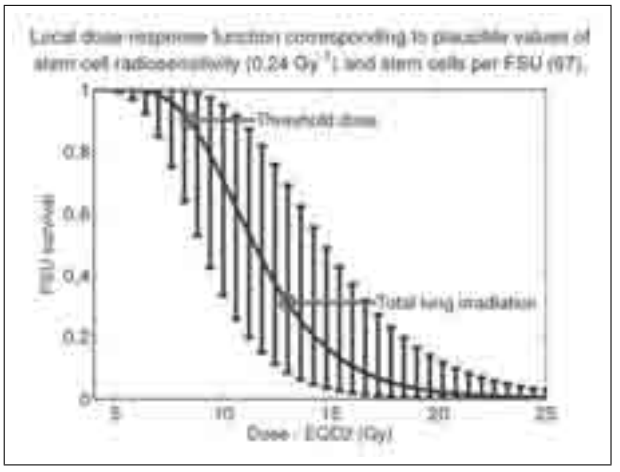
regions and influences the volume effect.



Conclusions: A mechanistic model of normal-tissue damage is an effective framework for summarising the radiobiological knowledgebase of radiation pneumonitis, and plausible parameter values have been derived. Future predictive mechanistic modelling would require more quantitative histopathological studies on relevant local dose effects, thereby providing stronger evidence for the local dose-response relationship. This would provide a stepping stone from which the mechanisms of organ function loss, as a result of 3D distributions of FSU inactivation, could be studied separately.

181 oral

ESTIMATED LIFE YEARS LOST DUE TO FATAL LATE COMPLICATIONS AFTER PHOTON OR PROTON RADIOTHERAPY

P. Brodin[1], I. R. Vogelius[2], M. Maraldo[2], M. Aznar[2], A. K. Berthelsen[3], T. Björk-Eriksson[4], P. Munck af Rosenschöld[2], P. Nilsson[5], L. Specht[26], S. Bentzen[72]

[1] COPENHAGEN UNIVERSITY AND COPENHAGEN UNIVERSITY HOSPITAL, Department of Radiation Oncology, Copenhagen, Denmark
[2] THE FINSEN CENTER - RIGSHOSPITALET, Department of Radiation Oncology, Copenhagen, Denmark
[3] THE FINSEN CENTER - RIGSHOSPITALET, Department of radiation oncology and the department of nuclear medicine, Copenhagen, Denmark
[4] SKÅNE UNIVERSITY HOSPITAL, Department of Radiation Oncology, Lund, Sweden
[5] SKÅNE UNIVERSITY HOSPITAL, Department of Radiation Physics, Lund, Sweden
[6] COPENHAGEN UNIVERSITY, Faculty of Health Sciences, Copenhagen, Denmark
[7] UNIV. OF WISCONSIN SCHOOL OF MEDICINE AND PUBLIC H, Department of Radiation Oncology, Madison WI, USA

