Poster

Young scientists ESTRO Poster Session: Trial design and data analysis

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DESIGNING A MULTI-CENTER DOSE-PAINTING TRIAL: METHODOLOGY AND PITFALLS

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Purpose: Intensity modulated radiotherapy has reached a status that is sufficient to test dose-painting (DP) in clinical trials, such as for head-and-neck and lung cancer. Both dose-painting by numbers (DPBN) or by dose painting by contours/volumes (DPBC) are hypothesized to individualize the treatment of cancer patients to provide the most optimal treatment. We will discuss the methodology and possible pitfalls for designing DP trials and use our currently ongoing multi-center randomised phase II PET-boost trial as an example.
Materials: Our multi-center DPBC trial for stage II-III non-small cell lung cancer patients (PET-boost trial: NCT 01024829) recently started. We hypothesised that DPBC based on pre-radiotherapy PET imaging improves local control of the primary tumour. The following criteria were taken into account in the design of this DP trial: 1) Forcing iso-toxicity is mandatory to prove that DP is superior compared to homogeneous dose delivery without the bias of more toxicity and/or more integral target dose in the experimental arm; 2) Standardization of the imaging techniques is of utmost importance as well as 3) standardized delineation of organs-at-risk (OAR) and 4) treatment planning techniques and delivery should be comparable in all centers.
Results: We designed a randomized phase II trial on dose-escalation of advanced NSCLC patients to the primary tumour. A two-arm randomized design was chosen. Arm A: homogeneous boost to the entire primary tumour target volume. Arm B: boost to the high FDG-uptake region (SUV max>50%) within the primary tumour without decreasing the minimal PTV dose below our current standard (66 Gy/ 24 fractions). 1) Both arms A and B are normalized, i.e. forced isotoxic for the mean lung dose (MLD) to each other by performing dual arm treatment planning for every patient and forcing a downscaling of the treatment plan with the highest MLD towards equal MLD of the other arm. 2) The FDG-PET imaging is standardized using the NEDPAS protocol (Boellaard et al. 2009) for all PET scanners used in the participating centres. 3) An atlas was created (freely downloadable at http://www.maastro.nl/web/show/id=62542/langid=43[2]) and is used to standardize delineations of the OARs. 4) A feasibility treatment planning study prior to start of the trial was performed to assure that the dose-escalation levels for identical patients were similar.
Conclusions: Designing a dose-painting trial is not trivial. Unbalanced or single arm studies will be biased against the fact that the integral dose in such DP trials is higher, hence leading to improved local control, thus not investigating dose redistribution in the PTV but also dose-escalation. A control arm with approximately equal toxicity and preferably also equal integral dose to the target structures might provide solid evidence that DP has an added value towards treatment outcome.

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INTERNATIONAL IMRT CREDENTIALING BY PHYSICAL PHANTOM IRRADIATION: THE EORTC ROG EXPERIENCE

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Purpose: For credentialing of an international IMRT head and neck cancer trial, three identical anthropomorphic head phantoms were obtained from an external dosimetry laboratory (EDL). The phantom's insert contains eight TLDs marking primary and secondary PTVs and one organ at risk (OAR; Figure 1). GAFchromic dosimetry film is placed through the primary PTV in the axial and sagittal planes and steel needles act as fiducial markers. Our objective was to investigate the timeliness, reproducibility and accuracy of reloading the insert independent of the EDL.
Materials: Four sequential CT simulation scans were performed; between each, the insert was completely disassembled, reassembled (TLD, film), and the scans were co-registered. KV-CT doses were separately extracted from TLD doses based on EDL procedures. Following the final scan, the insert was left intact; volumes were delineated and an IMRT plan created with the following dosimetric objectives: primary and secondary PTVs should receive 6.6Gy and 5.4Gy respectively, and maximum allowed dose to the OAR is 4.5Gy. The phantom was irradiated with this plan three times, with the insert reloaded each time. The fourth and final irradiation was to enable extraction of dose contributed by position verification (MV-CT).
Results: On average, it took 15-20 minutes to reload the dosimetry insert, which moved <2mm between CT acqusitions. The degree of exposure of GAFchromic film was not different from background compared to KV-CT. MV-CT dose based on TLD evaluation was <0.01Gy. For the three irradiations, the average ratio between the actual dose delivered to the primary PTV (measured by TLD exposure at the EDL) and dose prospectively planned was 0.96, 0.96 and 0.95 (acceptable range 0.93-1.07). Values for the secondary PTV were 0.95, 0.96 and 0.95. Film dose maps confirmed concordance (<0.5mm displacement) of the calculated and observed dose gradient in the region between the primary PTV and the OAR for each irradiation.
Conclusions: This confirms both the feasibility and equivalent accuracy of reloading of the dosimetry insert independent of the EDL, permitting parallel phantom irradiation via site visits for IMRT credentialing. To date, this has been completed in 14 institutions (seven each via site visits and direct shipment of phantoms from the EDL to participating institutions).

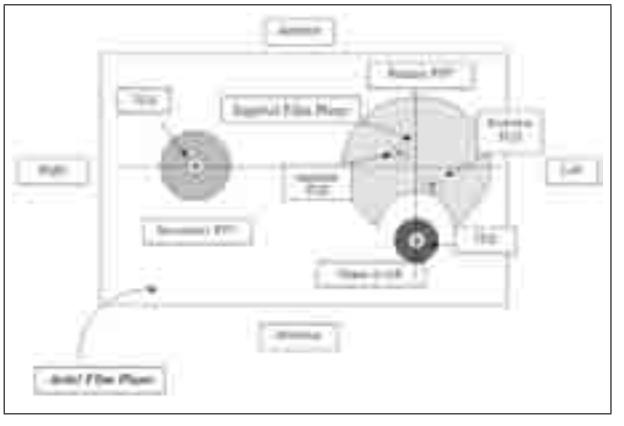

Figure 1. Cross-sectional view of the insert in the axial film plane as found in irradiation instructions of the EDL.

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AD-HOC DATA SHARING INFRASTRUCTURE FOR RADIOTHERAPY RESEARCH COLLABORATION: A TOOL FOR MULTICENTRIC CLINICAL RESEARCH

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Purpose: Extensive multifactorial data sharing is widely recognized as crucial for current and future radiotherapy research, clinical research in general, but the cost, time and effort it takes to share data is often a roadblock. The purpose of this work is to present a quick, ad-hoc data sharing infrastructure between two radiotherapy departments based on free or open source products.
Materials: A collaboration and data transfer agreement was signed which describes the type of data, the permitted use and the protection of the data. This agreement was submitted to and approved by the local ethical authority. On a research workstation (Windows XP 32-bit, Intel Xeon, 2.53GHz, 4GB RAM) the following software was installed: SQL Server 2008 (free Express version, Microsoft, Redmond, WA); Clear Canvas Image Server and Workstation (both free and open source, Clear Canvas, Toronto, Canada); DCMTK DICOM toolkit (free and open source, Offis, Oldenburg, Germany); RSNA Clinical Trial Processor CTP (free and open source, RSNA, Oakbrook, IL) and Matlab Runtime Component (free, Mathworks, Natick, MA). Nightly text and DICOM synchronization with the local clinical databases was implemented. Part of the synchronization mechanism is an extensive de-identification and the translation of local terms to a standardized terminology (SNOMED).

[2] http://www.maastro.nl/web/show/id=62542/langid=43