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Teaching Lectures

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Radiobiological treatment planningA.E. NahumClatterbridge Centre for Oncology, Bebington, Merseyside,
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The time is now ripe to start using models of TCP (Cattaneo *et al* 2001) and NTCP (Ten Haken 2001) and their associated parameters to make *predictions* of complications and to compare these predictions with the observed complication rates. Only in this way will NTCP models be used with confidence in the clinic. For those organs/endpoints for which a reasonable amount of reliable dose-volume-complication data already exists (e.g. radiation pneumonitis in the lung – Seppenwoolde *et al* 2003; proctitis in the rectum – Rancati *et al* 2003), treatment plans can start to be optimized on the basis of the calculated NTCP values. Two of the forms that active use of NTCP models can take are

i) Start with a treatment plan arrived at using, for example, dose-based criteria (e.g. PTV within 95-105% of D_{presc} , $V_{90\%}$ of OAR < 80% of D_{presc}) and then adjust D_{presc} until $NTCP_{OAR}$ is equal to a value specified in the local clinical protocol e.g. $NTCP_{proctitis} = 3\%$ (McGinn *et al* 1998; Sanchez-Nieto *et al* 2001).

ii) Use NTCP and TCP as part of the objective function in the optimization/inverse-planning process, thus allowing the mathematical and radiobiological properties of the models to drive the search for the optimum plan (e.g. Peñagaricano *et al* 2005).

Other variables such as fraction size, clonogen proliferation rate and the patient's performance status should ideally be incorporated into both the biological models and the optimization process (Glatstein 2001; Bentzen 2004; Fowler *et al* 2004). The high rates of uncomplicated local control in early-stage lung cancer achieved with the use of very large fraction sizes is a very interesting example of how dose distributions and fraction size are interrelated (e.g. Fowler *et al* 2004; Nahum and Bentzen 2004). Low-dose hypersensitivity (LDHRS) may also play an important role in our understanding of how certain complications depend on dose and volume. One likely consequence of LDHRS will be an increased contribution to overall NTCP from those normal-tissue volumes at 20% and lower isodoses. A significant increase in such volumes through the use of rotational techniques such as tomotherapy or many-field IMRT could therefore be undesirable for certain organs and endpoints in which the killing of cells exhibiting LDHRS play a significant role in causing the complication. There is also the question of secondary cancer induction (SCI) by radiotherapy. Concerns have been raised (Glatstein 2002; Hall and Wu 2003) that certain modern conformal techniques may increase SCI due to the increase in volumes irradiated at low doses compared to non-IMRT few-field techniques and especially compared to proton beams. Models of secondary cancer induction probability (SCIP) which take into account details of the dose distribution in different organs and also the patient's age and general prognosis are needed.

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Clinical Trial design an evidence based medicineS. Bentzen

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Defining national strategies in RTD. HollywoodAcademic Unit of Clinical and Molecular Oncology, Trinity
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The role and status of radiation oncology services as a component of modern multi-disciplinary oncology care is developed to varying degrees throughout Europe. In the last decade several countries, including the UK, Northern Ireland, and Holland, have completed significant 'national' analyses of existing clinical services and have recommended major investment in radiation oncology services together with the development of new structures of clinical service governance including clinical networks. Options that needed to be considered included academic-community hospital linkage programmes, hospital groupings facilitated by health management organisations and medical insurance schemes, or large private healthcare organisations. In addition the role of centralised or decentralised systems together with linked satellite services is of considerable interest to clinical groups, the general public, patients, and patient advocacy groups. In some cases such networks have been the result of recent 'consolidation' of pre-existing hospitals rather than the forward planning of completely new services. In contrast to the development of 'comparable' networked radiation oncology care schemes in the US, the catalysts for the development of oncology care networks within most European countries is primarily based on the 'clinical goal' of advancing clinical care, rather than the more complex interaction within a 'business model' of advancing clinical care together 'market-driven' elements of financial competitiveness. The development of 'business models' for investment in new radiation oncology services is a significantly new and challenging development in many European countries, for example in the significant service expansion within the UK, which has more recently explored variations of Public-Private Partnership (PPP) models of financial investment.

Against this background, Ireland initiated a formal review of radiation oncology services in 1999 in tandem with the development of a formal phased 'National Cancer Strategy'. The development of Radiation Oncology services became the most controversial element of the plan with concerted opposition to elements of the proposed expansion of radiation oncology services from clinical and political groups together with patient and 'local action groups' in certain geographic areas. A complex process and analysis which included a review of international experience and best practice, was undertaken and completed in 2003 together with the publication of a strategic report on the 'The Development of Radiation Oncology Services in Ireland'¹. The final element of analytical review and service plan recommendations to the Department of Health included a formal invitation to ESTRO to provide expertise on the international assessment panel. This was the first opportunity in its history for ESTRO to formally advise a EU member state government on radiation oncology service development. The process has recently resulted in a phased significant 480M euro investment package for Ireland to be completed by 2011.

¹http://www.dohc.ie/publications/expert_working_group_on_radiation_oncology_services.html

Radiobiology and mathematical modeling

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Outcomes modeling based on 3-D images and dose-volume data

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The revolution of 3-D treatment planning in radiation oncology translates into many opportunities to better understand the relationship between how we treat patients and their outcomes. Tools are now available to routinely capture 3-D image and dose-volume data, which, along with patient and disease related factors can be explored for new insights. Our research group has recently developed tools to facilitate gathering and analyzing radiation therapy outcomes data, as well as new methods of statistically modeling the data, and application to several clinical endpoints. We have released an open-source, Matlab-based software tool (CERR: A Computational Environment for Radiotherapy Research; see <http://radium.wustl.edu/cerr>) to conveniently extract data from treatment planning systems and to further generate a wide-range of geometric and dose-volume parameters for modeling. Statistical modeling with many candidate parameters is challenging. We use bootstrap resampling methods to guard against over-fitting (including too many model parameters). A common problem is when several models achieve similar performance. We will discuss these techniques in relation to xerostomia, esophagitis, pneumonitis, and tumor local control. Future challenges include the need to establish publicly available databases (or 'data banks') of anonymized patient treatment planning data and outcomes, which could crucially provide increasingly powerful datasets for outcomes modeling as well as effective reference datasets against which novel therapies could be compared.

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Radiobiological modelling & clinical trials

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Well-conducted randomised clinical trials are very useful for identifying those treatments which provide the best overall treatment to whole patient populations. Unfortunately, however, such trials take a long time to perform and analyse, may involve several thousand patients and, in some cases, may be incapable of detecting small differences in clinical effectiveness between two or more trial arms. Moreover, even a positive trial result, strongly supporting the use of a particular treatment, does not necessarily mean that the treatment is best for each and every patient. Radiobiological modelling, particularly when used in conjunction with reliable predictive assays, has the ability to rationalise patient selection for clinical investigations and to help reduce the time and effort which needs to be expended in pursuing a trial. This presentation will show how the wide spectrum of individual biological responses present within any randomised patient population has the effect of "diluting" the predictive power of a conventional clinical trial. It will also present examples of modelling processes which can be used to simulate clinical trials and will discuss the various parameters which may be used as input data. Issues which may be addressed using this approach include:

1. Investigation of the inter-relationship between overall time, interfraction, interval and dose per fraction and the current concept of optimised treatment.
2. Considerations relating to how best to sequence radiotherapy in cases where external beam treatment is combined with brachytherapy.
3. How to use the results of predictive assays to assign

patients to particular trial arms.

4. Assessment of the overall costs of complex radiotherapy and how this might be balanced against the reductions in the costs of continuing care which accrue from a reduction in the number of treatment failures.

It is stressed that computer modelling must not be considered as a replacement for clinical trials; rather it can effectively serve as a method for refining trial design and improving patient selection in order that the trial may then deliver clearer clinical identifiers with minimum time and effort and using relatively small patient numbers.

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Mathematical modelling of hypoxia and impact on RT outcome

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Hypoxia is an important factor that influences the outcome of radiotherapy through the radioresistance it confers to the affected tumour cells. Information regarding the tumour oxygenation is available from a multitude of sources and it is advised that it should be included into radiotherapy simulations in order to evaluate its influence on the outcome of particular treatment approaches. The questions that arise in relation to these simulations regard the relevance of the predictions and their dependence on the accuracy of the input parameters and the models used.

A mathematical model that simulates numerically the tumour oxygenation starting from the fundamental processes of oxygen diffusion and consumption was used to study the effects of diffusion limited and perfusion limited hypoxia. Averaging, resolution and other factors were investigated with respect to their influences on the predictions of treatment outcome for full fractionated treatments.

The description of the full distribution of oxygen in tissue by a black-and-white simplification with fully oxic and fully hypoxic cells could lead to erroneous predictions for treatment outcome. Furthermore, the averaging of the oxygen tensions in rather large regions involved by some measuring methods may also lead to systematic deviations from the actual oxygen distributions in the tissue. This may in turn lead to an overestimation of the tumour response from the RT simulations using directly the measured values. Another potential source of misinterpretations might be the issue of distinguishing between the radiobiological responses of acutely and chronically hypoxic cells.

All these results suggest that care should be taken when incorporating hypoxia information into the biological modelling of tumour response for making clinical decisions as the various factors may become critical in some circumstances. In spite of these difficulties, the mathematical modelling of tumour hypoxia has the potential to allow a better simulation of radiation treatments.