Purpose: To estimate and compare the shortening of life expectancy (LE) due to radiation-induced secondary cancers (SC) and cardiac events after photon or proton radiotherapy (RT). Estimating the Life Years Lost (LYL) for competing causes of treatment-related mortality allows direct long-term risk comparison between alternative radiotherapy plans or modalities.
Materials: The largest clinical data sets available are used to extract dose-response (DR) parameters for the excess relative risk (ERR) for each endpoint. The ERR is combined with the age- and gender-specific incidence in the general population (GP) to estimate the absolute excess risk (AER). The excess mortality rate (EMR) is then estimated by including the prognosis for each endpoint. The remaining LE for a person of a specific age in the GP gives the LYL for a patient dying at that age. Competing risks of death prior to a treatment-related event is taken into account from life tables of childhood cancer survivors. Integrating over all ages gives the LYL attributable to each complication. The LYL measure is sensitive to the associated mortality and age dependency of late complications, weighting early occurring events higher due to more years lost at younger ages. We apply the LYL measure for comparing treatment plans created with 3D conformal RT (3D CRT), arc therapy (RapidArc® (RA)) and spot-scanned intensity-modulated proton therapy (IMPT) for craniospinal irradiation (CSI) of 10 paediatric patients.A paired Monte Carlo method is used to test for difference in LYL between modalities. The main source of uncertainty lies in the DR relationship for the different endpoints. Samples are drawn from a log-transformed normal distribution matching the confidence intervals (CI) of the DR parameters. For each sample, the difference in LYL between pairs of modalities was calculated and the corresponding mean and CI for each patient was extracted from the distribution.
Results: Figure 1 shows the final LYL estimate averaged for all ten patients. The attributable LYL varies among endpoints as a function of treatment technique. The dominating causes of LYL appear to be secondary lung cancer and cardiac events as a result of the poor prognosis after these events. In the paired samples test the total LYL was significantly lower for RA than for 3DCRT, mainly due to substantially lower cardiac dose, and LYL with IMPT was significantly lower than for both photon techniques.

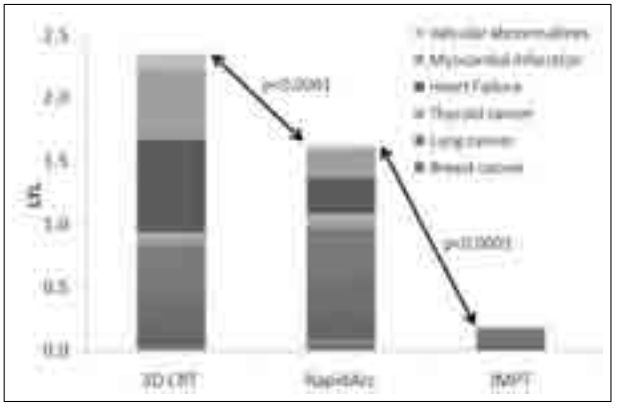


Figure 1. Estimated LYL attributable to various endpoints for the 3D-CRT, RA and IMPT techniques. LYL varies between treatment techniques due to differences in the distribution of non-target dose. The full bars represent the mean total LYL for the ten patients for each of the three techniques. Statistically significant p-values from the paired comparison of LYL between techniques show that these differences are relatively insensitive to uncertainty in DR parameters.
Conclusions: The LYL measure provides a framework for direct comparison of SC risks and risks of other adverse late complications and is readily applicable to other treatment techniques and endpoints provided the necessary model parameters are available. For the ten paediatric patients studied, we found a significant difference in LYL favoring proton over photon radiotherapy. We also found a difference favoring RA over 3DCRT, this ranking will however depend strongly on the relative weight of SC and cardiac events.

182 oral

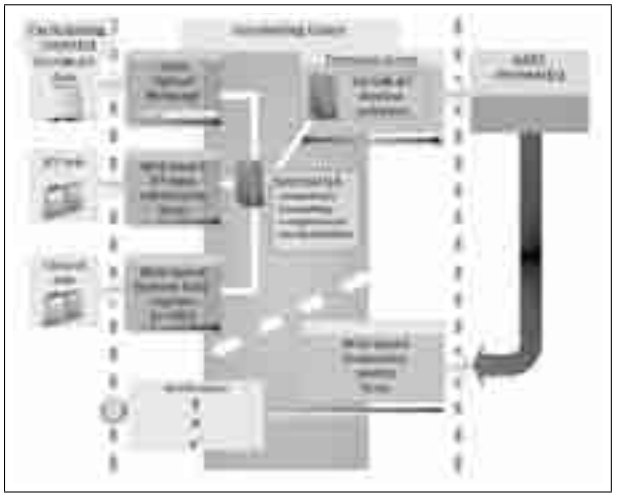
EORTC RADIOTHERAPY QUALITY ASSURANCE PLATFORM: ESTABLISHMENT OF AN INTEGRATED CENTRAL REVIEW FACILITY

