa-b) and 7 pts (group B) with lung metastases underwent tomotherapy with curative intent. Group A and B received 62.5 Gy (2.5Gy/fr) and 36Gy (6Gy/fr), respectively. Different combinations of chemotherapy were previously (>3 months) received by 2 pts of group A and 4 pts of group B. To assess the response to treatment, a PET/CT (PET_2) was performed at a median of 4 months (range:2-12 months) after the baseline (PET_1) and at a median of 2 months (range:1-4 months) after the end of tomotherapy. The metabolic response was defined by one nuclear medicine physician and one radiation oncologist as complete (CMR), partial (PMR), stable (SMD) and progressive (PMD) according to visual criteria and semiquantitative criteria. When more than one lesion was present at PET_1, the less favorable lesion response was used for coding the overall response of the patient. The [^{18}F]FDG maximum uptake (SUV_{max}) of the lesions was also quantified. Radiation induced inflammatory changes in normal tissue (radiotoxicity) were coded according to a visual scale. Side effects were monitored with the scale for the Common Terminology Criteria for Adverse Events (CTCAE).
Results: Visual analysis showed 4 PMR and 1 PMD (new lesion outside the target volume) in group A, and 2 CMR, 4 PMR, and 1 SMD in group B. Semiquantitative criteria yielded an identical classification. Only descriptive statistical is provided for the metabolic responder (MR, n=10) and non-responder (NMR, n=2) groups. At PET_1, the longest axial diameter of the lesion was 25.2±11.5 vs. 12.5±7.2 mm in MR and NMR, while SUVmax was 12.6±6.7 vs. 9.5±3.9, respectively. Percent SUVmax reductions in MR were 61.9±17.1% (range 40%-90%), while in NMR were 37% and 23% (PMD and SMD, respectively). In 2 MR, pleural [^{18}F]FDG uptake at PET_2 (SUV_{max} 2.54 and 3.57) was independently attributed to grade I toxic reaction by the two observers. Grade III radiotoxicity, a positive prognostic factor for the CMR, was detected in 2 MR. Acute CTCAE radiation toxicity occurred in 3MR (G1 lung and G1 esophagitis;G1 lung;G1 dysphagia).
Conclusions: A favorable metabolic response to tomotherapy was obtained with negligible clinical side effects in 10/12 patients with either unresectable NSCLC or lung metastases. In this limited sample, successful treatment does not appear dependent on the histology, size and magnitude of [^{18}F]FDG uptake of the examined lesions.

1288 poster

PHYSICAL CHARACTERISTICS OF THE SIEMENS 2.6 MM MODULEAF COLLIMATOR (MMLC)

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Purpose/Objectif: Conventional circular collimator or MLC is far from ideal for field shaping needs for highly irregular tumors. With reduced leaf resolution, the ability to deliver a high dose to the tumor with acceptable morbidity could be significantly improved. In this study, the physical characteristics of a Siemens moduleaf collimator (2.6 mm resolution) is investigated for potential application in the treatment of small but highly irregularly shaped tumors. The maximum field size achievable is 10x12 cm^2.
Materials/Methods: Dosimetric parameters (PDD, and Scp) are measured with a computerized water phantom system with micro diode detectors over the range of field size 1x1 - 10x10 cm2 for 6 and 15 MV x rays. The jaw openings are set at 10x12 cm2 throughout. Metal buildup caps are used for Sc measurements in air with an ion chamber. In addition, film dosimetry is used to measure the penumbra and the output factors. The results are compared with the regular 82-leaf MLC (MLC82) with 1 cm leaf width.
Results: For both 6 and 15 MV, the PDDs of the MMLC are consistently lower by 1-3 % than those for the MLC82 for field size ≤3x3 cm^2. For field size ≥4 cm^2, the PDDs are identical. The Scp values for the MMLC level off at field size≥ 7x7 cm^2. This is due to the shielding of the x rays scattered from the flattening filter by the MMLC. This effect, coupled with the lack of phantom scatter, result in Sc values approaching unity for field sizes ≥5x5 cm^2. The MMLC output factors are consistently higher than those of MLC82. As expected, the 80-20% penumbra is sharper for MMLC than for MLC82. For example, for 6 MV, the penumbra at dmax for the 1x1, 5x5 and 10x10 fields are 2.2mm, 3.6 mm and 4.1mm respectively. For MLC82, the corresponding values are 4.1mm, 3.6mm, and 5.6 mm respectively. The

interleaf leakage as measured from films is 0.85% for 6 MV and 1.4% for 15 MV. The accuracy of leaf positioning is within 1mm.
Conclusions: The MMLC provides improved physical characteristics compared to the conventional MLCs, and may be advantageous for field shaping of small irregular tumors. A drawback is that, being an optional accessory mounted on the block tray slot, the clearance to the patient is reduced, which may limit the ability to use certain non-coplanar fields.

1289 poster

PRODUCT DESIGN OF A PATIENT POSITIONING SYSTEM FOR TOTAL BODY IRRADIATION: THE "TIBIT"

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Purpose/Objectif: This abstract summarises a thesis made in 2005 at the Department of Consumer Goods. The goal was to design a positioning aid for fractionated total body irradiation including transmission blocks for lung shielding and the possibility to make megavolt images using (CR) cassettes.
Materials/Methods: Product idea: The main drivers for the design were: time reduction, reduction of effort and patient comfort. The main developed items are: A] reproducible, reliable and comfortable body support with fixation of the thoracic region, B] reproducible and reliable shielding of the lungs. Secondary items: system storage and mobility, access to the patient, communication with the patient and connectivity. Extra items: dimensions of the irradiated area, patient position, PMMA radiation diffuser, no radio-opaque material between source, patient and cassette, recognition of patient dependant parameter settings (eg fixation, shielding), patient friendly and easy to clean.
System design: Various existing methodologies were studied and tested. A cost analysis was made as well as a market study.
Results: Product concept: The unit consists of a rotating stand on a fixed base plate. The front of the unit supports the PMMA radiation diffuser and an adjustable block system. The patient rests on a reclining surface in carbon to which panels holding the thorax fixation, bottom and head rests are connected. The panels fit in a unique way to the surface. The back of the unit can hold a standard cassette at a selectable height. A number of switches interlocks to the linac to prevent erroneous irradiation. The patient has audio-visual communication with the control room and the progress of the treatment can be followed by the patient on a display in the unit. All cables are integrated in the frame of the unit including connections for in-vivo diodes.
The base plate locks into position and is not moved during treatment. For APPA treatment, the stand is rotated maintaining the patient position in the stand, the diffuser, block holder and cassette holder remain steady. The Tibit unit can be stowed away when not in use and fits through a standard size door.
Conclusions: The design tackles most problems that are encountered with Total Body Irradiation. The use of the Tibit system would add to the quality of the patient's treatment and reduce handling time by the nursing staff. The poster shows the design with detailed views of the various parts.

1290 poster

SHORT-COURSE HYPOFRACTIONATED ADJUVANT RADIOTHERAPY AFTER RADICAL PROSTATECTOMY WITH HELICAL TOMOTHERAPY

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Purpose/Objectif: A hypofractionated schedule for adjuvant (ADV) RT delivered with helical Tomotherapy (TT) unit (HiArt2, Tomotherapy Inc.) after radical retropubic prostatectomy (RRP) for prostate carcinoma (CaP) was recently activated in our Institute. Acute toxicity (TOX) data relative to the first 40 pts are presented.
Materials/Methods: Assuming an a/b ratio for CaP = 3, TT was prescribed to deliver 58 Gy to the tumoral bed in 20 fractions (2.9 Gy/fr; 2 Gy Equivalent dose EQD_2 = 68 Gy). Nonetheless, due to some controversial reports suggesting both a/b ratio much higher (up to 10) or lower (up to 1.5), the chosen fractionation scheme represents an excellent compromise to deliver an EQD_2 RT dose within the usually accepted range of dose in the ADV setting (from 73 to 62.5 Gy for a/b ratio between 1.5 to 10, respectively).
All 40 pts had undergone pelvic lymphadenectomy and RRP for a pT2R1 (n=12), pT3a (n=25) or pT3b (n=3), pN0 CaP. In pT3b patients the seminal vesicle bed was also irradiated to 53 Gy (2.65 Gy/fr) with a concomitant boost. No pts received NEO/ADV hormonotherapy (HORM). Megavoltage CT image-guide was used to decrease set-up errors, by matching bone structures on the daily scan with the planning scan.
Results: The mean rectal dose was 26 Gy, with a median % value of rectum volume receiving > 40 Gy of 24%. Bladder sparing depended on the degree of filling at the CT scan, with the mean dose ranging from 28 Gy for "full" bladders to about 40 Gy for the "empty" ones. The PTV fraction included in the 95% isodose was between 96 and 99.6%. After a median follow-up of 12 months (range 4-15), acute TOX were as follows: GU G1 50%, G2 15%, G3 2.5%; upper GI G1 23%, G2 2.5%; proctitis G1 25%, no G2-G3. By comparison, acute TOX in a cohort of 107 comparable pts (pT2 R1, pT3, pN0, no HORM), treated with ADV 3DCRT at 68-70 Gy were: GU G1 23%, G2 14%, G3 2%; upper GI G1 12%, G2 5%; proctitis G1 21%, G2 9%. The comparable incidence of acute GU TOX between TT and 3DCRT may derive from the similar bladder volumes included in the "high doses" region, whereas the significant reduction of acute GI G2/3 TOX with TT, which results from the steep dose-gradient achievable with TT, supports the recent data indicating the rectum as a "parallel" organ for acute G2-G3 TOX.
Conclusions: Although preliminary, these data suggest the possibility to safely deliver a hypofractionated adjuvant TT after RRP, with significant reduction of GI TOX and RT duration with respect to a conventional regimen.