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Modeling late rectal injury following RT

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A number of studies have been devoted to the analysis of volume effects in rectal injury with the consequent search of significant correlation between rectal dose-volume parameters and clinically observed toxicity. Thanks to this, the evidence of a significant volume-effect for partial irradiation of the rectum is today well established: in particular, correlations between late rectal bleeding (lrb) and the fraction of rectal volume receiving more than 65-75 Gy (V65-V75: high dose) and more than 40-60 Gy (V40-V60: intermediate dose) were reported. Although important differences exist among investigations in terms of treatment techniques, treatment procedures, use of different definitions of rectum (including filling, rectal surface, rectal wall) and possible impact of set-up and organ motion uncertainties, a

number of reported findings are quite consistent. Within the retrospective Italian cooperative study (AIROPROS01-01), the analysis of a large population of patients (550 pts) pooled from different institutions and treated mostly with doses between 68 and 78 Gy revealed strong correlation between grade 2-3 lrb and both high (V70) and intermediate doses (V50-V60). Different NTCP models were found to accurately fit these data and probably the main result emerging from maximum likelihood analysis concerns the volume parameter $n=0.23\pm 0.25$ for grade ≥ 2 lrb: this suggests that the rectum has a more parallel architecture than previously thought and this is congruent with the results of the previously performed analysis which established the high impact of the "intermediate" dose region (40-60 Gy) in predicting the risk of lrb. On the other hand, when considering only severe lrb (grade 3) the dose-response curve is substantially different: its slope becomes steeper (the parameter m decreases from 0.19 to 0.06) and the volume effect increases largely (n decreases from 0.23 to 0.06). Even if great caution should be maintained because of the low number of grade 3 lrb, when severe injury is considered the rectum seems to act as a more serial-like organ.

In addition the impact of different uncertainties (contouring, organ motion, set-up error) on the NTCP best fit parameters was investigated through iterative random sampling of modified DVH shapes. In this way, a distribution of best fit parameters was obtained. Results showed that the best fit parameters found were robust enough if grade ≥ 2 lrb was considered.

It is worth emphasizing that all this analysis cannot be considered as a validation of NTCP models: they are phenomenological models, for this reason the resulting dose-response curve cannot be considered as directly representative of rectum radiobiology, but rather a simplified representation of a complex clinical situation which is measured in terms of late rectal bleeding.

All the results presented above may be considered as a starting point which will be refined through the AIROPROS01-02 prospective investigation. The new study has completed the enrolment of about 1100 patients treated with 3DCRT (70-80 Gy) in 21 Italian Institutions: results on acute toxicity are now available, while the final results on lrb, prospectively assessed by self-reported questionnaire, are expected in 2006.

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The potential therapeutic gain of redistributing dose to hypoxic regions using dose-painting: a modeling study

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Introduction: Tumor hypoxia is considered a main cause of failure in radiation therapy due to the fact that hypoxic cells can be ~3 times more resistant to irradiation than aerobic cells. Hypoxia is a common feature of solid tumors and its presence is known to be highly heterogeneous at the cellular level. The aim of this study is to quantify the expected gain in treatment efficacy by redistributing dose from well-oxygenated to poorly oxygenated areas of the tumors using dose painting techniques. In our analysis, we accounted for the underlying cellular oxygen distribution that contributes to the oxygenation measurements obtained using available imaging techniques. In addition, we developed methods to evaluate the potential complications of transient hypoxia and necrosis.

Methods: Two models were designed to simulate the underlying oxygen distribution of each oxygen measurement (voxel). The first is a binary model, in which cells within the voxel are considered simply as hypoxic (maximally radiation resistant) or aerobic (maximally radiation sensitive) with an OER of 2.8. The second is a diffusion model in which the cellular oxygen levels are determined by the radial distance

of each cell to its nearest capillary. In this model, cells exist at a continuous range of oxygen concentrations with variable OER's. For simplicity we assigned tumor voxels to one of 9 oxygenation categories and for dose-painting each category received a unique dose. We held the mean dose per fraction constant at 2Gy. Equations were composed to describe the surviving fraction of the entire tumor after 30 doses, SF30, as a function of the applied dose to each of the voxels in the 9 oxygenation categories. These equations were minimized by an optimization algorithm that allowed the dose to vary to each category between several upper and lower limits (with a mean dose of 2 Gy). The optimum SF30 was then compared with the SF30 after a uniform dose of 2 Gy. We also developed an extension of this model to evaluate the effects of various degrees of necrosis and the presence of transient hypoxia.

Results: Redistribution of dose to hypoxic areas by dose-painting results in a significantly lower SF30 compared to applying a uniform dose of 2 Gy. Interestingly, the expected gain from dose-painting is significantly larger when a more realistic distribution of oxygenation is assumed within each measurement voxel. The absolute amount of benefit is not strongly dependent on the α/β ratio, but is influenced by the intrinsic radiosensitivity (SF2).

Conclusion: These results quantify the maximum benefit expected to be obtained from dose-painting based on realistic assumptions of oxygenation measurements. They suggest that redistribution of dose to hypoxic areas is capable of influencing the cure-rates for certain tumors.

Dosimetric methods

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Practical approaches to small field dosimetry

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The dosimetry of small fields has become increasingly important in recent years, for both stereotactic radiotherapy and for sub-fields for IMRT, using MV photon beams. There is also interest in small fields in other modalities. However measurements are difficult because of the sizes of available detectors, as well as other problems such as lack of lateral equilibrium. A range of measurement methods and detectors have been investigated and are summarized here, where the aim is to acquire data with accuracies of at least $\pm 2\%$ and to verify delivered doses to $\pm 3\%$. These studies include exploring the limitations and methods required for in-air measurements (caps and mini-phantoms for small field use, e.g. for S_c) and in-phantom measurements, as well as comparing different small detectors. Detectors include a range of 'micro' and 'pinpoint' ion chambers, standard and 'stereotactic' semiconductor detectors, diamond detectors, conventional and Gafchromic film.

The main measurements in this series have been carried out on a Varian 600CD 6 MV x-ray beam, in small fields set with conventional collimators down to $1 \times 1 \text{ cm}^2$, similar fields set with MLC down to $0.5 \times 0.5 \text{ cm}^2$ and in circular stereotactic fields down to 0.5 cm diameter. Head scatter factors, total scatter factors, depth doses and profiles have been investigated, as well as verification of delivered doses. For head scatter factors, a number of approaches to forward and side build up were investigated. Additional measurements have been carried out on other linacs, other beam qualities and also in electron beams and kV x-rays.

Comparison of the results and of the characteristics and performance of the different detectors and methods in small fields produces practical recommendations on approaches, limitations, methods and problems.

The results can be used to model and evaluate correction factors for detector sizes and to separate out effects. Finally Monte Carlo modeling is necessary to fully understand the behaviour of practical systems in these situations.

252**Monte Carlo study on IMRT and Radiosurgery dosimetry performed by ionization chamber**

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Treatment Planning Systems (TPS) represent an important advance in Radiotherapy due to the possibility of knowing the dose distribution prior to treatment. In consequence, the best strategy can be selected to cover the target appropriately and to protect the organs at risk (OAR). Nevertheless, TPS is not a final product due, among others reasons, to the weak consideration of tissue interfaces. This problem may be magnified when using Intensity Modulated Radiotherapy (IMRT) techniques, due to the high complexity of these treatments that might imply a considerable amount of beamlets. For these cases the only guaranty for the correctness of the pre-calculated dose, is the empirical absolute and relative verification in a phantom. However, the absolute dosimetry performed is far from reference conditions and, therefore, represents an important inconvenient. This also applies to Radiosurgery.

We have demonstrated that the correction factor necessary to take into account the departure from reference conditions, to obtain accurately the dose delivered by a single segment, may vary strongly depending on its position with respect to the position of the ionization chamber (IC). We have also studied the clinical implications in the Planning Target Volume (PTV) and in OARs. A worse behaviour would be expected in the later, due to the increase on the number of off-axis beamlets in the point of evaluation.

Our conclusions, based on this experience, are:

- A) Experimental verification of the absolute dosimetry is essential previous to each IMRT treatment.
- B) Measurements with IC, far from reference conditions, could not have the required accuracy for this purpose.
- C) It may be demonstrated easily that the real dose, due to the contribution of a single segment, is strongly dependent on the relative position of the IC with respect to the beamlet, having an error up to 9% or even larger.
- D) In the case of the PTV, as a point of interest for a complete treatment, the error is negligible, resulting that the less contribution to the dose comes from the situations where the divergence is larger.
- E) Finally, in the worst scenario that represents the clinical implication of the absolute dosimetry in the OARs, we have obtained larger errors, but always below 3% for 6 MV.

A systematic new project with more clinical cases and detectors is being carried out to better clarify this crucial aspect of the IMRT. No important differences, with respect to the previous studies, are being found so far.

253**Low energy dose measurements performed in a new type of scintillator dosimeter**

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Introduction: For absolute dosimetry is mandatory use cylindrical ionization chamber for energy over 70 kVp, while below 70 kVp parallel plate ionization chamber is common

used to provide minimal perturbation. A recent technological improvement able us to check orthovoltage photon beams parameters by a small plastic scintillator detector. Reduction dimension, good accuracy and very good resolution are most important characteristic of this dosimeter.

Materials and Methods: An orthovoltage X-ray system with energy range from 50 kVp to 250 kVp is used to test the plastic scintillator. For energy over 70 kVp dose measurements were carried out with a Farmer-type ionization chamber in polystyrene and parallel plate (below 70 kVp) embedded in polystyrene phantom.

All measurements have been developed with low energy photon beam centered in geometrical center of the dosimeters. Dose measurement results obtained with ionization chamber are the our reference respect to scintillator detector data.

Detector reader has a shutter with two positions: close (Dark signal) or open (Source signal). Measurements performed has been: output factor, short and long term stability, energy dependence and linearity, dose dependence, field dimension dependence and dose rate dependence.

Results: Output factor of the detector has been evaluated for all energies and for a delivered dose of 100 MU.

Short term stability shows a mean value of 0.58 (range: 0.12 - 0.25) and 0.13 (range: 0.03 - 0.33) respectively for Dark Count and Source Count. Long term stability shows a mean value of 0.40 (range: 0.20 - 0.52). Detector has a linear dependence for energy from 100 kVp to 250 kVp, but is independent at very low energies (50 kVp to 70 kVp). Our results show linear increment in function of monitor unit increment. Field size dependence is linear between 100 kVp and 250 kVp. All our data respects inverse square law and we can consider the detector independent of dose rate.

Discussion and Conclusion: This investigation shows a good result for this type of scintillator detector. Good results in short term stability assure us to obtain a good constant in dose measurements at low energy tested. System scintillator-electrometer speed to response and the time that occur to obtain a stable response is about 15 minutes. Pre irradiation is not request.

Its quick use and implementation advice a use in quality assurance for low energy devices, like Plesio – Roentgen units, Brachytherapy sources and Radiological sources.