A. Gulyban[12], P. Fenton[23], A. Fairchild[2], E. Aird[4], V. Grégoire[5], D. Lacombe[2], O. Matzinger[6], P. Poortmans[7], B. Baumert[8], R. Pascal[2], D. C. Weber[9], C. Hurkmans[10]

[1] UZ-BRUSSEL, Brussel, Belgium
[2] EORTC HEADQUARTERS, Brussels, Belgium
[3] SOUTHAMPTON UNIVERSITY HOSPITAL NHS TRUST, Southampton, United Kingdom
[4] MOUNT VERNON HOSPITAL, Northwood Middlesex, United Kingdom
[5] UCL CLINIQUES UNIV. ST.LUC, Brussels, Belgium
[6] CENTRE HOSPITALIER UNIV. VAUDOIS, Lausanne, Switzerland
[7] DR. BERNARD VERBEETEN INSTITUUT, Tilburg, Netherlands
[8] MAASTRO CLINIC, Maastricht, Netherlands
[9] HÔPITAL CANTONAL UNIV. GENÈVE, Geneva 14, Switzerland
[10] CATHARINA ZIEKENHUIS, Eindhoven, Netherlands

Purpose: Quality assurance (QA) in multi-centre clinical trials is essential to ensure treatment is safely and effectively delivered. As QA requirements have increased in complexity in parallel with evolution of radiotherapy (RT) delivery techniques, a pressing need to facilitate digital data exchange and timely review has emerged. Our objective is to present the platform developed for the integration and standardization of QART activities within our pan-European academic clinical trial organization.
Materials: Based on 30 years of RT clinical trial and QA experience, the central coordinating team and QART strategic committee identified the essential requirements for the platform: secure and easy access to data without on-site hardware installation; integration within the coordinating centre's existing clinical remote data capture system; and the ability to both customize the platform to specific studies and adapt to currently unforeseen future needs. After retrospective testing within several clinical trials, the platform was introduced in phases to participating sites and QART study reviewers.
Results: The resulting QA platform, integrating RT analysis software installed at the coordinating centre, permits timely, secure, and fully digital central DICOM-RT based data review (Figure 1). Participating sites submit requested data through a standard secure upload webpage. Supplemental information is submitted in parallel through web-based forms such as type of treatment planning system and description of the treatment verification protocol. An internal quality check by the coordinating team verifies data consistency, formatting, completeness, and anonymization. Personnel responsible for QART reviews have remote online access to DICOM-RT data through a terminal server, and receive relevant clinical data as well. Reviewers evaluate submissions for protocol compliance through a standardized online evaluation

matrix. Comments are collected by the coordinating centre after which participating institutions are informed of the results.



Conclusions: This integrated, web-based central review platform facilitates the performance of rapid, extensive, and prospective QART patient review within large multinational clinical trials. Timely central review completed in this manner allows reduction of the risk that trial outcomes are compromised through inadequate radiation delivery.

RTT Proffered Papers 2: Head and Neck Cancer Treatment

183 oral

IS THERE A CORRELATION BETWEEN SMOKING AND LATE SIDE EFFECTS FOR HEAD AND NECK CANCER PATIENTS?

D. Wiinholdt[1], C. Pisinger[2], B. Frederiksen[2]
[1] COPENHAGEN UNIVERSITY HOSPITAL, Department of Radiation Oncology, Copenhagen, Denmark
[2] GLOSTRUP HOSPITAL, Research Centre for Prevention and Health, Glostrup, Denmark