1291 poster

TARGET VOLUME DEFINITION FOR STEREOTACTIC RADIOTHERAPY OF LUNG METASTASES : A COMPARISON BETWEEN PET/CT AND 4D-PET/CT

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Purpose/Objectif: Four-dimensional PET/CT data acquisition (4D-PET/CT) could offer the opportunity to improve image quality and to precisely define target shape and its motion during the entire respiratory cycle. The aim of this study is to compare PET/CT and 4D-PET/CT for target volume definition in the stereotactic treatment of lung metastases
Materials/Methods: Five patients affected by a single lung metasta-

sis were studied. A PET/CT scanner was used to acquire "standard" PET/CT images from the base of the skull to the pelvis and PET/CT images in 4D-mode on the region of interest in the thorax. All images where acquired during free breathing , digitally reconstructed and coregistered. Two image data sets were obtained on the target region: "standard" PET/CT and "integral"PET/CT representing all the phases of the respiratory cycle.Treatment volumes were generated and compared for each data set. A "standard" Gross Target Volume (GTVst) was contoured on "standard" PET/CT; GTVst was expanded (+2 mm) for microscopic infiltration to a "standard" Clinical Target Volume (CTVst), to a "standard" Internal Target Volume (ITVst, +5-15 mm, according to GTV location) for organ motion and to a "standard" Planning Target Volume (PTVst , +3,3,5 mm) for set-up errors. An "Integral" GTV (GTVint) was contoured on "integral" PET/CT and expanded to a CTVint (+2 mm) for microscopic infiltration and to a PTVint (+3,3,5 mm) for set-up errors.

Results: The following volumes were calculated: GTVst = 17.51±30.83 cc; GTVint = 19.64±31.86 cc. To evaluate the grade of spatial reproducibility of these volumes, a reproducibility index (R), defined as the ratio between volume intersection and volume union, was calculated. A R = 1 was expected in case of the highest reproducibility; a R = 0 was expected in case of the lowest reproducibility between the volumes. GTVst was smaller than GTVint (64±24%) in accordance to organ motion; a R = 0.33-0.86 was calculated between GTVst and GTVint. PTVint was smaller than PTVst ; a R = 0.12-0.41 was calculated between PTVint and PTVst.

Conclusions: GTVst and PTVst inadequately reproduce GTVint and PTVint . PTVint could represent patient-specific target volume in order to ensure correct dose coverage when free breathing is present during beam delivery. Further patients need to be studied to validate these data.

1292 poster

TOTAL BODY IRRADIATIN: THE MIDDELHEIM PARADIGM

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Purpose/Objectif: In this study we describe a technique used for fractionated total body irradiation. The patient is treated with 12 Gy in 6 fractions over 72 hours with the dose to the lungs limited to 9 Gy

Materials/Methods: After comparison of several techniques for positioning the patient (antero-posterior irradiation with patient laying on his side, free standing, sitting or crouching, left-right irradiation with patient in supine position) and positioning the lung shields, we have opted for a standing position of the patient, fully stretched with adjustable crouch and armpit supports and hand grips. A reclining back support at 15 degrees gives the effect of a resting position. The "treatment cabin" is positioned at 3 meters from the linac's isocenter. For the lung shields we use transmission blocks cut out of lead sheets. The blocks are glued on a plastic foil which is fixed by two clamps to the 2 cm thick PMMA screen used to homogenise the surface dose. To track the position of the blocks and make it reproducible, during simulation a 8mm steel ball bearing is put on the patient on the projection of a central mark on the PMMA screen. This mark (or rather the ball bearing) shows up on an "x-ray" taken with 12 MU (18 MeV) on a CR screen. The magnification known, a reduced copy is printed to give the size of the lung blocks and their position relative to the central mark. Once the blocks are cut, they are glued on the foil relative to the mark. Positioning the mark on the foil onto the mark on the PMMA screen gives a reliable reproducible position of the blocks relative to the patient. During treatment, each session starts with a verification "x-ray" of the blocks and the lungs.

Results: Only small (1-4 mm) adjustments of the position of the block foil are necessary depending on the general status of the patient. The reclined standing position combined with the support and individual head rest gives a very reproducible position for both anterior and posterior irradiation. Patients experience the position as rather comfortable.

Measurements and calculations: Depth dose and transmission were measured at the effective distance of the treatment. Lung dose relative to central dose is measured on line by diodes every treatment fraction. TLD measurements track central dose and dose to extremities.

Conclusions: After a series of 25 patients we can conclude that the described paradigm allows for routine TBI treatment. The specially designed treatment cabin is easy to use and can be put away during the rest of the treatments. The block system gives reproducible results and is easy to use.

1293 poster

VIRTUAL SIMULATION AND FIELD JUNCTION VERIFICATION FOR CRANIOSPINAL AXIS IRRADIATION IN SUPINE POSITION

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Purpose/Objectif: Craniospinal axis irradiation (CSI) is a complex treatment technique requiring the use of at least two isocenters to cover completely the volume of treatment. The process is classically done with the patient in prone position in order to verify the adequacy of the matching of adjacent fields. We propose a method for CSI in supine position using virtual simulation and a procedure to check the junction of the fields.

Materials/Methods: The patient was a boy, 7 years old. Patient is immobilized lying supine over a cushion with a head mask fixation. CT images 5 mm width are taken and used for virtual simulation, where treatment volumes and organ at risk (OAR) are delineated. The treatment technique uses two isocenters: the first one located in the cervical region the more caudal as possible to avoid irradiating the oral mouth and superior airway-path. Half blocked parallel-opposed fields are used to irradiate cervical and cranial region while the cervical-dorsal region is irradiated with a direct posterior half blocked field open caudally to 20 cm. The second isocenter is located 20 cm apart from the first one, the table is then rotated 90 degrees and the gantry to 169 to correct for the divergence of the cervical-dorsal field and using again a half-blocked field. Treatment was delivered for all beams with 6 MV X-Rays and MLC to spare OARs. Daily electronic portal image (EPID) for corrections of possible misalignment of the spinal cord was taken. Shifts of the matching line can be easily implemented opening the jaws adequately without changing the position of the isocenter. Verification films were positioned daily under the patient for the second isocenter and tapped on the EPID for the first cervical isocenter. Films were exposed during the complete session and visually analyzed before next fraction was given. Before the treatment of the first patient the procedure was checked using a plastic phantom with films sandwiched between the plastic slabs.

Results: In the phantom verification films was observed that although visual matching was exact there was a systematic underdosing gap in the junction lines of 1.3 mm measured as the 80 % width. On each session to give confidence that the second isocenter is correctly located, the cervical-dorsal field, after delivered, is rotated to 0 degrees and marked the edges on the patient skin. Digital table readout is used to position the second isocenter and rotated to 90 degrees. Then the gantry is rotated to 11 degrees and visually verified that the axis of the beam coincides with the caudal edge marked on the skin. 26 verifications films were obtained for this paediatric patient (13 sessions times 2 films) visually verifying that no overlap between adjacent fields in both isocenters occurs.

Conclusions: Supine position is better accepted for patients and

technicians, being more comfortable and having access to superior airway-path. The use of virtual simulation and QA with weekly verification films/daily visual inspection during the treatment make this technique appropriate to be incorporated in cases when prone position is not well tolerated.

Posters Upper GI

1294 poster

CLINICAL RESULTS OF THREE-DIMENSIONAL CONFORMAL RADIOTHERAPY FOR PORTAL VEIN OR INFERIOR VENA CAVA TUMOR THROMBUS IN PATIENTS WITH INOPERABLE HEPATOCELLULAR CARCINOMA

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Purpose/Objectif: To evaluate the treatment results of prognostic factors affecting tumor response and survival of patient with hepatocellular carcinoma (HCC) complicated with portal vein (PV) or inferior vena cava (IVC) tumor thrombus treated with three-dimensional conformal radiotherapy (3D-CRT).

Materials/Methods: From 1998 to 2006, 21 patients with inoperable HCC complicated with tumor thrombus were treated with 3D-CRT. The median age was 68.5 years (range: 46-80). The performance status (PS) according to the Eastern Cooperative Oncology Group scale was 1 in twelve patients, 2 in eight, and 3 in one. Liver cirrhosis was present in 20 patients (95%). The Child-Pugh classification was A in 7 patients, B in 6, and C in 8. Ascites was present in 9 patients before radiotherapy. Serum AFP was positive in 20 patients, with 15vpatients having an AFP level > 400 IU/ml. 13 patients had tumor thrombus in first branch of portal vein, and 6 in main trunk, and 2 in IVC. The target volume was defined with a 2 cm cranial-caudal margins and 1-1.5cm other margins of the tumor volume. Radiotherapy was delivered by 6- or 10-MV linear accelerator using 3-5 coplanar ports. The median radiation dose was 46 Gy (range: 30-60 Gy) in a daily fraction of 2-3 Gy. The median biologic effective dose (BED) at $\alpha/\beta=10$ was 56.4 Gy (range: 44-74Gy). The various factors associated with tumor response were evaluated by using the Mann-Whitney U-test. The factors associated with survival were also evaluated by using the Cox regression model. Acute toxicity was evaluated by using CTCAE v3.0, and subacute or chronic toxicity was evaluated by using Radiation Therapy Oncology Group criteria (version2.0).