254**A new 2D ionization chamber array for dosimetry verification of IMRT**

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Introduction: The aim of this study was to analyze the dosimetry properties of a new 2D ionization chamber array (IMRT MatriXX from Scanditronix-Wellhofer, Germany) and to assess its capability in routine IMRT QA. The device consists of a 32x32 matrix of 1020 vented plane-parallel (single volume 0.07 cm³, $\phi = 4.5$ mm, h=5mm, pixel to pixel distance is 7.62 mm) ionization chambers arranged in a square of 24x24cm² area. Each of the 1020 ionization chambers is independently read out with a custom microelectronic chip with no dead time and automatically compensated for temperature and pressure variation. Minimum integration time is 20 msec. The entire array factory is calibrated to allow for measurements in absorbed dose.

Material and Methods: The MatriXX response was evaluated as a function of dose, dose rate, beam energy including influence of accumulated dose to the uniformity of the individual calibration factors. Basic parameters of radiation beams (TMR, OF, penumbra, field size, flatness, symmetry, start-up behaviour) were compared to ion chamber measurements in water for high-energy photon and

electron beams. The MatriXX response in the steep dose gradients is compared with the film data and the results of Monte Carlo simulation. The analysis of measured (Film, MatriXX, Ionization chamber) versus calculated absorbed dose distribution has been performed for IMRT fields in a number of clinical cases for various Linac/TPS combinations. Capability to perform dosimetry verification of dynamic fields, including start up performance of Linac, has been verified for different speed of MLC leaves, EDW and clinically tested in D-IMRT.

Results: The signal reproducibility of the MatriXX has been tested in a Co60 beam and it was found constant within 0.5% over a 3 month period. Short term stability The dose response is linear ($R^2=1.00$) up to 10 Gy. The dose rate dependence response variation is within 0.5 % in the range 0.1 – 10 Gy/min. The TMR data measured in a Co60 and 15 MV x-ray beam and compared with an ion chamber have shown agreement within 0.5 % (up to 20 cm). Output factors measured with MatriXX and an ionization chamber agreed within 1% for field sizes in the range from 4x4 cm to 25x25 cm. Comparison of penumbras measured by film and MatriXX for various IMRT fields shows a clear correlation with differences below 1 mm. The leaf speed variation between 0.07 - 2cm/s influenced the MatriXX response within 0.6%.

Conclusions: The time necessary for setup and analysis of IMRT beams is typically below 15 min, depends on number of fields. The MatriXX offer reliable dosimetry verification of static and dynamic radiation fields and is very well suited for the pre-treatment IMRT QA as well as standard LINAC QA.

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The off-axis response of an amorphous silicon electronic portal imaging device

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The aim of this work is to determine the off-axis dose response of an amorphous silicon electronic portal imaging device (EPID), and develop a correction method to improve EPID dosimetry.

The uncorrected or raw pixel response of the aS500 amorphous silicon EPID shows differences in response (sensitivity) of individual pixels as well as a large off-axis over-response compared to the beam profile measured with ion-chamber. Both can be corrected by division of raw images by the flood-field (FF) image. However this leads to two problems for dosimetry, 1) the beam profile is in both the raw image and FF image and hence is "washed out", and 2) mismatch of EPID position between dosimetry and FF-calibration means that the off-axis response in the raw image and FF are misaligned. This causes artifacts in FF division and dosimetric errors. A method was developed to measure the off-axis response and pixel sensitivity differences separately to apply these at any EPID position. To measure the pixel sensitivities, multiple raw images of the same symmetric field were acquired with the detector displaced laterally and these were combined. The off-axis over-response was quantified by acquiring off-axis raw images and removing the off-axis beam fluence and previously determined pixel sensitivity differences. The new correction method was then applied to images with the detector laterally displaced and compared to conventional FF correction results. EPID profiles were then compared to beam profiles measured with ion-chamber in water for open fields, asymmetric fields, and step and shoot breast compensator IMRT fields.

The off-axis over-response of the EPID was large for 6 MV increasing to 10% at 15 cm off-axis and 3% for 18 MV. The dosimetric errors introduced by detector displacement with conventional FF-calibration were found to be approximately 2% per cm of lateral detector displacement. These were reduced to less than 1% for any position with the new correction method. Comparison of corrected EPID images

with ion-chamber measurements showed good agreement for a variety of field sizes and asymmetric and compensator IMRT fields, except for the penumbra region where the EPID scatter kernel causes differences in the profiles.

The amorphous silicon EPID has a large off-axis over-response particularly for 6 MV. The difference in over-response off-axis with beam energy suggests that this is due to the energy response of the high atomic number phosphor with the softer beam off-axis. Monte Carlo modelling is being employed to further investigate this effect. The new correction method gives accurate dosimetry for any EPID position and retains beam profile information in the image.

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A low-density normoxic polymer gel dosimeter: Basic studies

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Introduction: Gel dosimetry offer a great potential for quality assurance in radiation therapy, as it measures the integrated dose distribution in 3D. For most applications, a gel with a density close to water is used. However, in several situations, a gel with the possibility to simulate different electron densities is of great interest.

The aim of this study was to investigate the basic dose response characteristics of a low-density normoxic polymer gel. In addition, depth dose data for clinical photon beams have been measured and compared with Monte Carlo calculations. The feasibility of using low-density gel in large volumes for 3D measurements was investigated as well.

Method: The gel consisted of 86% deionized ultra pure water, 8% gelatin and 6% methacrylic acid. The concentration of the anti-oxidant (THP) was varied between 50 and 150 mM. The reduced density was achieved by mixing the gel with Styrofoam™ spheres. All gel samples in this study were manually kept in rotation until the gel was set. The CT-number as well as the mass density was measured for the gel samples.

A Varian 2100 C/D linear accelerator was used for irradiation. Monte Carlo calculations of the absorbed dose to the low-density gel were performed using the dosrznrc module of the MRI was used for evaluation of the gel.

Results: The CT-number of the samples were approximately between -400 and -500 Hounsfield units and the mass density varied from 0.58 to 0.63 g/ml. The absorbed dose response was approximately linear for doses between 2 and 8 Gy. There was no systematic dependency on the slope of the dose response curve for different concentrations of THP. Calibration of the depth doses was performed using the equation for the linear fits (between 2-8 Gy) of the corresponding dose response curves. This is acceptable as the absorbed doses in the test tubes were ranging from 2 to 4 Gy. The gel depth doses were compared with Monte Carlo calculations. No pronounced difference in depth doses with varying concentrations of THP was seen. The gel data were found to be in good agreement with Monte Carlo calculations, however for some of the samples the gel curves decrease faster than the Monte Carlo curves. This may be due to inhomogeneous distribution of gel and Styrofoam™ spheres. For the large volume central depth dose data and profiles at three various depths were extracted. Background subtraction was performed using a background value from the unirradiated part of the phantom.

Conclusion: The study shows that a normoxic polymer gel with a reduced density can be obtained by adding Styrofoam™ spheres. However, in order to get reliable results it is of utmost importance to have a uniform distribution of gel and Styrofoam™ spheres in the volume. We therefore suggest a mechanical rotation of the containers after they are filled with gel until the gel is set.

The application with the phantoms shows that it is feasible to manufacture this low-density gel also in larger volumes.

257**Dosimetry of ion beams using lithium formate EPR dosimeters**

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The use of accelerated hadrons in radiation therapy has become increasingly popular, largely due to their superior physical properties in comparison with photons and electrons. Following the introduction of such techniques in radiotherapy, it is essential to perform detailed analyses of the resulting energy depositions. In this work, dosimetry using Electron Paramagnetic Resonance (EPR) spectroscopy has been employed for dose determinations and further characterizations of ion beams.

Recently, lithium formate has emerged as a promising EPR dosimeter, as high concentrations of stable radicals are formed in this substance following photon irradiation. However, the usefulness of this dosimeter material in ion beam dosimetry has yet to be demonstrated. In the current study, the EPR response (i.e. the amount of radicals produced per absorbed dose) of lithium formate dosimeters following irradiation with ⁶⁰Co γ -rays, 3-8 MeV electrons, 35-163 MeV protons and 340-550 MeV nitrogen ions has been examined. Ion chamber dosimetry (following water-based dose standards) has accompanied the EPR measurements.

The EPR response of dosimeters irradiated with electrons was practically equal to the response following γ -irradiation. For nitrogen ions, the resulting dosimeter response was reduced by about 30 % in comparison with γ -rays. For dosimeters irradiated with protons, a similar but much smaller reduction was observed. Most important, dosimeters irradiated with nitrogen ions displayed a significant increase in the line width of the EPR resonance constituting the dosimeter signal.

The effects observed are very likely to be caused by the increased ionization density resulting from irradiation with high LET particles (e.g. nitrogen ions) in comparison with irradiation using (low LET) γ rays and electrons. Although a relatively high level of recombinations following irradiation with nitrogen ions was found, the characteristic changes in the dosimeter signal may be used to correct the dosimeter reading in order to provide more accurate dose estimates. Lithium formate is therefore a good candidate for solid-state EPR dosimetry of ion beams.

RT departments of the future**258****Design of a new RT department: the Dublin approach**

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Background: Radiotherapy in Ireland was significantly under funded for many decades. This resulted in a severe national shortage of both departments and equipment, long waiting lists and a sub optimum rate of usage of radiotherapy as a treatment modality. In May 2002 the Government established an Expert Working Group to advise on the development of radiotherapy services nationally. This group met 25 times culminating in the publication of the report The Development of Radiation Oncology Services in Ireland. Following acceptance of the report the government issued a "Request for Outline Proposals for the Development of Radiation Oncology Services in the Eastern Region (North and South)" to the academic teaching hospitals in Dublin.

Method: A project team was established with the remit of preparing a submission in accordance with the criteria laid

down in this request. The project team was chaired by Professor Donal Hollywood and included, in addition to myself, representatives from the main oncology related disciplines in the hospital. An architectural team was put in place to draw up plans in accordance with the defined requirements, equipment specifications were drafted and a full costing exercise carried out. Relevant government publications from other countries were reviewed and visits made to several centres. Advice was sought from international experts where appropriate. The final submission was forwarded to the Department of Health and Children in October.