Purpose: In 2006, 937 new cases of cancer in larynx, pharynx and cavum oris were registered in Denmark. Because the disease has often spread to the lymph nodes, the patient is normally treated with radiotherapy. The primary causes of these diseases are smoking and alcohol and, thus, most patients are smokers or newly quitters. Every head and neck cancer patient treated with radiotherapy gets side effects. Currently, we do not know whether smoking has an influence on the severity of these side effects, and this question is what we seek an answer to in this thesis.
Materials: 795 patients with head and neck cancer who are registered in the Danish Head and Neck Cancer Group's database and treated with radiotherapy in the period from 2000-2009 at Copenhagen University Hospital (Rigshospitalet), are included in the study. The patients are divided into 3 groups: never smokers, ex-smokers and smokers. In logistic regressions, we have looked at smoking and its effect on the side effects 6 and 12 months after end of treatment, respectively. The 6 types of side effects considered are: voice, fibrosis, dryness, dysphagia, atrophy and edema.
Results: A significant correlation between smoking at baseline and the side effects dysphagia and edema after 12 months have been observed. We also found a significant correlation between the amount of smoking per day and the number of moderate to severe side effects. Also, quitting smoking during treatment results in a significant reduction in the probability for experiencing the side effects voice and edema.
Conclusions: The results are based on, as far as we know, the biggest data material on smoking and late side effects of radiotherapy. We can conclude that smoking cessation before or during treatment will have a positive effect on the severity and amount of side effects.

184 oral

DYSPHAGIA REDUCTION WITH OPTIMIZED PHOTON AND PROTON INTENSITY-MODULATED RADIOTHERAPY FOR HEAD AND NECK CANCER

H. P. van der Laan[1], T. van de Water[1], H. van Herpt[1], M. Christianen[1], H. P. Bijl[1], C. Schilstra[1], H. Langendijk[1]
[1] UNIVERSITY MEDICAL CENTER GRONINGEN / UNIVERSITY OF GRONINGEN, Department of Radiation Oncology, Groningen, Netherlands

Purpose: To compare the probability of dysphagia (swallowing dysfunction) with standard intensity modulated radiotherapy (st-IMRT), swallowing sparing IMRT (sw-IMRT), standard scanned beam intensity-modulated proton therapy (st-IMPT) and swallowing sparing IMPT (sw-IMPT).
Materials: Five patients with oropharyngeal cancer were treated with bilateral irradiation on the primary tumor and the neck and were selected for this planning comparative study. For each patient, st-IMRT, sw-IMRT, st-IMPT and sw-IMPT simultaneous integrated boost treatment plans were created. In 35 similar fractions, a total dose of 70 Gy was delivered to the boost planning target volume (PTV) and 54 Gy was delivered to the elective nodal PTV. The st-IMRT and st-IMPT treatment plan optimization was performed to obtain adequate target volume coverage, limited dose in critical structures such as the spinal cord and sparing of the parotid glands as much as possible. These primary objectives were similar for sw-IMRT and sw-IMPT, except that specific attempts were made to spare the organs at risk related to swallowing dysfunction (SWOARs, Table 1). For all plans, normal tissue complication probabilities of physician-rated and patient-rated dysphagia were calculated with predictive models that were recently developed at our institute.
Results: All plans had adequate target volume coverage and the dose to critical organs was within accepted limits. The mean dose to the parotid glands was similar for st-IMRT and sw-IMRT, and lowest with st-IMPT and sw-IMPT. With sw-IMRT and sw-IMPT, the dose to the various SWOARs was reduced when compared to st-IMRT and st-IMPT, respectively. In general, the lowest dose to the SWOARs was obtained with sw-IMPT. The predicted mean probability of grade 2-4 physician rated dysphagia (RTOG) was 47%, 36%, 45% and 31% with st-IMRT, sw-IMRT, st-IMPT and sw-IMPT, respectively. Patient rated moderate to severe complaints with regard to the swallowing of solid food, soft food, liquid food and aspiration with sw-IMRT and sw-IMPT were similar (Table 1).
Conclusions: The predicted probability of different dysphagia-related endpoints with IMRT and IMPT was reduced by limiting the dose in the SWOARs. The lowest probability of dysphagia was predicted with sw-IMPT.