Results: The mean follow-up was 3 months (2-27 months). Out of 21 patients, 6 patients (28%) got partial response (PR), 10 (48%) got stable disease (SD), 5 (24%) got progressive disease (PD), and no patient got complete response (CR). The tumor response rate (CR+PR) was 28%. Radiation dose was the only significant factor for tumor response on Mann-Whitney U-test ($p<0.05$). During follow-up period, 4 patients had local recurrence. The progression free survival at 1 year was 75%. The over all survival rate at 1 and 2 year was 39.6% and 0%, respectively (median survival 3 months). On univariate analysis, PS, Child-Pugh classification, and ascites were significant factors for survival rate ($p<0.05$). Tumor response was not significant factor. There was no Grade 3 or 4 acute toxicity and gastric or duodenal ulcer.

Conclusions: Radiation dose was significant factor in tumor response. Additional efforts for dose escalation may be warranted to improve the treatment results.

1295 poster

EXCLUSIVE CHEMORADIATION FOR NON OPERABLE PATIENTS WITH STAGE I AND II ESOPHAGEAL CANCER

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Purpose/Objectif: Surgery is a standard treatment for patients with stage I/II oesophageal cancer (OC). As far as the comparison between surgery and exclusive chemoradiation (CRT) is concerned, any valid comparison for stage I / II OC is available. Thus, exclusive CRT could be considered as an alternative to surgery in a curative intent. The aim of this retrospective study is to analyse results of exclusive CRT delivered to non operable patients with stage I/II OC.

Materials/Methods: From January 1993 to December 2001 eighty-eight patients (pts) were reviewed. Mean age was 65.8 years (y) (range 46-85.5y). Most patients had SCC (81.6%). At baseline, WHO performance status was : 0 - 1 : 60 pts (68.2%); 2 - 3 : 25 pts (28.4%) and weight loss was : < 10% : 63 pts (71.6%); [3] 10% : 25 pts (28.4%). According to the current UICC classification, tumours were recorded as follows : stage I : 17 patients; stage IIA : 35 patients; stage IIB : 36 patients.

Results: Median follow-up was 11.4 months (range 0.3 - 82.8 months). Survival rates at 1, 2 and 3 y were respectively 48.9%, 25% and 10.2%. Median survival were respectively 14.4, 10.8 and 9.3 months for stage I, IIA and IIB. Prognostic factors identified by univariate analysis were : dysphagia and histology. Dysphagia was the only prognostic factor identified with multivariate analysis ($p=0.013$).

Conclusions: Exclusive CRT is an alternative treatment for non operable patients with stage I / II oesophageal cancer. Despite poor results, due to unselected patients with a poor performance status at baseline, there is a need for a randomised trial comparing surgery to CRT in patients with localized oesophageal cancer.

1296 poster

FACTORS INFLUENCING SURVIVAL IN PATIENTS WITH LOCALLY ADVANCED ESOPHAGEAL CANCER TREATED WITH CURATIVE RADIOTHERAPY

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Purpose/Objectif: To investigate the predictive and prognostic factors influencing overall survival in patients with locally-advanced esophageal cancer treated with definitive concurrent chemoradiotherapy (CRT).

Materials/Methods: A total of 47 patients with locally-advanced unresectable esophageal cancer, who had been treated in the Radiation Oncology Department of Uludag University between 1995 and 2004, were included in this analysis. There were 26 males and 21 females with a median age of 55 years (range: 24-78). The most common histological diagnosis was squamous cell cancer being detected in 42 patients (89%). Lymph node involvement was seen in 12 patients (26%). Six patients (13%) had T1-T2 tumor, and 41 patients had T3-T4 tumor (87%). Radiotherapy (RT) was delivered with 1.8 Gy daily fractions (5 days a week) bringing to a total median dose of 59.4 Gy (range: 49-72 Gy). Concurrent chemotherapy (CT) with weekly cisplatin (30-40 mg/m2) was given in 33 patients (70%). Response assessments were carried out one month after RT

with endoscopical and appropriate radiological examinations. Adjuvant 5-fluorouracil plus cisplatin CT regimen was administered in 18 patients, who showed stabile disease or tumor progression after RT/CRT. Overall survival was estimated with Kaplan-Meier method. Potential prognostic factors were analyzed with univariate and multivariate analyses.

Results: The median survival was 13 months (95% CI 8.35-15.65). The overall survival for 1 and 3 years were 52% and 13%, respectively. Occurrence of pathological complete response, lower tumor grade and existence of <T4 primary tumor stage were demonstrated to be the significant prognostic factors affecting survival as positively (p=0.043, p=0.026 and p= 0.029, respectively). Complete response rates were observed to be higher in patients with ≥65 years old, when the factors predicting pathological complete response were analyzed (p= 0.043).

Conclusions: Pathological complete response to RT is an important predictive factor influencing overall survival. Pathological complete response rates and survival was impaired in patients older than 65 years.

1297 poster

INTENSIVE NEOADJUVANT RADIOTHERAPY FOR GASTRIC CANCER: 30-YEARS SINGLE INSTITUTION EXPERIENCE

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Purpose/Objectif: The survival of patients with gastric cancer especially locally-advanced, poorly differentiated and diffuse types remains poor. To improve the outcome of surgical treatment neoadjuvant radiotherapy was used.

Materials/Methods: Between 1974 and 2004, 804 patients were operated on with curative intent. 332 patients underwent surgical treatment while in 472 patients radiotherapy precedes the operation. Neoadjuvant radiotherapy was given as a short-term course, 3 schemes were used. The first one was so called "concentrated" radiotherapy: 20 Gy/5 fractions/5 days (225 patients). The second one was the same scheme plus metronidasole as a radiosensitizer (67 patients). The third one was uneven or dynamic fractionation: 27 Gy was delivered for 7 days, 2 fractions per day, the first (7 Gy) and the last (5 Gy) fractions were the largest (180 patients).

Results: The radiation therapy was completed in 461 patients (97,6%). No increase in postoperative morbidity or mortality was seen in radiotherapy group. Definite but statistically insignificant increase in overall survival existed for multimodal vs surgical treatment for the entire group: 5-YS was 55±2% vs 49±3%, 10-YS was 44±2% vs 36±3%, median survival was 6,9 vs 4,8 years; p=0.058. Subgroup analysis showed that surgical treatment never provided better survival while multimodal treatment did. Equal long-term results were obtained when the tumor was within gastric wall (T1-2); regional lymph nodes were negative (N0); in UICC stage 1, 3B and 4; and when the tumor represented well or moderately differentiated adenocarcinoma. In contrast we have identified clinical situations when neoadjuvant radiotherapy provided statistically significant improvement in long-term results. There were: UICC stage 2 and 3A (p=0.017); N+ cases (p=0.014); tumors more than 3 cm in diameter (p=0.021); and Borrmann 3-4 type tumors (0.024). The most impressive survival advantage was registered in poorly differentiated adenocarcinoma and signet ring cell carcinoma: 5-YS was 56±3% vs 42±4%, 10-YS was 47±3% vs 27±4%, median survival was 7,1 vs 3,3 years; p=0.004.

Conclusions: In patients with poorly differentiated and signet ring cell carcinoma, diffuse-type carcinoma, N positive tumors, long-term results of surgical treatment may be improved by neoadjuvant radiotherapy. Further studies of neoadjuvant radiotherapy should be focused in these "target" groups of patients.

1298 poster

IODINE-125 IMPLANTATION IN THE TREATMENT OF UNRESECTABLE PANCREATIC CARCINOMA WITH INTRAOPERATIVE GUIDANCE

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Purpose/Objectif: Preliminary assessment of feasibility, efficacy and morbidity of ^{125}I seed interstitial brachytherapy for pancreatic carcinoma with intraoperative ultrasound guidance.

Materials/Methods: 27 patients with unresectable pancreatic carcinoma was undertaken interstitial implantation of ^{125}I seeds with intraoperative ultrasound guidance. The matched peripheral doses (MPD) of ^{125}I seeds implantation ranged from 110Gy to 160Gy. The ^{125}I activity of per seed ranged from 0.4 mCi to 0.6mCi. The total number of sources implanted ranged from 10 to 75 (imedian 38)j. External beam radiotherapy (EBRT) was given to 6 patients, the total doses of EBRT were 4500~5000cGy, 200~300cGy/f, 5f/w. The intervals between ^{125}Iseed implantation and EBRT were 3~4 w. 8 patients were received 5-fluorouracil based chemotherapy, 2~4 cycles.

Results: All patients could well tolerated seed implantation. At the time of this analysis, the local-regional controls were 74%, the survival of 1- and 2- year survival rates were 25% and 15% for II/III stage patients, respectively, the median survival was 8 months (95% CI,5-11). 1-year survival rates were 8.3% for IV stage patients, the median survival was 5 months (95% CI,3-7).

The major late complications included GI bleeding and was seen in three patients. Two patients died from local recurrence after 6 and 8 months,respectively. One patient developed late radiation enteritis and three patients developed chylifaction. Overall late complications were seen in 7/27 patients (25.9%) alive beyond 6 months.

Conclusions: ^{125}I seed implantation can be successfully used for salvage in patients with unresectable pancreatic cancer by intraoperative ultrasound guidance. Patients with localized advanced pancreatic carcinoma are most likely to benefit from ^{125}I seed implantation, at the same time, it can relieve pain but did not show survival benefit for metastatic patients.

1299 poster

OPTIMIZATION OF RADIOTHERAPY TREATMENT PLAN FOR HEPATIC TUMOR

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Purpose/Objecti: Radiotherapy treatment plans for hepatic tumor are significantly limited by the adjacent normal organs at risk (OAR), which become major restriction on the total dose of the target. In this study, we try to find the optimal treatment plans for hepatic tumor according to the intra-hepatic location of the target tumors and its relationship to OARs.