Results: An expert group appointed by the Government visited each submitting hospital during the 13th-17th December and site visits together with presentations of the proposed plans were made. Question and answer sessions were held following the presentations. The proposal in which I was involved was successful.

Conclusions: The design for the new department is innovative and based on optimum delivery of service. During this presentation I will describe the approach to equipment and staffing in the proposed department.

259**Introducing new technology – a team approach**

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This presentation will discuss the introduction of new technology into a radiotherapy department and the requirements for the changes in practice associated with changes in technology. The radiotherapy department at the Rosemere Cancer Centre has progressed from a single clinical Linear Accelerator in 1997 to six Linacs and full pre-treatment equipment in 2005. The need for changes in practice and departmental processes has been an almost constant pressure as new technology has been introduced. At the same time there has been a decline in the availability of radiation technologists, physicists and clinical oncologists which has required a more flexible approach to change and a greater need for prioritisation of resources.

Some of the areas covered will include the advantages of a multi-disciplinary approach, some obstacles to changes in practice and planning for future advances in technology. Radiotherapy technology continues to advance quickly and these changes present an on-going challenge to the radiotherapy team that has to adapt in order to improve the quality of treatment provision for patients.

260**Replacing equipment**

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The turn of the century brought the large scale break through of 3D conformal and intensity modulated radiation therapy techniques in the clinical setting. During the 90's, new technologies were introduced for high-resolution dose delivery. These delivery techniques have nearly reached maturity. However to fully use the power of high-conformal dose delivery up to its potential, the main focus of innovation today is mainly on target volume definition and localization. Definition and localization of the target volume requires advanced image acquisition technology for visualization of anatomy. Some of the required technology and know-how is available in the radiology industry. An integration process of this technology into radiation therapy was commenced and input from technological innovation in radiology became one of the driving forces for innovation in radiation therapy. As a consequence, these new devices found their way to application in radiation therapy much faster than during the previous decades. The last few years, the speed of technological evolution in radiation therapy increased and this process will probably continue in the future. Radiation therapy innovating at larger speed influences the process of replacing equipment.

Beside the installation of new equipment there seems to be an almost continuous process of upgrading hardware and software in our departments. To handle this continuous process of change one has to incorporate change into the daily routine. Radiation therapy being a complex working environment with its different disciplines working together, is a particularly difficult environment to implement new approaches to change. The radiation therapy department of the University Hospital Gasthuisberg Leuven is at the moment going through the motions of changing about 75% of its equipment. This talk is about the impact of such a project on a working radiation therapy department with a heavy workload of treating 2400 patients every year on 5 treatment units.

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Distributed radiotherapy - the use of telemedicine as a tool for decision making in paediatric radiation oncology ? a report from SWPR

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SWPR is the Swedish Workgroup for Paediatric Radiotherapy who initiated this project in 2004. Members of the group comes from six University Hospitals in Sweden; Umeå, Uppsala, Stockholm, Linköping, Gothenburg and Lund.

Approximately 300 children are diagnosed with cancer annually in Sweden. About 115 of these patients will receive radiotherapy, which is given in six major radiotherapy centres in Sweden. Only a few radiation oncologists deal with these patients, most often one or two in each centre. Since the incidence is low, each paediatric radiation oncologist only sees a few patients per year. A network has been formed to assist in standardising treatments, evaluating study protocols and to discuss these, often rather complicated cases. The network members meet twice a year but are in phone contact whenever needed. To satisfy the need to be able to see what's being discussed and to learn from each others experience the idea of online conferences emerged.

The paediatric radiation oncologists were interviewed, regarding a peer-review platform for radiotherapy that could be readily implemented into the clinic. They all agreed that the implementation of a conference system could raise the level of competence, give support for new ideas and help in developing new standards. It would also be helpful for discussing individual cases. The oncologists also saw teaching/learning within the group as a possible gain as well as an opportunity to invite others into the field of paediatric radiation oncology. Other needs asked for was the ability to work with medical images and treatment plans in an interactive way using conferencing tools and shared applications.

A system is under construction in which patient cases from the participating clinics can be submitted for online conferences. It will include a simple conference part, a server with application sharing software and the TPS (treatment planning system, viewing only). The participating clinics will temporary upload treatment plans for the conference to this server. A coordinator will serve the online members with the information needed for each case. This group and its experiences will also serve as a pilot for distributed radiotherapy within the national proton project, in which all Swedish clinics will be connected.

The presentation will describe our first experience with this system.

Acknowledgments: We thank the physicians, physicists and engineers who contributed to this project in its initial phase.

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Distributed radiotherapy in Northern Sweden

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In 1996 an official report concluded that cancer patients in Sweden are offered radiotherapy to a lesser extent than patients in several other countries. This situation is partly due to the low population density and the long distance patient transport that follows. Previously the only radiotherapy department in northern Sweden was situated in Umeå and the reception area covered 55% of the country area, over 225 000 km². The population of this area is only ca. 900 000.

In order to reduce the need for long distance patient transports and to be able to offer radiation treatment to patients unable to travel long distances a radiation treatment department in Sundsvall in the southern part of the region was built up.

The treatments given in Sundsvall in the initial stage was palliative treatments later followed by curative prostate and tangential postoperative breast irradiation together with certain brain and lung treatments.

Patient conferences with Umeå are held twice a week through videoconference. Common patient information and check and confirm systems are used in order to make transfer of patient data fast and secure. This is done using replicated databases rather than a common database for each system. The main reason for this is to reduce the risk of treatment interruption because of problems with computer communication.

Treatment simulation in Sundsvall is done using virtual simulation and all patient information in the Sundsvall clinic are digital (no film or paper), partly because of the common patient conferences. The patient fixation and CT-scanning for virtual simulation are done in Sundsvall.

CT-data is sent to Umeå where the treatment planning is performed. The setup parameters are then stored in the database for use in Sundsvall.

The radiation treatment department in Sundsvall is a complete department with oncologists, radiation therapists, physicists and technicians. This means that the joint center, apart from dose planing, works as a cooperation between independent clinics rather than main and satellite clinic.

A common treatment method book is currently under development and it will secure the same treatment regardless of at what clinic the treatment is given.

Quality assurance

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Failure Modes and Effects Analysis (FMEA) applied to two modern radiotherapy centres

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FMEA is a Quality improvement technique, generally applied to industry, that can provide an efficient, structured approach to assessing interconnected system failures. It is a bottom-up analytical process, which identifies process hazards.

According to this technique, each potential failure mode in the system is analysed to determine its effect and to classify it according to its severity. The objective is to identify reliability-critical areas in the system for which modifications to the design or maintenance procedures are required to eliminate single point failures and any catastrophic or critical consequences of such failures. Each individual component of the system is considered separately for each of its failure modes.

The procedure involves the following steps:

1. Define the system and its required reliability performance.
2. Construct functional block diagrams to define and illustrate how the different sub-systems are interconnected.
3. List the components, identify their failure modes and where available their modal failure rates.
4. Complete a set of FMEA worksheets analysing the effect of each sub-assembly or component failure mode on overall system performance. Severity rankings are then assigned to each failure mode.
5. Review the worksheets to identify the reliability-critical components and make recommendations for design improvements or amendments to maintenance schedules

In this work authors are presenting a FMEA study of two recent radiotherapy centres in Lisbon (Centro Oncológico Dra. Natália Chaves and Hospital CUF-Descobertas), where there are two very different radiotherapy equipments: Varian accelerator, VarisVision network and Eclipse TPS (in the first centre) and Elekta accelerator, Impac network and Xio TPS (in the second centre). This study covers a time-period of one year (all the 2004 year), and allows some very interesting conclusions related to the way the equipment behaves and how one may prevent some problems.

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Acceptance Test Procedures (ATP) and preliminary results of a Quality Assurance Program (QA) for a Helical Tomotherapy (HT) unit

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Introduction: Image-guided HT is a new modality for delivering IMRT with helical irradiation: the slip ring continuously rotates while the couch moves into the bore. The radiation source (Linac, 6 MV) is collimated into a fan beam and modulated by means of a binary MLC. A xenon detector array, opposite the radiation source, allows an MVCT acquisition of patient images for set-up verification.

Aim: To define the -ATP and -QA programs for the physical and dosimetric characterisation of an HT unit recently

installed at our Institute and clinically activated on November 2004.

Materials and Methods: Conventional Linac ATP and QA protocols were adapted to HT with additional items reflecting important differences between the two irradiation modalities. Geometrical, mechanical and dosimetric tests may be summarized in 5 categories: a) Mechanical and geometrical characterisation of the system's components: evaluation of alignment among radiation source-gantry rotation plan-jaws-MLC-MVCT; b) Treatment beam configuration in static condition: PDD and profiles, output factors, output reproducibility and linearity; c) Dynamic components characterization: accuracy and reproducibility of MLC positioning; rotational output reproducibility and linearity, leaves latency, couch movement constancy; d) Gantry-couch and MLC-gantry synchronisation; e) MVCT image quality.

Based on ATP results, a QA protocol was defined: daily tests (output in static and IMRT condition, energy and cone-profile constancy), bi-weekly tests (synchronisation), monthly tests (source-jaws-MLC alignment), quarterly check (MVCT alignment and image quality). Ionisation chambers (Exradin A1SL 0.056cc), films (XV-Omat/EDR2), water and solid water phantoms were used.

Results: All ATP results were within reference limits: $\leq 1\text{mm}$ or $\leq 1^\circ$ for alignment tests, and $< \pm 2\%$ for dosimetric parameters. Over a 5 months period, an average output variation equal to $-0.1\% \pm 1\%$, both for static and rotational condition, and an average energy variation of $-0.5\% \pm 0.2\%$ were found. Daily IMRT plan absolute dose verification showed a dose reproducibility of $0.7\% \pm 1.2\%$ and $1.3\% \pm 1.8\%$, for low and high dose gradient regions. Source-jaws-MLC and MVCT alignment results and jaw and leaves positioning accuracy were $\leq \pm 1\text{mm}$. Couch-gantry-MLC synchrony tests showed good stability ($\leq \pm 2\text{mm}$).