Materials/Methods: We divided the liver into four groups according to the frequency of tumor location that our institute had treated. These groups correspond to Couinaud segment system as follows: (I) segment 1, (II) segment 2, 3, 4; (III) segment 5, 6; (IV) segment 7, 8. We acquired a CT image data of a healthy liver and drew virtual targets and OARs (right kidney, normal liver, stomach and duodenum) using Pinnacle3 (ADAC Laboratories) radiation treatment planning

system. The centers of the each virtual target were picked as isocenters and field margins were given 1.5 cm for organ movements and setup margins. We made several plans for each virtual target and compared the dose-volume histograms (DVH) and normal tissue complication probabilities (NTCP). For NTCP calculation, we used system TCP/NTCP model of the Pinnacle3.

Results: For group I, NTCP got better as the number of the beam ports increase. However, plans with more than 5 ports had little advantage. For group II, plans with the beam directions from anterior side only showed better results compared with the multi-directional plans, particularly in view of protecting liver and stomach. Group III represents the presence of many OARs near the target, which gave restrictions to the beam-directions. Multi-directional plan allowed significantly higher dose to the OARs than simple 2-port plan using RAO, PA (as shown in table). For group IV, no significant differences were noted among the plans. Simple 2-port plan was good enough for the target conformity and protection of OARs. In spite of these optimal beam directions according to the target position, small number of the ports appeared rather suitable as the target size gets bigger.

Conclusions: Better NTCP can be achieved through individualized radiotherapy treatment plan according to the intra-hepatic location of the tumor.

Table. Group3 NTCP (Total Dose 63 Gy)

Beam Configuration	Remained Liver	Duodenum	Right Kidney
RAO/PA	27%	2%	97%
RAO/RPO/PA	73%	17%	100%
AP/PA/RT	83%	65%	98%
AP/PA/RAO/RPO	79%	35%	99%

AP : anterior to posterior beam PA : posterior ot anterior beam

RT : right side beam

RAO : right anterior oblique beam, entering between the anterior and right axes

RPO : right posterior oblique beam, entering between the posterior and right axes

1300 poster

POSTOPERATIVE ADJUVANT 5-FU/CISPLATIN AND CHEMORADIATION WITH CAPECITABINE FOR ADVANCED GASTRIC CANCER

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Purpose/Objectif: To evaluate the efficacy and toxicity of adjuvant 5-FU/cisplatin and chemoradiation with capcitabine after radical gastrectomy for advanced gastric cancer.

Materials/Methods: Fourty patients who had underwent a radical gastrectomy (D2 lymphadenectomy) for stage III and IV(M0) gastric cancer were enrolled. Therapy consists of one cycle of FP (continuous infusion of 5-FU 1000 mg/m^2 on day 1-5 and cisplatin 60 mg/m^2 on day 1) followed by 4500 cGy (180 cGy/d) with capcitabine (1650 mg/m^2 daily throught radiotherapy). Four weeks after completion of the radiotherapy, patients received three additional cycles of FP every three weeks. The median follow-up was 25 months.

Results: The 3-year disease free and overall survival in this study were 65.4% and 82.1%, respectively. Eight patients (20%) showed relapses during follow-up. Thirty two patients (80%) completed all planned adjuvant therapy. Grade 3/4 toxicities included neutropenia in 45%, anemia in 15%, thrombocytopenia in 2.5%, nausea/vomiting in 5% and adhesive ileus requiring operation in 5%. Neither grade 3/4 hand-foot syndrome or treatment related febrile neutropenia or death were observed.

Conclusions: This postoperative adjuvant chemoradiation regimen appears well tolerated and offers a comparable toxicity profile to the chemoradiation regimen utilized in INT-0116 study. This treatment modality allowed successful loco-regional control rate and 3-year overall survival for advanced gastric cancer.

1301 poster

POSTOPERATIVE CHEMORADIATION WITH WEEKLY GEMCITABINE FOR PANCREATIC ADENOCARCINOMA: A PHASE II TRIAL.

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Purpose/Objectif: Surgery is the most important treatment in pancreatic carcinoma. Despite local relapses are high, adjuvant radiochemotherapy has not yet shown a clear benefit in completely resected tumours. We report the clinical outcome and treatment-related toxicity of a phase II study on an alternative schedule of gemcitabine-based chemoradiation followed by adjuvant gemcitabine in resected pancreatic cancer patients.

Materials/Methods: Eligibility criteria included: histologically proven pancreatic carcinoma, pathological stage II-III, no liver, heart or kidney comorbidity, age 18-75 years, ECOG performance status (PS) ≤ 2, written informed consent. Patients (pts) received postoperative 3D conformal radiotherapy on the surgical bed and regional nodes (39.6 Gy 1.8 Gy/fr) followed by a boost on surgical bed (10.8 Gy 1.8 Gy/fr) plus concurrent chemotherapy (gemcitabine: 100 mg/m^2 continuously infused for 24 h, weekly, weeks 1-5). A dose reduction scheme was applied based on observed toxicity: grade 1: 80%; grade 2: 60%; grade >2: no chemotherapy. Chemoradiation was followed by 5 courses of adjuvant gemcitabine (1000 mg/m^2, days 1-8, every 21 days). Toxicity was evaluated according RTOG/EORTC score systems. Survival analysis was calculated from the time of diagnosis with Kaplan-Meier method.

Results: Thirty pts have been enrolled from September 2000 to December 2004 (M/F: 18/12, median age: 59.4 yrs [range 40-73]). Twelve pts (40%) were stage IIA, 15 pts (50%) IIB and 3 pts (10%) III. Pretreatment ECOG PS was 0 in 22 pts (73.3%) and 1 in 8 pts (26.6%). Nineteen pts (63.3%) completed radiotherapy without any interruption. Seven pts (23.3%) interrupted the treatment for less than 7 days (median 3 days) and 4 pts had definitive interruption of radiotherapy (>40 Gy delivery dose). Twenty-seven pts (90%) received 4-5 cycles of concurrent gemcitabine. The median dose of administered gemcitabine was 80% of prescribed dose. Adjuvant chemotherapy was completed in 23 pts (76.6%). Grade 3-4 haematological acute toxicity was observed in 3 pts (10%), whereas 4 pts had G3-4 gastrointestinal toxicity. No patient showed late toxicity. Four pts (13.7%) showed local recurrence and 14 pts (48.2%) had distant metastasis. With a median follow-up of 38 months (range 14-76), actuarial local control was 84% at 2- and 5-years. Actuarial 2- and 5-years distant metastasis free survival was 54% and 38% respectively , median 20 months. Actuarial 2- and 5-years overall survival was 56% and 37% respectively, median 32 months.

Conclusions: Postoperative combined modality therapy with continuous infusion of gemcitabine plus adjuvant chemotherapy seems safe and feasible. Three dimensional radiotherapy resulted in an acceptable rate of acute toxicity, which allowed the majority of pts to receive further adjuvant chemotherapy. The study proved to be effective in terms of local control and survival, compared to standard results.

1302 poster

POSTOPERATIVE CHEMORADIOTHERAPY OF KLATSKIN TUMOR

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Purpose/Objectif: To analyze the outcome of adujvant chemoradiotherapy (CRT) for patients with Klatskin tumor and to identify prognostic factors for these patients.

Materials/Methods: Between April 1991 and July 2003, 35 patients underwent adjuvant chemoradiotherapy after resection for Klatskin tumor at the Department of Radiation Oncology, Seoul National University Hospital. One patient was excluded from analysis due to incomplete treatment. There were 24 males and 10 females, and median age was 58 years. Hepatobiliary resection (extended hepatectomy and hilar bile duct resection, N = 18) or bile duct resection (N = 16) was performed with curative intent. Thirteen patients had en-bloc resection with negative margin (R0), whereas 18 patients had microscopically positive margin (R1) and 3 patients had gross residuum (R2). Radiation dose range was 40-50Gy with median 40Gy. Radiation target volume included tumor bed and regional lymph nodes. Radiation field was extended to include paraaortic lymph nodes in 22 patients. Concomitant 5-fluorouracil was administered during radiotherapy in 33 patients, and maintenance chemotherapy was offered to 22 patients after adjuvant radiotherapy. Interval between surgery and chemoradiotherapy was 27-102 days (median 41).

Results: Median follow-up period was 42 months. Two year and five year overall survival rates were 59% and 34%, respectively. Two year loco-regional control rate was 55%. The 5-year survival and 2-year local control were 35.9% and 67.7% in R0 group and 32.4% and 47.0% in R1 group (p=0.5922 and p=0.6750, respectively). Nodal involvement, lengthened treatment interval and limited radiation field were found to be significant adverse prognostic factors for survival with multivariate analysis (p=0.031, 0.010, 0.004, respectively). Resection margin involvement, lengthened treatment interval and limited radiation field significantly worsened loco-regional control in multivariate analysis (p=0.034, 0.016, 0.042, respectively).

Conclusions: After adjuvant CRT for Klatskin tumor, survival and loco-regional control of patients with microscopic residuum after resection was comparable to those of complete resected patients. Furthermore, results from this study show earlier adjuvant CRT after resection and extended target volume could increase not only loco-regional control but survival as well.

1303 poster

PROGNOSTIC FACTORS FOR DISEASE-FREE AND OVERALL SURVIVAL IN PATIENTS TREATED WITH CHEMORADIATION THERAPY FOR LOCALLY ADVANCED PANCREATIC CANCER

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Purpose/Objectif: Non-metastatic locally advanced pancreatic cancer portends an extremely poor prognosis. Patients are typically treated with chemoradiation. Prognostic factors for disease-free survival (DFS) and overall survival (OS) are inadequately defined.

Materials/Methods: Between December 1993 and July 2005, 247 patients with locally advanced, non-metastatic, pancreatic adenocarcinoma were treated at our institution with concurrent chemoradiation therapy. Patients treated with bevacizumab chemotherapy on protocol were excluded from this analysis. Median radiation dose was 30 Gy (range 15 - 52.2 Gy). Radiosensitizers included 5-FU (54%), gemcitabine (33%) and capecitabine (13%). Fourteen patients received adjuvant gemcitabine chemotherapy while the remaining received no adjuvant chemotherapy. Actuarial survival was calculated from the start of radiation treatment. Potential prognostic factors analyzed included age, gender, race, tumor grade, KPS, percent weight loss, jaundice at presentation, pretreratment hemoglobin level (Hgb), radiation dose, and concurrent chemotherapy regimen. Actuarial univariate and multivariate statistical methods were used to determine significant prognostic factors for DFS and OS.

Results: Median follow-up was 4.3 months (range 1-63 months). Median DFS and OS were 3 months and 8.5 months respectively. On univariate analysis, prognostic factors for improved DFS were KPS >80 (p=0.008) and less than 5% weight loss in the preceding 3 months (p=0.034). On multivariate analysis, KPS (odds ratio, OR=1.17, p=0.049) was the only independent prognostic factor for DFS. Median DFS was 3.8 months among patients with KPS >80 and 2.4 months among those with KPS <80. On univariate analysis, prognostic factors for improved OS were Hgb ^{3}12 (p=0.017), KPS >80 (p=0.001) and less than 5% weight loss in the preceding 3 months (p=0.033). On multivariate analysis, Hgb (OR=0.68, p=0.028) and KPS (OR=1.25, p=0.006) were independent prognostic factors for OS. Median OS was 10.3 months among patients with KPS >80 and 7.6 months among those with KPS ^{3}80. Patients with a pretreatment Hgb <12 had a median OS of 7.3 months compared to 9.0 months for those with Hgb ^{3}12.

Conclusions: KPS is an independent prognostic factor for DFS and OS among patients treated with chemoradiation for locally advanced pancreatic cancer. Pretreatment Hgb is an additional independent prognostic factor for OS. These factors could be used in the stratification scheme of future chemoradiation trials for pancreatic cancer.

1304 poster

RADIOCHEMOTHERAPY AFTER SURGERY IN GASTRIC CANCER. RESULTS OF 92 PATIENTS.

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Purpose/Objectif: Local relapse after curative surgery in gastric adenocarcinoma is high. The benefit of adjuvant treatment is to improve locoregional control and survival. A randomized multicentric assay (SWOG-9008), established a significative benefit of relapse free and overall survival , in treating patients in a postoperative setting. To describe the results of a serie of 92 patients, diagnosed of gastric adenocarcinoma, treated with surgery and radiochemotherapy.

Materials/Methods: From August-00 to desember-05 92 patients (53 men and 39 women), diagnosed of gastric adenocarcinoma, received radiochemotherapy after surgery. Histologic diagnoses showed in all cases adenocarcinoma. Mean age was 62,1 ± 11,1 years. A total gastrectomy was performed in 40 patients, and a partial in 52. Only 7 esplenectomies were done. Mean nodes resected were 20,9 ± 12,3. Staging was as follows: 4 IB, 27 II, 35 IIIA, 17 IIIB y 9 IV. There were 12 complications after surgery. Mosty all patients received chemotherapy. A CT scan was made to all patients, so as to delineate the planning target volume, and was delivered using

high energy photons being the total dose administered 45 Gy with a dose per fraction of 1,8 Gy/d. Organs at risk (liver, spinal cord and both kidneys), were delineated too.
Dose volume histograms were performed to PTV and organs at risk.
Results: Toxicity was recorded following the RTOG criteria. Acute toxicity was mild in most cases. There were 8 patients with neutropenia and in 4 patients was necesary to stop treatment. Cronic toxicity appeared in 20 patients. We excluded 10 patients for the analysis because of positive residual disease. With a mean follow up of 2,2± 1,2 years, overall survival and specific survival at 3 years were 67,8 ± 13 % and 69,9± 13% respectively. The local and distance disease free survival at 3 years was:86,5± 9,1% and 71,4± 11,6% and the disease free survival at 3 years was: 87,4± 9,7%.
Conclusions: In our serie of patients, the treatment, was well tolerated in terms of acute and late toxicity. A good nutritional suport is basic for patients.Our results show a benefit in survival and local control adding chemoradiation after surgery.

1305 poster

RADIOCHEMOTHERAPY FOLLOWED BY GEMCITABINE AND CAPECITABINE IN EXTRAHEPATIC BILE DUCT CANCER (EBDC): A PHASE I/II-TRIAL

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Purpose/Objectif: The prognosis for patients with not curative resectable EBDC is very poor with a median survival of 13 - 21 months. Phase II trials demonstrated that advanced EBDC respond to both chemotherapy with gemcitabine and capecitabine and to radiotherapy. Our objective was to define a feasible and effective postoperative simultaneous therapy in patients with EBDC.
Materials/Methods: Patients were eligible after surgery for EBDC. Surgery included resection of lymph node positive cancer (5 patients), incomplete resections (2 patients) and diagnostic laparotomy in unresectable tumors (11 patients). Patients received a fractionated 3D-conformal radiotherapy of the tumorregion and the locoregional lymphnodes with a single dose of 1.6 Gy, 6x per week, to a dose of 40 Gy. Afterwards the primary site received a local boost to a cumulative dose of 49.6 Gy (sinlge dose 1,6 Gy). Silmutaneously the radiation was accompanied by gemcitabine 100 mg/m^2 weekly x 5. After a two week rest patients were treated with gemcitabine (1000 mg/m^2 IV D1+8 q3w) and capecitabine (1500 mg/m^2 PO D1-14 q3w) on a 3-week cycle. Treatment continued for 6 cycles in nonmeasurable disease or until disease progression or intolerable toxicity. Primary endpoint was toxicity; secondary endpoints were response rate in measurable disease and overall survival.
Results:18 Patients (resectable/unresectable disease 7/11) were enrolled. Radiotherapy was completed in all patients and a total of 66 cycles of chemotherapy were applied. The observed toxicity was generally relatively mild. Whereas the severe adverse events (grade 3 and 4) especially cholangitis (4 patients) and cachexia (4 patients) were mostly shown by patients with unresectable tumors. Other grade 3 and 4 toxicity were fatigue, nausea, duodenal ulcer in 1, 2, 2 patients, respectively. Median overall survival was 7.9 months in patients with unresectable tumors. Median overall survival in patients after resection has not been reached after a median follow-up of 19.5 months.
Conclusions: Radiochemotherapy with gemcitabine followed by gemcitabine and capecitabine is an active regimen with manageable toxicity after resection of EBDC but has significant toxicity in unresectable disease.

1306 poster

ROLE OF ADJUVANT CHEMORADIOTHERAPY FOR DUODENAL CARCINOMA

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Purpose/Objectif: Although the prognosis of duodenal cancer is reported to be better than those of other periampullary malignancies, loco-regional failure still account for more than half of cause of failure and the role of adjuvant treatment including radiotherapy and chemotherapy has not been clarified as in other periampullary malignancies. Its rarity, however, precludes prospective clinical trials for the confirmation of the role of adjuvant treatment. The purpose of this study was to evaluate the role and feasibility of adjuvant chemoradiotherapy for duodenal carcinoma after curative resection.
Materials/Methods: Between January 1991 and December 2002, twenty four patients with duodenal cancer underwent curative resection at Seoul National University Hospital . There were fourteen males and ten females, and median age was 60 years (range; 33-75). Ten patients underwent Whipple's operation, while fourteen had pylorus-preserving pancreaticoduodenectomy. Nine patients received postoperative chemoradiotherapy (RT (+) group), and fifteen did not (RT (-) group). Postoperative radiotherapy was delivered to tumor bed and regional lymph nodes up to 40Gy at 2Gy per fraction with a two-week planned rest. Intravenous 5-fluorouracil (500mg/m^2/day) was given on day 1 to 3 of each split course. The median follow-up period was 32 months (range; 5-170).
Result: Age, sex, type of operation, T stage, tumor size, number of examined lymph node, and degree of histologic differentiation were similar in each group. N stage and stage group, however, were significantly advanced in RT (+) group ($p = 0.0894$ and 0.0361, respectively). According to the treatment modality, 5-year overall survival rates of RT (-) and RT (+) group were 46.7% and 29.6%, respectively ($p = 0.3799$). Five-year loco-regional relapse-free survival rates of RT (-) and RT (+) group were 64.2% and 80.0%, respectively ($p = 0.4188$). No patient suffered grade 3 or higher toxicity during postoperative chemoradiotherapy. Multivariate analysis revealed nodal involvement to be of marginal significance for over-all survival ($p = 0.072$) and radiotherapy for loco-regional relapse-free survival ($p= 0.075$). Furthermore, distant metastases accounted for four out of five documented failures for RT (+) group, whereas loco-regional failure accounted for four out of seven documented failures for RT (-) group.
Conclusions: Postoperative adjuvant chemoradiotherapy is feasible and may enhance loco-regional control in advanced-staged duodenal cancer after curative resection.

1307 poster

SHOULD ALL PATIENTS WITH AMPULLARY CANCER RECEIVE ADJUVANT THERAPY?