Conclusions: During ATP all parameters were below the pre-defined tolerance levels; QA results indicated good reproducibility of all HT mechanical/ dosimetric performance.

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Optimization of output measurement frequency of linacs based on acceptable radiobiological risk

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Purpose: The aim is to develop a method to optimize the output measurement frequency for linacs on the basis of an acceptable radiobiological risk. Output is defined as the absorbed dose per monitor unit at a given point of the beam. Radiobiological risk is defined as undesirably high drop in tumour control probability (TCP) caused by alterations in the output. An optimal measurement frequency is defined as the minimum frequency ensuring an acceptable fraction of undesirably low TCP values.

Materials and methods: Output variations for photon beams were estimated for different output measurement frequencies and for different constancy checking acceptance limits. This was achieved by modelling the output behaviour of the linacs based on the data from local quality control (QC) measurements, collected for 8 treatment units for five years. The output behaviour was modelled by empirical curve fitting to the QC data points. The output variations were converted into TCP distributions by using normalized dose-response slope of 2.5 (% TCP/% dose). This slope was derived by averaging slopes of breast and prostate cancers and of lymphoma estimated by applying linear-quadratic-Poisson (LQ) model with parameters taken from literature. Acceptable risk level was defined so that decrease in TCP due to the output drifts was $\leq 5\%$ in 95% of the treatments.

Results: The estimated optimal output measurement frequency is 6 and 3 months with constancy checking

acceptance limits of ± 2 and ± 3 %, respectively. With the frequency of 6 months, the estimated treatment dose variation due to output drifts is about 1.4 % (1STD). The output modelling revealed that a drift of 2 % occurs in 18 \pm 12 months with the shortest time of only 2 months observed just after commissioning of a new linac. Even at long term, the modelling described the outputs well with maximal errors of ≤ 1 %. Output levels of new linacs stabilized during the first 2-3 years.

Conclusions: Radiobiological risk based optimization of the output measurement frequency includes uncertainties and may be cancer-specific. The frequency can be prolonged to several months if the long-term drift in the calibration of constancy checking device is known. The presented output modelling provides a useful tool to estimate linac-specific output trends. The results indicate that the implementation of linac-specific time intervals for output measurements would be more optimal than the using of a common output measurement frequency.

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Simple Daily QA with an amorphous silicon EPID

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Purpose: To evaluate the effectiveness of simple daily imaging with amorphous silicon EPID for linear accelerator QA.

Methods: For a complete year daily images of 24x24cm open and wedged beams have been collected on a dual energy, 6 and 8MV, photon linear accelerator using the Elekta iViewGT amorphous silicon imager. Images have been collected using the standard image capture routines and without additional build up on the imager plate. The images have been used to assess the imager effectiveness as measuring variations in output, flatness, symmetry and wedge factor.

Results: Output results have been compared with daily ion chamber readings. Simple normalisation of the imager results shows that the standard deviation between image and ion chamber results is 0.65% for both 6 and 8MV. The EPID proved a sensitive monitor of relative changes in flatness & symmetry, able to detect both systematic changes and gradual drifts in these parameters over time. Adjustments in machine parameters during QA and service days were apparent in the data. Absolute measurements of symmetry and flatness were more problematic as the calibration of the imager plate with a flood field corrects for the flatness of the beam as measured by the imager. A simple correction was implemented to account for the 'horn suppressing' and flatness/symmetry showed good agreement (within 1%) between EPID and a diode array. However, some inconsistencies were found in the daily images requiring further investigation.

Comparison of the open and wedged field showed little variation in wedge factor demonstrating consistent wedge and imager positioning.

Conclusion: Simple images collected daily have proved a sensitive measure of output, symmetry and flatness constancy. With the increasing availability of amorphous silicon technology and the continued need for efficient linear accelerator test procedures the role of daily EPID imaging in QA programmes should be considered.

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Obtaining optimal double exposure settings for the Elekta iView GT electronic portal imaging system

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Introduction: Electronic portal imaging (EPI) is an important tool in the placement and verification of treatment

portals (TP), ensuring coverage of target volumes. Users of the Elekta iView GT system at our centre noticed inconsistencies when acquiring double exposure images on successive days. They also questioned whether 'image quality' could be improved. The aim of the study is to investigate the reason for and thus reduce inter fraction variation in images and determine whether image quality can be improved. Parameters investigated were monitor units (MU), beam energy, port weight, field size of 'open' portals (OP), dose rate and EPI panel position.

Materials and Methods: An Elekta Precise linear accelerator with amorphous silicon EPI and iView GT software was used. Phantoms included a anthropomorphic thoracic phantom used to evaluate MU variations: total number of MU (minimum of 2) and ratio of TP to OP MU, beam energy, size of OP relative to TP, and Elekta Las Vegas phantom used to evaluate port weight: a weighting factor that affects the display of OP and TP, dose rate and panel position.

Results: Variation in both the total number of MU and the ratio of TP to OP MU had no effect on image quality. A noticeable improvement in image definition for both anterior and lateral projections was seen with 6MV compared to 10MV. A variation in port weight showed a change in the intensity of the TP but did little to improve image quality. Variation in OP size relative to TP size significantly affected image contrast, with a small difference in portal sizes giving the best image, while dose rate and image position had no effect on image quality.

Conclusion: Whilst no quantitative image analysis was performed, the subjective quality of images is the determining factor and a number of conclusions /recommendations can be drawn from this work. It is likely that inter-fraction variation in image quality is due to a variation in the relative size of the OP. It is recommended that the same OP size be used each time and that this be kept as small as possible. Monitor units should be kept to a minimum and it is recommended that 6 MV be used for all double exposure images. The port weight should be reduced to improve TP visualization. Normal treatment dose rate can be used for all exposures and panel position makes no difference to image quality. It is intended to continue this work with further studies using an anthropomorphic pelvis phantom.

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Dosimetrical verification of treatment planning system in radiotherapy departments of Estonia

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Purpose: A group of participants of the IAEA coordinated research project "Development of procedures for quality assurance for dosimetry calculation in radiotherapy" developed a number of clinical test cases to verify the treatment planning system (TPS) dose calculations for photon beams during commissioning. This set of test cases was applied in radiotherapy departments of Estonia to evaluate its feasibility for possible application in TPS dosimetrical verification audit.

Methods and Material: CIRS thorax phantom (Model 002LFC, CIRS inc., Norfolk, VA) has been used to verify the dose calculated by TPS with measurements. The phantom was scanned twice using CT. The first scan was performed to derive the relative electron densities to CT numbers conversion. The second scan was used for treatment planning. The proposed clinical test cases were designed to check the wide range of conditions. The doses were measured both on axis and off axis with 0.125cm³ ionisation chamber placed inside the CIRS phantom. More detailed information about the tests will be presented in the poster. Four TPSs - 2 CMS XiO (3 photon algorithms), Helax TMS and Theraplan 500 installed at two radiotherapy departments of Estonia have been tested. The different beam qualities, including Co-60 and 6, 10, 18 MV photon beams were used.

Results: The electron densities to CT numbers conversion curve was adjusted for all TPS tested. In general, the results of proposed test cases were in agreement with the results of commissioning measurements performed in water. However, the limitations of TPS algorithms were much more pronounced and clearly seen in proposed clinical test cases. The superposition algorithm (CMS XiO) had the smallest differences between measured and calculated doses for all beam qualities tested. The largest deviation of 13% for point in lung was found for Co-60 beam and convolution (CMS XiO) algorithm. The time required for the whole chain of activities: setting up the phantom, CT scanning, planning, measuring and analysing the results was 12.5 h for dual photon energy machine and TPS with three different photon algorithms.

Conclusion: The proposed clinical tests proved to be useful to verify the TPS calculations with measurements and to estimate the magnitude of algorithm limitations in situations close to clinical settings. The amount of time required to perform the tests is reasonable to conduct them as a TPS dosimetrical verification audit for the number of hospitals in the region.

Imaging II

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Potential interest in integrating functional MRI (fMRI) in 3D RT planning for grade 2 unfavorable and grade 3 gliomas: first results with 10 patients

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Introduction: Among new imaging techniques potentially useful in radiotherapy (RT) of patients (pts) with brain gliomas, fMRI is supposed to add informations to conventional MRI (cMRI). Among its possibilities, fMRI could modify Gross Tumor Volume (GTV) delineation, visualize inside a low-grade glioma small focuses of higher activity (for an eventual RT boost) and identify sites essential for memory and language, to be eventually avoided, these functions being potentially altered by RT. fMRI was evaluated for pts with gliomas of intermediate prognosis, in addition with computed tomography (CT) scan and cMRI, routinely used for RT planning (RTP). The main goal was to evaluate if fMRI could modify CT / cMRI-based RTP.

Description: After biopsy / surgery, 10 pts with gr. 2 unfavorable or gr. 3 supra-tentorial glioma were entered in the study. CT scan and cMRI (T1 Gado, T2-weighted sequences) were performed in RT position. fMRI was subsequently performed in the same position using (1) a diffusion tensor imaging (DTI)-based fiber tracking technique, visualizing major white matter tracts (2) a perfusion-weighted imaging identifying higher perfused areas (3) cortical activation with memory and language paradigms. **Firstly**, only CT scan and cMRI were used for RTP, contouring of GTV was based on T1 Gado for gr. 3 and T2 for gr. 2 gliomas, organs at risks (OaR) were delineated. Then, RTP was made, optimizing GTV coverage and minimizing irradiation of OaR. Pts were treated according to this conventional RTP and baseline neurocognitive functions were evaluated before RT, then bi-annually. **Secondly**, fMRI images were analysed and used to define a « functional » GTV for comparison with the conventional one.

Results: 10 pts with a mean age of 42 yrs were included in 6 months, all with an oligodendroglioma component. First symptom was epileptic seizure in 8 pts. In 6 pts, glioma was

located in the left-temporal area with a mean size of 6 cm in T2-cMRI, 6 showed a mild signal enhancement. In 7 pts, highly active focuses were identified, within homogenous T2 hypersignal areas. In 5 patients, DTI fiber-tracking showed warped white matter fibers, strongly suggesting brain infiltration beyond cMRI images. Overall, the ballistic of RT could be potentially modified in 4 pts.