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Purpose/Objectif: The role of adjuvant chemoradiation therapy in

the treatment of cancers of the ampulla of Vater remains controversial. Retrospective series have identified potential adverse prognostic factors that could direct the choice of adjuvant treatment. This study retrospectively compares treatment outcomes in patients treated with pancreaticoduodenectomy alone versus those who received additional adjuvant chemoradiation therapy.

Materials/Methods: Between May 1990 and January 2006, 96 patients with ampullary adenocarcinoma were treated with curative intent with pancreaticoduodenectomy. Fifty-four of these patients also received adjuvant chemoradiation therapy. Twenty-nine patients received preoperative chemoradiation therapy and 25 received postoperative chemoradiation therapy. Median preoperative radiation dose was 45 Gy (range 30-50.4 Gy) and median postoperative dose was 50.4 Gy (range 45-55.8 Gy). Concurrent chemotherapy included 5-flurouracil (52%) and capecitabine (43%) primarily. No maintenance chemotherapy was administered. Median follow-up was 30 months (range 1-150 months). Actuarial survival was determined from start of first treatment. Univariate and multivariate statistical methodologies were used to determine significant prognostic factors for local control (LC), distant control (DC) and overall survival (OS). Patients were stratified into historical low- and high-risk groups based on pancreatic invasion, tumor grade, margin status, and nodal involvement. The effect of adjuvant therapy was also evaluated based on identified prognostic factors.

Results: Actuarial 5-year LC, DC, and OS were 76%, 68%, and 63% respectively. On univariate analysis, age, gender, race, tumor grade, use of adjuvant treatment, historical risk grouping, and sequencing of adjuvant therapy (preoperative vs. postoperative) were not significantly associated with LC, DC or OS. However, on univariate analysis, T3/T4 tumor stage was prognostic for poorer LC and OS (p=0.023 and 0.001 respectively) but not DC (p=0.15); node-positive disease was prognostic for poorer LC (p=0.021) but not DC and OS (p=0.084 and 0.25 respectively). On multivariate analysis, T3/T4 tumor stage was independently prognostic for decreased OS (p=0.002). Among patients with T3/T4 tumor stage (n=34), those who received adjuvant therapy had a trend towards improved overall survival (p=0.063). Median survival was 17 months without adjuvant therapy and 36 months with adjuvant therapy in patients with T3/T4 tumors.

Conclusions: Ampullary cancers have a distinctly better treatment outcome than pancreatic head adenocarcinomas. Higher primary tumor stage (T3/T4) is an independent adverse risk factor for poorer treatment outcomes in patients with ampullary cancer. The addition of adjuvant chemoradiation therapy to pancreatico-duodenectomy demonstrated a trend towards improved OS in patients with T3/T4 tumors. Our data suggest a role for selective treatment of higher-risk patients with adjuvant chemoradiation therapy.

1308 poster

THE ROLE OF POSTOPERATIVE ADJUVANT RADIOTHERAPY IN RESECTED STAGE II AND III ESOPHAGEAL CANCER

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Purpose/Objectif: A retrospective study was performed to evaluate that postoperative adjuvant radiotherapy(PORT) can improve survival and decrease the recurrence as compared with surgery alone(S) group in resected stage II and III esophageal cancer with squamous histology.

Materials/Methods: From Mar. 1996 to Dec. 2003, among 97 patients of resected stage II and III esophageal cancer with squamous histology, thirty-eight patients were received PORT. The postoperative adjuvant radiotherapy was performed 4 weeks after surgery and a total dose of 36-60Gy in 1.8 Gy daily fraction, median 45 Gy over 5 weeks, was delivered in primary tumor bed, the mediastinal + both supraclavicular lymph nodes or celiac lymph nodes according to the tumor location and anastomotic site. Postoperative adjuvant chemotherapy was administered to 12 patients for S group and 9 for PORT group. The median follow-up period was 21 months(1-111 months). Postoperative risk factors and tumor characteristics were similar between two groups.

Results: 5-year overall and disease-free survival(DFS) were 21.7%, 20.1% for S group and 31.1%, 28.7% for PORT group (p>0.05). 5 year DFS of stage IIA, IIB and III were 29.8%, 16.7%, 18.8% for S group and 33.0%, 50%, 25.7% for PORT group (p>0.05). 5-year loco-regional recurrence free survival rates was 33.4% for S group and 69% for PORT group (p=0.013). There was no radiation-induced gastritis more than grade II.

Conclusions: There is no statistical significant difference in either the overall survival or DFS between S group and PORT group for resected stage II and III esophageal cancer with squamous histology. PORT has reduced loco-regional recurrence significantly without significant RT-induced complication.

1309 poster

TOLERANCE AND EFFICACY OF HIGH-DOSE 3D-CONFORMAL RADIATION THERAPY (CRT) IN CIRRHOTIC PATIENTS WITH SMALL HEPATOCELLULAR CARCINOMAS (HCC) NOT SUITABLE FOR CURATIVE THERAPIES

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Purpose/Objectif: Some patients presenting with small hepatocellular carcinoma (HCC) benefit from curative therapies (liver transplantation, surgical resection or percutaneous destruction) while others are only candidates for palliative options. Although conventional external beam radiation therapy of the liver is regarded as little efficient and potentially toxic in cirrhotic patients, 3D conformal radiotherapy (CRT) demonstrated promising results in previous studies.

Materials/Methods: Prospective phase 2 trial was conducted in 26 patients with small HCC (1 nodule below 5cm, or 2 nodules below 3cm) not suitable for curative therapies, Child Pugh A (15) or B (8), mean age 70 years, TNM stage I or II, mean tumor size 3.2 cm. Primary endpoint was the rate of complete tumor response assessed by contrast enhanced spiral tomodensitometry showing complete disappearance of the arterial blush on 2 successive examinations at 3 mo interval. Secondary endpoint was assessment of toxicity (NCI and RTOG EORTC Soma Lent toxicities). 66 Gy (2 Gy per fraction, beam energy above 10 MV) were delivered with CRT, with or without respiratory gating. Liver dose volume histograms and normal tissue complication probability values were used to evaluate tolerance of 66 Gy.

Results: 18 over 23 (78%)currently evaluable patients achieved a complete tumor response, and 5 absence of response (stability of size but residual hypervascularisation). With a median follow up of 17 months, 2 patients relapsed on the irradiated tumor bed at 12 and 30 months respectively. No grade 4 toxicity was observed in 16 Child Pugh A patients. Grade 3 asymptomatic biochemical toxicity was observed in 2 patients. Grade 4 biochemical toxicity was observed in 2 over 9 patients Child Pugh B (thrombocytopenia, hyperbilirubinemia). Biochemical toxicity grade 3 was observed in 4 patients. One patient developed a grade 3 clinical toxicity (portal hypertensive bleeding) requiring blood transfusion. One patient developed a jaundice with edema and ascitis at 1 mo, which spontaneously resolved.

Conclusions: This study has shown for the first time in Europe that High Dose 3D Conformal Radiation Therapy can induce a complete tumor response of most of small HCC, with a low rate of local relapse and a good tolerance especially in Child-Pugh A cirrhotic patients. The future study will compare percutaneous destruction to 3D CRT

using an accelerated fractionation, in patients presenting with small HCC.

1310 poster

GEMCITABINE-BASED CHEMORADIATION FOR INOPERABLE PANCRATIC CANCER: A PHASE II STUDY

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Purpose/Objectif : Aim of this study was to evaluate the effect of chemoradiation with an alternative schedule of gemcitabine in a subset of inoperable patients (pts).

Materials/Methods: Eligibility criteria included: histologically proven pancreatic carcinoma, cT3N1 and cT4N0-1, no distant metastasis, no major comorbidities, age 18-75 years, ECOG performance status (PS) < 2, written informed consent. Treatment consisted of 3D conformal radiotherapy (PTV2: T + regional nodes + 1-1,5 cm: 39.6 Gy; PTV1: T + 1-1.5 cm: 50.4 Gy, 1.8 Gy/fr) plus concurrent chemotherapy with weekly gemcitabine, 100 mg/m^2, 24-hours i.v. infusion, week 1-5. A dose-reduction scheme was applied for concurrent chemotherapy based on observed toxicity: grade 1: 80%, grade 2: 60%, grade > 2: no chemotherapy. After chemoradiation, compliant pts with an ECOG PS <3 were administered further 5 cycles of gemcitabine (1000 mg/m^2, days 1-8, every 21 days). Toxicity was evaluated according to the RTOG/EORTC score systems. Clinical response was evaluated by the WHO criteria. Survival analysis was calculated from the time of diagnosis with Kaplan-Meier method.

Results: Forty-three pts (M/F 24/19; median age 62 years, range 36-76) with T3 (n=7;16.2%) or T4 (n=36; 83.8%) pancreatic cancer were enrolled into the study. Seventeen pts (39.5%) presented node positivity at the staging work-up. Twenty-nine pts (67.4 %) completed radiotherapy without any interruption. Only one patient had definitive interruption of radiotherapy. The mean dose of administered gemcitabine was 76% (range 32-100%) of the prescribed dose. Grade-3-4 hematological toxicity was observed in 15 pts (34.8%); 10 pts presented G3 gastrointestinal or hepatic toxicity (23.2%). Thirty pts (69.7%) received further gemcitabine-based chemotherapy after chemoradiation. Late gastrointestinal toxicity was observed in 3 pts, represented by duodenal stenosis/perforation.

Clinical evaluation of the response was performed 6 weeks after the end of treatment. A complete clinical remission (CR) was observed in 5 pts (11.6%), who achieved radical surgery (pathological CR in 2 cases); a clinical partial remission (PR) was recordered in 8 pts (18.6%), whereas 20 pts (46.6%) obtained a clinical stabilization of the disease (NC). Ten pts (23.2) experienced a progression of the disease (PD) when on treatment.

With a median follow-up of 43 months (range 4-71), 3-year local control was 58%, median not reached; 3-year progression-free survival was 33% (median 11 months). Three-year overall survival was 23%, (median 16 months).

Conclusions : Concurrent chemoradiation with weekly gemcitabine seems well tolerated, and showed favourable results in terms of local control and survival. The overall clinical benefit (CR+PR+NC=76.8%), associated with a clinical remission of symptoms, documented by a reduction or withdrawal of analgesic drugs observed in 21 pts (48.8%), proved that this combined treatment can be considered as a valid therapeutic option for these pts, whose prognosis remains severe.

Posters Urological Tumours

1311 poster

BLADDER EXTENSION VARIABILITY DURING PELVIC EXTERNAL BEAM RADIOTHERAPY WITH A FULL OR EMPTY BLADDER

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Purpose/Objectif: The bladder is an organ with varying fillings during a fractionated pelvic radiotherapy, leading to a changing dose-volume load to the bladder and neighbouring structures (like small bowel, sigma, rectum, prostate) compared to the primary treatment plan. The aim of the study was to define the extent of bladder wall movements during a series with a full bladder (FB) and a second series with an empty bladder (EB).

Materials/Methods: A total number of 340 serial treatment planning CT scans (supine patient position, slice thickness of 5mm) were performed in 50 prostate cancer patients (30 primary and 20 postoperative). Each patient underwent a CT scan with FB and EB before the start of treatment and 2-3 times during radiotherapy. The data was transferred to a commercially available stereotactic planning system (Brainlab®, Heimstetten, Germany). The scans were matched by alignment of the pelvic bones. Displacements of the bladder wall were compared at the anterior, posterior, superior, inferior and lateral borders and a correlation with changing bladder fillings was calculated.

Results: The mean bladder volumes of FB and EB for the pretreatment (225cc and 82cc) and consecutive CT scans (217cc and 79cc) did not change considerably, but the variability of the FB volume was larger compared to the EB volume (standard deviation for the difference of 124cc and 56cc; p<0.01). Significant difference of bladder wall displacement variabilities were found only at the anterior and superior borders (table). After a complete emptying of a full bladder (mean voiding volume 146cc), a mean bladder wall displacement of 23mm, 12mm, 9mm and 8mm resulted superiorly, anteriorly, posteriorly and laterally.

		full bladde	empty bladder	p-value
sup.displ./ mm	M±SD*	0.1±19.3	0.9±16.3	0.005
	range**	-26.5-23.1	-15.4-13.5	
inf.displ./ mm	M±SD*	-1.0±4.7	-0.8±4.9	1.000
	range**	-6.8-4.1	-7.5-5.2	
left displ./ mm	M±SD*	-0.3±4.5	1.0±4.5	0.731
	range**	-6.0±5.9	4.8±7.0	
ant.displ./ mm				

Conclusions: Treating the pelvis with EB compared to FB, organ wall displacement can be significantly reduced at the superior and anterior border (influence on small bowel and sigma position). No difference results at the remaining borders, regarding for instance the rectum or prostate position.

1312 poster

CLINICAL RESULTS OF A CONCOMITANT BOOST RADIOTHERAPY TECHNIQUE FOR MUSCLE INVASIVE BLADDER CANCER

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Purpose/Objectif: To update the effect of a concomitant boost radiotherapy technique on local control and bladder function in patients with muscle invasive bladder cancer.

Materials/Methods: From 1994 to 2005 a total of 92 patients, not suitable for radical surgery, with T2-4 N0-1 M0 transitional cell carcinoma of the bladder were retrospectively evaluated. Median age was 79 year. This study was an update of the previous published series of Pos et al. (Radiother Oncol 2003) with nearly a doubling of the patient number. All patients were treated with a dose of 40 Gy/2 Gy to the small pelvis with a concomitant boost of 0.75 Gy to the tumor plus a margin of 1,5-2 cm. Total tumor dose was 55 Gy in 4 weeks.

Results: Three months after treatment there was a complete remission at cystoscopy in 78% of patients. The actuarial 3 years local control rate was 56% and the 3 years overall survival 35%. The median survival after a local recurrence was very low (7 months). The mean functional bladder capacity was slightly improved after radiotherapy, with a post-treatment bladder capacity of more then 200 cc in 81% (n= 63). The late toxicity rate (> grade 3) was only 8,6%. Tumor size, grade, T-stage, haemoglobin and hydronefrosis were not statistically significant for local control at univariate analysis.

Conclusions: The actuarial local control rate after external beam radiotherapy with a concomitant boost for muscle invasive bladder cancer was 56% at 3 years. Functional bladder outcome was good. Radiotherapy with a concomitant boost technique is a good alternative for radical cystectomy in patients not willing or unable to undergo surgery.

1313 poster

IMPACT OF CONCURRENT CHEMOTHERAPY ON OUTCOME OF PATIENTS WITH INVASIVE BLADDER CANCER TREATED WITH AN ORGAN PRESERVING MULTIMODAL APPROACH:THE ERLANGEN EXPERIENCE.

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Purpose/Objectif: To evaluate the impact of concurrent chemotherapy on the long-term outcome of patients with invasive bladder cancer treated with a combined modality approach and selective bladder preservation. Moreover late toxicity and quality of life due to bladder function were assessed with a short questionnaire.

Materials/Methods: Between 1982 and 2005, 525 patients with bladder cancer (high-risk T1, n =142; T2 to T4, n = 383) were treated with radiotherapy alone (RT; n = 156) or radiochemotherapy (RCT; n = 368) after transurethral resection of the tumour (TURBT). Since October 1985, chemotherapy was applied in the first and fifth week of RT and consisted of cisplatin (25mg/m^2/d) in 153 patients or carboplatin (65mg/m^2/d)) in 106 patients with decreased creatinine clearance (<60 ml/min) or congestive heart disease. Since 1993 a total of 110 patients received a combination of cisplatin (20mg/m^2/d) and 5-flourouracil (600 mg/m^2/d) with the same time schedule. Six weeks after RT/RCT, response was evaluated by restaging-TURBT. In case of complete response (CR), patients were observed at regular intervals. In case of persistent or recurrent invasive tumor, salvage-cystectomy was recommended. Median follow-up was 42 months (range: 2 to 260 months).

Results: CR was achieved in 71% of all patients (RT = 57%; RCT = 76%). Freedom from muscle invasive recurrence after CR for all patients was 70% at 10 years (RT = 69%; RCT = 71%). Ten-year disease-specific survival after CR was 60% for all patients (RT = 52%; RCT = 63%) while overall survival after CR was 39% (RT = 25%; RCT = 45%). About 90% of survivors preserved their bladder. Early tumor stage and a complete TURBT were the most important factors predicting CR and survival. Salvage cystectomy for local failure was associated with a 45% disease-specific survival rate at 10 years. Cystectomy because of a contracted bladder was restricted to 2% of patients, all of them have had multiple transurethral resections. For bladder function 152 patients completed the questionnaire. 72% stated an excellent or good result for bladder sparing treatment. Only 2% declared a dissatisfying or very dissatisfying outcome.

Conclusions: The addition of cisplatin based chemotherapy to RT was more effective than RT alone in terms of CR and survival. TURBT with RCT is a reasonable option for patients with invasive bladder cancer and an alternative to radical cystectomy. Ideal candidates are those with early-stage and unifocal tumors, in whom a complete TUR-BT is accomplished.

1314 poster

LOW DOSE PARA-AORTIC AND PELVIC IRRADIATION FOR STAGE I TESTICULAR SEMINOMA.

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Purpose/Objectif: Over the past decade irradiation only to the paraaortic region has been proposed, by some groups, for the treatment of stage I seminoma. The best treatment dose is still undefined. The purpose of the present study is to determine the treatment results and morbidity with low dose paraaortic and hemipelvis irradiation for stage I seminoma

Materials/Methods: 155 patients with stage I seminoma were seen at our institution between January 1997 and December 2005. Patients were treated to the paraaortic region with AP/PA fields high-energy 18-20 MV photons and to the hemipelvis with an AP field only, with 6MV photons, dose specified between 6 - 8 cm, depending on depth of the lymph node chains. The total dose was 2505 cGy in 15 fractions. 3D simulation or pyelogram was used in all patients for kidney localization. The median age for patients was 35 years (17-70) and the median follow up was 2 years. Three patients presented with bilateral seminoma and were treated to the whole pelvis. Morbidity was scored according to the Common Toxicity Criteria for Adverse Events CTCAE v.3.0 scale.

Results: All patients are alive without disease. There are no failures in the irradiated area, para-aortic or pelvis. Only one patient developed distant failure in the right lateral supraclavicular region with bone invasion. The patient was rescued with chemotherapy and local radiotherapy. Acute toxicity was nausea G1 and G2. No long term toxicity or second malignancy has been reported

Conclusions: 25 Gy in 15 fractions resulted in 100% locoregional control, with moderate acute toxicity, nausea, and no long-term toxicity. Hemipelvis irradiation avoids the risk of pelvic failure and does not seem to increase toxicity. Further follow up is necessary to confirm the present results.