Conclusion: The preliminary results of this study strongly suggest that the entire spectrum of fMRI can play a major contribution to improve the accuracy of 3D RT in pts with non-glioblastoma gliomas.

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Workflow for the integration of biological information into radiotherapy planning

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Radiotherapy planning is largely restricted on structural images. New diagnostic imaging techniques – like MR perfusion imaging and PET – provide information about tumour microcirculation, tumour metabolism and other biological parameters, which can be used to improve detection of vital and aggressive tumour areas. This information can be incorporated into individualized safety margins and into dose optimisation. However, morphological data sets are still the gold standard in the planning of radiotherapy.

We introduce an in-house software platform for radiotherapy planning with a specific workflow, offering a standardized usage of biological images in the course of radiotherapy planning. This workflow is open for different imaging modalities and analysis methods. It comprises (a) data import from DICOM for 3D and 4D (for temporally resolved data) data sets; (b) data analysis for quantification and the generation of parameter maps, which allow the oncologist to interpret biological information with spatially resolved images; and (c) image registration based on Mutual Information to match the parameter maps with planning CT. The capability of the workflow is demonstrated exemplarily for patients with meningioma. The data for these patients were examined with a pharmacokinetic analysis of T1w DCE-MRI and with a calculation of the standardized uptake value (SUV) of DOTATOC-PET.

The pharmacokinetic analysis examines changes in MR image intensities following the injection of Gd-DTPA. Meningiomas are well perfused and show a stronger and faster contrast enhancement, compared to normal tissue. The analysis of intensity-time courses allows the quantification of kinetic parameters (visualized as parameter maps), representing different aspects of tissue microcirculation and microvasculature. With the calculation of the SUV the activity in the tissue is normalized to the injected dose. DOTATOC-PET is very sensitive in imaging meningiomas and therefore the SUV in tumour is very high. The generated parameter maps were compared to the segmentation results from clinical RT plans. The parameter maps with high perfused areas and high SUV give additional information about tumour characteristics within PTV, which have the potential to improve segmentation and dose optimisation.

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The value of respiration corrected PET for determination of the standard uptake value of FDG in lung tumors

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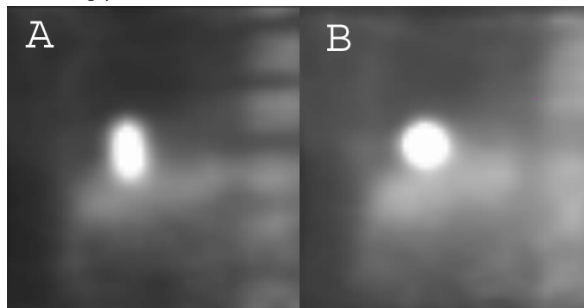
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Purpose The maximum standard uptake value (SUV_{max}) of FDG in lung tumors is a prognostic factor for response to

radiotherapy [Borst et al. Eur.J.Cancer, 2005]. However, PET images are blurred due to respiratory motion, resulting in SUV values that might be lower than the actual SUV depending on the amplitude of motion. The purpose of this study is to eliminate respiratory motion in 4D PET scans, providing a more accurate SUV estimation that predicts treatment response more reliable.

Method For 10 patients, an emission PET scan at a single bed position was acquired in cardiac gating mode. A respiratory signal from a thermo-couple placed below the nostrils was used to generate a trigger pulse to the scanner, halfway inhalation in each respiratory cycle. Between two trigger pulses data were retrospectively binned into 16 time-equidistant phase bins and reconstructed into a 4D respiration-correlated PET scan. In addition, data from all phases were used to reconstruct a single non-gated (blurred) scan. In the 4D PET scan, the tumor was manually segmented in the first phase and registered to the tumor in the subsequent phases, yielding the tumor translation as function of respiration phase. This phase-dependent translation was applied back to each phase scan, and a motion-corrected (MC) scan was created by averaging over the breathing phases [Wolthaus et al. PMB, 2005]. From the MC-PET scan the SUV_{max} was determined and compared to the value in the non-gated PET.

Results For motion amplitudes larger than 1 cm, the average SUV_{max} in the MC-PET was about 30% higher (right panel) than in the non-gated PET (left panel). For amplitudes smaller than 1 cm, the difference was up to 10%. The variation of SUV_{max} in the 16 phases was 10% (1 SD). There was no relation between the SUV_{max} and the breathing phase when no attenuation correction was used. However, for patients with the tumor close to the diaphragm, applying attenuation correction using a non-gated transmission scan resulted in SUV_{max} that showed variations up to 10% with breathing phase.



Conclusions We implemented a new and simple method for accurate determination of the SUV in PET scans of lung tumors taking tumor motion into account. The large variation in SUV_{max} indicates that measurements based on a specific single phase scan are not sufficient. The relation of SUV_{max} with the breathing phase after 3D attenuation correction indicates the need of 4D attenuation correction, i.e. as function of breathing phase.

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Respiration gated cone beam imaging and fluoroscopy at a linear accelerator

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Purpose: To study the correlation between diagnostic 4D-CT data for breathing motion with 4D-cone beam CT (CBCT) data and fluoroscopic kV-images of the same patient acquired for dose delivery at the linac. The respiratory gated CBCT and fluoroscopic images are employed to study the feasibility of tumor tracking and gated dose delivery concepts.

Material and Methods: A lung cancer patient was selected to study the correlation between diagnostic 4D-CT data and

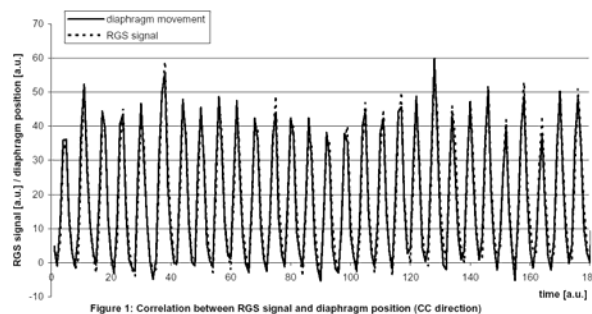
various respiratory gated images obtained in treatment position at the linac. The tracking of the patient's breathing phase was achieved with a respiratory gating system (RGS) from Anzai Medical based on a pressure sensor attached to the patient's abdominal region with a fixation belt. The linac integrated fluoroscopy and 4D-CBCT were performed with the in-line imaging approach, where an x-ray tube is mounted opposite to the treatment beam while the flat panel imager is located directly below the multileaf collimator.

Projections for fluoroscopy and CBCT were acquired simultaneously with the breathing signal of the RGS. 3DCBCTs of the patient were reconstructed for different breathing phases and compared to the respective data from the 4D diagnostic CT scanner. Furthermore, the position of the diaphragm was determined for each cone beam projection and correlated with the breathing signal of the RGS.

Results: The in-phase reconstructions of the commercial 4D-CT and the CBCT were matched with a resulting shift vector of 8 mm in CC direction and -0.3 mm in LR direction as an interfractional setup error. Also, the tumor region at the inhale and exhale phase was matched to determine the tumor motion during the image acquisition, which had increased from about 3 mm during 4D-CT acquisition to 5 mm in the 4D-CBCT. The position of the diaphragm in CC direction of each cone beam projection correlated well and stable in motion-amplitude and breathing phase with the RGS signal throughout the whole imaging process (Fig. 1). It therefore seems feasible to employ the RGS for gated dose delivery applications. As the tumor position could be identified in the fluoroscopic projections these images could be used as verification of the dose delivery.

Conclusions: The combination of linac-integrated in-line kV-imaging with the RGS seems to provide a reliable technology to monitor respiratory organ motions. The correlation between 4D-diagnostic CT data and these images might form the bases for dynamic dose delivery techniques.

Figure 1: Correlation between RGS signal and diaphragm position (CC direction)



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IGRT Clinical Experience using Siemens Primatom®

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Purpose/Objective: We report our experience in IGRT using the CT-on-rails and linac combination in one treatment room (Siemens Primatom®).

Materials/Methods: Fifty five patients were treated using IGRT based CT-on-rails imaging: 23 prostate, 20 head, 7 thorax and 5 abdomen patients. All patients had CT prior to each fraction to align for treatment. Some of these patients had CT before and after treatment to assess motion during treatment.

Of the 20 head patients we analyzed eleven patients who had stereotactic frameless radiation therapy treatments. We used IGRT to localize the isocenter and compare to orthogonal port films localization. For the stereotactic brain patients only the isocenter was verified against the bony anatomy.

Of the 7 thorax patients, we analyzed six patients for esophageal movement during their treatment. In the thorax patients, the tumor, lungs and the esophagus were contoured.

Of the 23 prostate patients, we analyzed four patients before and after the treatment to monitor patient and organ motion during treatment. The following regions of interest were identified in prostate patients: prostate, seminal vesicles, bladder, and rectum.

Results: For the stereotactic brain patients, it was observed that using a bite block inside the head cast significantly improved patient immobilization and decreased the magnitude of IGRT shifts. Orthogonal port film validation of the isocenter is adequate for an accuracy of 5mm for frameless stereotactic treatments.

We assessed the esophageal motion during lung treatments and verified that all patients had negligible esophageal motion. Greatest levels of motion are found in the anterior and towards patient's right. A maximum shift of 6.6 mm is found in one patient toward the patient's right. The average daily shifts for all the measured directions, at measured three locations, are within 1mm.

For the prostate patients the amount of inter-fraction motion was calculated by comparing the organ Center of Mass (COM) from the pre-treatment scan to the average position over all pre-treatment scans. To calculate intra-fraction motion, the position of the organ COM in each post-treatment scan was compared to its position in the pre-treatment scan. The average time between pre- and post-treatment CT scans was 28 minutes.

Conclusion: CT based IGRT provides an adequate verification of the isocenter for frameless stereotactic treatments to within 2-3mm accuracy, while esophagus motion are negligible for all clinical purposes.

The change in prostate position from the beginning of treatment to the end was measured to be at least as large as that from day to day. Systematic changes were seen during each fraction, such as bladder filling. These results could play an important role in developing techniques to manage organ motion during radiation therapy for prostate cancer.