1315 poster

OPTIMISING RADIOTHERAPY FOR SEMINOMA USING FIELDS BASED ON SURGICAL TEMPLATES FOR RETROPERITONEAL LYMPH NODE DISSECTION

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Purpose/Objectif: Radiotherapy to the para-aortic and ipsilateral pelvic lymph nodes is an established and effective therapeutic option in the adjuvant management of stage 1 seminoma. The associated toxicity of this treatment is both dose and volume dependent. Radiotherapy is currently delivered using standard para-aortic strip relative to bony landmarks (T10/11-L5/S1) and trials have shown the effectiveness of a short strip (T11/12-L4/5). These are larger than the surgical templates for retroperitoneal lymph node dissection (RPLND) used in nonseminomatous germ cell tumours.AIM: Assess the dosimetric consequences of planning radiotherapy according to surgical templates used for RPLND compared to standard and short para-aortic fields.

Materials/Methods: The RPLND template is bounded by the aorta medially, ureter laterally, renal artery superiorly and common iliac artery inferiorly. Allowing for adequate margins and uncertainty in the location of the ureter on planning CT, we tested an equivalent radiotherapy template: 1cm superior to renal artery (sup); 0.5cm contralateral to aorta/common iliac artery (med); 0.5cm lateral to renal hilum (lat); 1cm inferior to common iliac bifurcation (inf). Radiotherapy plans for five patients treated with standard para-aortic strip adjuvant therapy (20Gy/10F) were compared to: short strip, right-sided template and left-sided template. Parameters examined were: integral dose to all tissue, liver and stomach (mean dose), both kidneys (V15). Matched pairs t-tests were used to compare parameters.

Result: Using templates reduced integral dose by 5Gy-cm^3 (left template) and 4.3 Gy-cm^3 (right) compared to a standard strip. This was significant for both templates compared to standard and shortened strips ($p<0.005$). Significant reductions ($p<0.05$) were seen in liver and stomach dose using a short strip compared to a standard strip. Templates significantly reduced stomach dose compared to both standard and short strips, and reduced liver dose compared to the standard strip. There was no significant difference in the V15 to both kidneys.

Conclusions: Using the surgical templates for RPLND to define radiotherapy fields can significantly reduce dose to normal tissue. Although reductions are modest to individual organs, reduction in integral dose may be important in the context of reducing the risk of secondary malignancy. This study provides the rationale for the development of future trials.

1316 poster

PALLIATIVE RADIOTHERAPY FOR BLADDER CANCER: THE LEEDS TEACHING HOSPITALS EXPERIENCE

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Purpose/Objectif: Three-dimensional virtual simulation for radiotherapy planning has the potential to enhance accuracy of target localisation. This is especially important when the clinical target volume includes organs which are mobile or of a varying shape such as the bladder. As our radiotherapy centre has moved from standard (two dimensional) simulation to three dimensional virtual simulation planning for palliative radiotherapy we report a retrospective audit of a single institution's experience of delivering palliative radiotherapy for carcinoma of the bladder.

Materials/Methods: A retrospective audit was carried out of 43 patients who received palliative radiotherapy for carcinoma of the bladder during a three-year period. Nine patients were node positive, nine patients had T4 disease, 12 patients had a performance status of 3. All patients were treated using anterior-posterior parallel-opposed fields with a mid-plane dose of 20 Gy in 5 fractions delivered to the majority (n=36) and an 8 Gy single fraction delivered to the remainder (n=7). Sixteen patients had their radiotherapy planned using a standard two-dimensional simulator based on bony landmarks, with fields extending from just below the sacroiliac joints to the obturator fossa and laterally to the pelvic side walls. Twenty-seven patients were planned using three-dimensional virtual simulation (GE Advantage Sim v.4.0) with fields encompassing the bladder with a margin of 1.5-2 cm. All patients were followed-up in the outpatients department or until we received notification of their death.

Results: The median age was 85 years (range 70-92). Median overall survival was 6 months for male patients and 13 months for male patients. The 12 month overall survival rate was 31% (53% in females; 12% in males). Seven patients were re-irradiated with a dose of 17.5-20Gy in five fractions, and this was generally well tolerated. Use of virtual simulation did not alter survival but did demonstrate a trend towards decreased treatment volumes for female patients and increased treatment volumes for male patients.

Conclusions: Three dimensional virtual simulation is an effective radiotherapy planning technique for palliative radiotherapy for carcinoma of the bladder. A small cohort of patients have long-term palliation from this treatment.

1317 poster

THE IMPACT OF DRINKING INSTRUCTIONS AND BLADDER OUTFLOW MEASUREMENTS ON BLADDER VOLUMES DURING RADIOTHERAPY FOR BLADDER CANCER

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Purpose/Objectif: Background and Purpose: Organ motion is a major challenge in conformal radiotherapy of bladder cancer. In this study we have investigated the impact of drinking instructions (i.e. fluid intake restrictions) and pre-treatment bladder outflow measurements on bladder volume variation during a course of radiotherapy for bladder cancer.

Materials/Methods: Twice weekly CT scans were acquired from 7 patients during radical, conformal bladder irradiation (52.5 Gy/20 fractions/4 weeks). Pre-treatment uro-dynamic testing was performed on 6 patients, 4 male and 2 female. All patients were asked (on alternating weeks) to either drink normally or to not drink the last 3 hours prior to the treatment session. The bladder volume (i.e. the volume inside the outer bladder wall from dome to apex) was outlined in all repeat scans by the same observer. The bladder volumes were calculated, and comparisons were performed both between the weeks with vs those without drinking instructions and between patients with low vs. high bladder outflow scores.

Results: A total of 63 CT scans were available for analysis (7 planning scans, 56 during treatment). For the weeks that patients drank normally the median bladder volume was 105cm^3 and the median variation in bladder volume was 48cm^3. For the weeks when patients had limited fluid intake the median bladder volume was 92cm^3 and the median variation was 23cm^3. Urodynamics in the 2 women were not helpful as the volumes voided were unsatisfactory. Urodynamics were performed in 4 men. Three had good function and 1 had poor function. When these patients were compared, those with good function had a median variation in bladder volume of 49cm^3

when drinking normally and a median variation of 35cm^3 when fluid restricted. The patient with poor urodynamics however had a median variation of 93cm^3 when drinking normally and a median variation of 41cm^3 when fluid restricted.

	Normal fluid intake	Restricted fluid intake
	Median bladder volume and variation cm 3	Median bladder volume and variation cm 3
All patients n= 7	105 +/- 48	92 +/- 23
Good urodynamics n=3	158 +/- 49	99 +/- 35
Poor urodynamics n=1	305 +/- 93	334 +/- 41

Conclusions: This study shows that in patients undergoing conformal radiotherapy for bladder cancer fluid restriction does lower the overall volume and variation of volume of the bladder, and this reduction in variation is particularly marked in a patient with poor urinary function. This generates the hypothesis that fluid restriction and the use of alpha receptor antagonists to relieve outflow obstruction in men may allow smaller treatment volumes and hence reduce irradiation to normal pelvic tissue in this setting.

714 bis poster

SALVAGE SECOND CONSERVATIVE TREATMENT FOR LOCALLY RECURRENT EARLY BREAST CANCER: FOURTEEN-YEAR RESULTS OF A NON-RANDOMIZED COMPARISON WITH MASTECTOMY

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Purpose/Objectif: To report the long term results obtained in a prospective group of patients treated for local recurrence after conservative treatment of breast cancer treated by a second conservative surgery and brachytherapy or by total mastectomy.

Materials/Methods: Between 12/1990 and 04/2003, 81 patients with small size, low-risk local recurrence after conservative treatment for breast cancer were offered total mastectomy as salvage treatment. 44 of them refused mastectomy and were treated by a second lumpectomy followed by HDR brachytherapy implant to the tumor bed plus a 3 cm safety margin. Brachytherapy was given between 1 and 3 weeks after excision. Implants were done at the time of surgery in 38 cases and in the remaining 6 patients at the time of beginning treatment. The average number of implanted tubes was 8 (range 4-16) and the average volume of the reference isodose curve was 56 cc. HDR brachytherapy doses were 30 Gy in 12 fractions in 5 days. Patients treated by mastectomy had no further radiotherapy treatment.

Patients with positive oestrogen receptors were treated with tamoxifen for 2-5 years, premenopausal patients with negative receptors had chemotherapy and postmenopausal patients with negative receptors had no systemic treatment. No patient was lost for follow-up. Special attention to local, regional or distant recurrence, survival, fibrosis, late effects and cosmesis was done during the follow-up period.

Results

All patients completed treatment. During the 14-year, 1-year minimum follow-up, in the 2nd conservative group there were 8 patients who had regional (2 cases) or distant metastases (6 cases) as their first site of failure. Three of them experienced a differed local recurrence and 1 of them died from the disease. In the total mastectomy group, there were 2 local recurrences, 1 regional recurrence and 5 distant metastases as first site of failure. One patient died from the disease. Actuarial results at 14-year for 2nd conservative and total mastectomy were respectively: local control 84.2% and 71.7%; disease free survival 65.4% and 63.8%; and survival 90.7% and 88.2%. Cosmetic results were satisfactory in 89.4 % treated conservatively. No patient experienced arm edema or grade 3-4 early or late complications. Between the 14 patients that were followed-up for at least 10-years, 13 of them were with their breast still in place.

Conclusions: Second conservative treatment by HDR brachytherapy was a safe and effective method of treatment for small-size, low-risk, local recurrence after local excision in conservatively treated patients. The dose of 30 Gy given in 12 fractions along 5 days at 2.5 Gy/fraction, 2-3 times every day was safe in patients previously treated. The good results achieved justifies the initiation of randomized trials exploring its use as standard treatment in selected patients with low-risk recurrent breast tumors.