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Comparison of set up errors measured in 2D and 3D using EPI and cone beam CT

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Introduction: This study compares bony set up error measurements made in 3D using cone beam CT (CBCT) images to measurements made in 2D using EPI. The magnitude of errors introduced by bony anatomy rotations, not accounted for in the 2D method, is investigated.

Methods: CBCT scans were acquired daily using Elekta Synergy™ immediately following treatment for fifteen patients undergoing conformal radiotherapy for prostate cancer (total 199 CBCT scans). The CBCT scans were automatically registered to the planning CT scan based on bony anatomy in order to determine set up error in terms of translations and rotations. EPI's were also acquired through the anterior and right lateral beam portals at each fraction. These were used to determine set up error in terms of translations only by manual template matching between the EPI and DRR's produced from the planning CT scan. Differences between the set up translations measured by these two methods were assessed. Possible correlations with the set up rotations as measured by the 3D method were investigated.

Results: The mean differences between the set up translations measured using the two methods were found to be less than half a millimetre in all directions. The standard deviation of the difference between the methods was 1mm in the LR and CC directions and 2mm in the AP direction. Some

patients were found to show good agreement between the two methods for all fractions, while others have large difference for all fractions. Patients with large differences tended to be those with a large systematic set up rotation. The discrepancy between the two methods was found to be significantly correlated with set up rotation for certain combinations of rotation axis and discrepancy direction. The strength of the correlation was typically 1mm per degree of rotation.

Conclusion: Systematic differences between the 2D and 3D set up error measurements were small, but the random component of the differences was significant, particularly in the AP direction. This can be explained due to the random variability of manual EPI to DRR template matching, and due to errors introduced into the 2D method by set up rotations. These errors in the 2D set up error measurement can be significant if large set up rotations are present.

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Measurement of small volumes and the partial volume effect in PET images

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Purpose: New technologies in radiotherapy enable better dose conformation to the target and therefore better sparing of normal tissue. This requires accurate tools for quantifying dimensions. PET imaging devices normally have a spatial resolution of 6 to 12mm (FWHM) and an image resolution (pixel size) of about 4mm. The purpose of this work is to improve the accuracy of reconstructed images of volumes affected by the partial volume effect.

Material and Method: The Point Spread Function (PSF) in an imaging system is a gaussian function several millimetres wide and reaches over several pixels. It can therefore be used to reconstruct the real dimension of small lesions of sub-pixel size.

A NEMA phantom with a cylindrical insert of diameter 44mm filled with F-18 (100kBq/ml) was used to measure a reference profile. The profile was used to model the PSF for the system. PET images generated by integrating the PSF of different diameters from 1 to 40mm. To cover all possible positions of the source in the PET image grid, from "centred" on a pixel to "between" two pixels of the 4.25mm image grid, the image was calculated every 0.2mm in relation within the grid.

For the evaluation these calculated PET images the profile was scaled to 100% to the peak. In an iterative process the threshold was adjusted taking into account the diameter and the position of the source but not the activity since this is unknown.

The iterative formula was verified with measurements in water using sources of different activities in various background activity and signal to background ratios.

Results: The reconstructed diameters were accurate down to 3mm. The SD increased from < 2mm (0.8mm to 1.9mm) for the standard measurement to 2.6mm (2.1mm to 2.6mm) for diameters of 5mm to 1mm. The systematic error due to the partial volume effect was reduced from 5mm to less than 0.3mm for diameters down to 3mm with the iterative measurement. The figure shows the improvement in the reconstructed diameter of up to 5mm.

Measurements in water with various activities of sources and/or background showed in a first series of measurement good agreement with the calculations down to 6-8mm. Results of cylindrical and spherical sources will be presented.

Conclusion: Using measured profiles and an iterative reconstruction, the accuracy of definition of small volumes in PET images can be improved to well below 1cm.

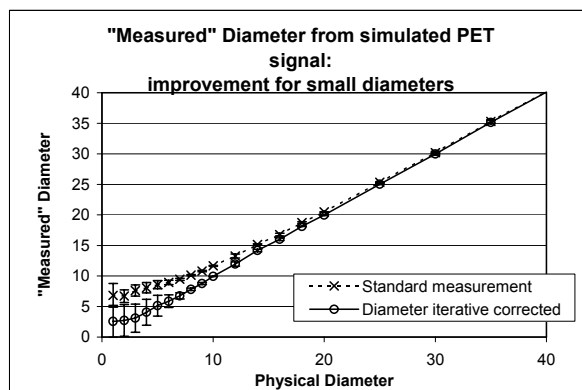


Figure: The lower curve shows the diameter measured with the iterative reconstruction. Below 3 mm the measured diameter is almost constant at 2.5 to 3mm. Without the iterative correction, a levelling off and an offset can be observed for about 15mm sources.

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Megavoltage conebeam CT to complement prostate planning CT in presence of hip prosthesis

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Purpose/Objective: The treatment plan for external beam radiation therapy is based on the delineation of the anatomy presented to the dosimetrist in the planning CT scan. However, when implanted objects of high-Z material are present, important image artifacts are generated, strongly hindering the ability to delineate some organs. This is particularly the case for the planning of prostate patients with hip prostheses. The purpose of this study is to exploit the penetrability of high-energy photons of Megavoltage ConeBeam CT systems (MVCBCT) to obtain 3D images of the anatomy in the presence of a hip replacement prosthesis in order to provide anatomical information and complement the Planning CT.

Methods and Material: A MVCBCT system integrated onto a clinical Linac was used to acquire 3D images in treatment position of 5 prostate patients with hip prostheses with exposures ranging from 2 to 8 cGy. The MVCBCT of a pelvic sized water cylinder was used to measure and calibrate the patient scatter-induced spatial cupping artifact in the CBCT. A scatter correction was then applied to facilitate the adjustment of window/levels. For each patient, the MVCBCT images were imported in the planning system and compared side by side or registered with the original planning CT. The PTV, GTV and organs at risk for prostate treatment were contoured.

Results: The presence of a hip prosthesis generates several striking artifacts that overcast the anatomical structures on a regular CT. The MVCBCT images clearly show the hip prosthesis, the bony anatomy and relevant soft-tissue structures and provide sufficient contrast to delineate the bladder and rectum. The MVCBCT image was particularly helpful for delineating the anterior rectum wall, the bladder neck and the lateral extension of the prostate in the median plane. The prostate volume contoured with the help of MVCBCT was often smaller than what could be guessed from the regular CT in presence of artifacts, preventing overdosage of the rectum. The MVCBCT image quality in the presence of the large metallic object is slightly degraded compared to the image of a regular prostate patient.

Conclusion: MVCBCT can complement missing information

and facilitate segmentation for planning purposes when hip prostheses are present. Compared to the kV energy range, the presence of high-Z material has relatively little impact on image quality of MVCBCT. The application of MV CBCT for patients with tooth fillings, dental implants or implanted gold markers in the prostate will also be discussed.

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A ray-driven approach to generate a deformed image for image-guided radiotherapy

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Purpose: To create an image in a geometrically resolved view based on deformable image registration for multi-modality, image-guided radiotherapy and augmentation of pre-treatment 3D images with prior images by resolving their geometric differences.

Methods and Material: A ray-driven approach is employed in this technique. An image voxel grid is generated for the deformed image and the image intensity values are determined by finding the corresponding voxel on the initial image, based on an assigned deformation map. A deformation map was created based on a multi-organ finite element model-based deformable registration technique, which has non-uniformly spaced node and displacement data. The deformation map is interpolated onto the image voxel grid to determine the correspondence of each voxel to the undeformed image. Several methods of interpolation were tested to determine their effect on speed and accuracy, including linear and nearest neighbor 3D interpolation and reduced 3D interpolation grids to 50, 33, and 25% followed by 2D interpolation to fill in the missing grid points. The ray-driven approach allows shear in the image deformation by permitting independence in the prior location of neighboring voxels in the final image. The interpolation effects on the

integration of the shear are substantially reduced by segmenting the nodes in the deformation map and their application to the image into the sheering components.

Results: The accuracy and time required for the image deformation depends on the interpolation method, number of nodes in the deformation map, and resolution of the image. For a constant number of nodes and image size, the time required scales linearly with increased interpolation grid precision. The loss of accuracy with decreased interpolation precision is minimal in visual observation. The percent of voxel variation between the 100% grid and 25% grid is 20 - 27%. The time required scales linearly with increasing number of nodes, with a constant image size and interpolation procedure. Real-time image augmentation can be achieved by generating a limited number of slices at a reduced interpolation grid.

Conclusions: A ray-driven approach for the generation of deformed images based on a deformation map has been described. Techniques to reduce the time burden have a minimal effect on the qualitative accuracy. Sheer and independent motion between organs is permitted, which can be important in deformable registration of the lung and breast.

Conformal RT

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A new, empirical optimisation approach to the determination of treatment margins for any source of geometrical uncertainty in radiotherapy

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Purpose: Determining treatment margins for geometrical uncertainties of moving and deformable radiotherapy targets remains a major challenge. This paper describes and applies an optimisation algorithm designed to derive such margins for individual or populations of patients.

Material and methods: The algorithm works by expanding the CTV defined in a patient's planning scan to enclose any further observed CTV positions for the patient. These other CTV positions may be the result of an inter-observer outlining study, and/or CTV positions observed during treatment using, e.g. repeat CT scanning and/or repeat electronic portal imaging (EPI). The algorithm derives margins that minimise the excess volume outside the envelope that encloses all observed CTV positions (the CTV envelope). Initially, margins are set such that the envelope is more than adequately covered when the planning CTV is expanded. The algorithm uses an iterative method where the margins are sampled randomly and then either increased or decreased randomly according to a probability level. It has been tested on a set of bladder cancer patients that underwent weekly repeat CT scanning and EPI throughout their treatment course. The algorithm can be applied to both individual patients and to a set of patients.

Results: From repeated runs on individual patients, the algorithm produces margins within a range of $\pm 1-2$ mm that lie amongst the best results found with an exhaustive search approach and agree within 3 mm with margins determined by a previously published manual approach on the same data. The algorithm can be used to determine margins to cover any specified geometrical uncertainty and allow for determination of reduced margins by relaxing the coverage criteria, e.g. disregarding extreme CTV positions, an arbitrarily selected volume fraction of the CTV envelope, and/or the patients with extreme geometrical uncertainties.

Conclusion: An optimisation approach to margin determination is found to give reproducible results within the accuracy required. The major advantage with this algorithm is that it is completely empirical and does not depend on any assumptions of the nature of the geometrical uncertainties.

The approach should therefore be particularly useful for margin determination in situations where the geometrical uncertainties are difficult to model, such as organ motion of the bladder and the rectum, and inter-observer variation in outlining of GTVs and CTVs.

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Predicting 2D transmitted dose maps using a 3D treatment planning system

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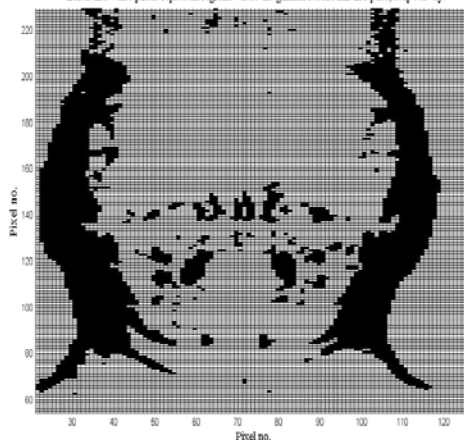
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Introduction: Patient dose verification is becoming increasingly important with new complex radiotherapy techniques such as conformal radiotherapy (CRT) and intensity-modulated radiotherapy (IMRT). An electronic portal imaging device (EPID) is a useful tool for dose verification and was modelled using a convolution/superposition based 3D treatment planning system (TPS), to calculate transmitted dose maps for comparison with measured transmitted dose maps obtained with an EPID.

Methods: The transmitted dose maps were calculated using Pinnacle³ for homogeneous, inhomogeneous and anthropomorphic phantoms. For the homogeneous study, phantoms of varying thickness were used to investigate changes in transmitted dose and were compared with equivalent EPID measurements, using the gamma method of Low *et al.* In the curved phantoms study, two different sized cylinders and a homogeneous pelvis phantom were used to simulate patient misalignment and the effects of surface curvature on transmitted dose maps. In the inhomogeneous phantom study, shifts in the position of an inhomogeneous object inside a homogeneous phantom were used to determine the spatial resolution in the position of the object. In addition, the size of the object was varied. Finally, a breast phantom and a head and neck phantom were used to further simulate patient misalignment. MLCs were also incorporated into the TPS simulations to determine the effects of misaligned leaf positions on the transmitted dose maps.

A gamma map (binary) for 2.5 mm shift in the position of the head neck phantom for 2.5 mm, 3 % pass criteria. Black and white pixels represent regions where the gamma results fail and pass, respectively.



Results: For the flat homogeneous phantoms, the calculated and measured transmitted doses on CAX agree to within 2 % (on average). More than 90 % of the points (excluding field edges) result in $\gamma \leq 1$ for 4 %, 3.8 mm pass criteria. The noise level in the transmitted dose maps is less than 0.1 % on CAX for all phantom thicknesses. Phantom thickness changes of less than 1 mm can be detected in the predicted transmitted dose maps. Phantom misalignment of at least 7.5 and 5 mm can be detected for the large and small homogeneous cylinders, respectively. For the homogeneous

pelvis phantom, about 5 mm patient shifts can be detected. The spatial resolution in the position of the inhomogeneity is less than 2.6 mm. The minimum size of the inhomogeneity along CAX that can be detected is 5 mm. For the head and neck (see figure) and breast phantoms, patient shifts of at least 2.5 mm and 5 mm can be detected, respectively. For the MLC study, 0.5 mm displacements of individual leaf positions can be detected in the calculated transmitted dose maps.

Conclusions: Pinnacle³ can be used to model an EPID for the prediction of 2D transmitted dose maps, for various phantom geometries. Phantom thickness variations, position misalignment and surface curvature were investigated, as well as changes in size and position of inhomogeneities.

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Fast Interactive Segmentation of Organs at Risk with Active Contours

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Segmentation of organs at risk is a time consuming task within radio therapy planning. In the framework of adaptive radio therapy an efficient and accurate segmentation tool is necessary for re-segmentation of verification images. Therefore we implemented an interactive segmentation tool based on the T-snakes approach.

Segmentation with snakes is interpreted as an optimization of an energy functional including terms for image features and contour properties. The Segmentation starts with an initial two or three dimensional contour template which allows for locally defined segmentation parameters. Segmentation is an iterative optimization using gradient descent. The T-snakes approach was extended by calculating the image features separately for the x- and y-direction leading to a better point distribution on the contour. This results in more accurate segmentation results and better preservation of the topology of the points during segmentation. A reparameterization of the contour during segmentation ensures the topological adaption of the contour to the image data and a uniform distribution of the points on the surface. The final segmentation result can be influenced by user-defined weighting of smoothness of the contour and its alignment to edges in the image data.

The method was tested on CT scans of the prostate region with special emphasis on the segmentation of the bladder. The segmentation tool was evaluated with respect to its accuracy and efficiency. The results show that the algorithm is capable of separating the bladder from the prostate and that it can cope with moderate image artifacts. The efficiency of the algorithm can be described by the time it takes to segment an organ at risk. With the implemented approach a bladder can be segmented within three seconds on a standard PC (3 GHz) and a 3D cylindrical template as initial contour.

The semi-automatic segmentation with the adapted snakes algorithm proved to be a flexible and fast segmentation tool for the delineation of organs at risk. It can be used for the evaluation of shape and position of organs at risk in adaptive radio therapy planning. Future work will include more elaborate template models as initial contours to further automate segmentation.

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Intra-prostatic gold markers for position-verification of the prostate gland in dose escalated external beam radiotherapy (EBRT)

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Purpose: To examine and correct for day to day movement of the prostate gland to secure safe margins in dose escalated EBRT

Methods and Materials: Under transrectal ultrasound guidance 4 gold markers were placed in the prostate gland

transperianally in local anaesthesia in 60 patients (pts). Two markers were placed ventrally and two dorsally in the right respectively left side of the prostate gland. Thereafter, the pts received EBRT to a mean absorbed dose of 78.9 Gy (74 - 80 Gy).

After performing a CT-scan for dose planning, DRR-images were used at the simulator to localise the prostate gland. On each treatment day pts were positioned by using laser alignment and reference marks on the skin. EPID- and simulation images were matched at the first three fractions of EBRT and thereafter twice a week. If alignment differed more than 1 mm in the vertical (ver) or 2 mm in the longitudinal (long) or lateral (lat) direction, the pts were moved to a position in agreement with simulation images. Thereafter, a new EPID image was taken to verify isocenter position in relation to gold markers.

Realignments and changes in mm in all three directions were recorded. Comparison of treatment delivery times between pts with and without gold markers was performed.

Results: A minimum of 1600 images were analyzed in 44 pts. 60%, 49% and 37% of the pts were realigned in the ver, long and lat directions, respectively. The frequency of movement's ≥ 5 mm were 23% (SD 3.9 mm), 20% (SD 3.4 mm) and 13%, (SD 3.1 mm) in the ver, long and lat directions, respectively. After re-evaluation of realignments, the isocenter position was found to be correct in relation to gold markers in 94% of the pts according to criteria's for movements of pts positions. There was no change in treatment delivery times between pts with and those without gold markers, although differences in treatment procedures. No complications due to implantation of gold markers were seen.

Conclusion: Intra-prostatic gold markers appear to be an accurate method to assess intra-individually differences in prostate movements during dose escalated EBRT. To secure safe margins to the prostate gland frequent matching of gold marker positioning with reference images should be performed.

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Qualitative determination of errors causing portal transit dose differences using gamma evaluation parameters

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Introduction: Electronic portal imaging devices (EPIDs) are used for patient setup verification and for detection of organ motion on a large scale. In our department, also pre-treatment and in-vivo dosimetry measurements are performed for all curative irradiations using electronic portal imagers. Based on measured two-dimensional (2-D) portal transit dose distributions, errors can be detected in treatment parameters, in machine output, and errors due to patient setup, patient shape changes and organ motion. The aim of this work was to investigate the feasibility of a qualitative automatic error detection method based on parameters from the gamma evaluation which can be used to evaluate deviations in dose and position.

Methods: A simulation study is performed where portal dose images (PDIs) are generated with homogeneous and inhomogeneous areas in the presence of noise. Perturbations due to output variations, setup errors and organ motions are imposed to the images and a gamma evaluation is applied with varying dose difference and distance-to-agreement criteria. In nearly homogeneous regions of a PDI, dose differences are calculated; in regions with dose variation, displacement is determined. In our approach, where we want to distinct between dose and position variations, output variations are determined first, then the perturbed image is corrected and displacements are detected. Because a portal dose distribution is not invariant to setup errors and organ motion, portal dose images are also simulated using a 2-D portal dose prediction model based on pencil beam scatter kernels. Using this model, changes in PDIs due to patient

perturbations could be simulated. Finally, the method to qualify errors is tested on clinical portal dose images.

Results: Using the gamma evaluation with varying criteria, a distinction can be made between errors caused by dose differences and displacement of patient or visible targets. Errors in simulated portal dose images are detected and can be qualified. Changes in portal dose distribution caused by patient or organ displacements do not influence the sensitivity of the error qualification method.

Conclusion: The method that was developed looks promising for qualitative automatic error detection. The method is currently being tested on clinical data.

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Dose calculation including uncertainty estimation

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Introduction: Modern radiotherapy includes an increasing complexity in the given fields. Fields can be shaped almost arbitrary with the MLC, and the energy fluence map can be varied with IMRT. From a verification perspective this development implies an increased need for verifications, and also that traditional verification methods becomes more difficult or unfeasible. An independent calculation tool (ICT) for MU verifications, can be an effective method to catch errors, not only from the TPS, but also introduced in for example the R&V system. When using an ICT one will find the occasions with mismatch between the TPS and the independent calculation. To be able to investigate these deviations in a uniform way at a department, there will be a need for specified levels where different actions/investigations are meaningful. A single, fix action level is not an optimal solution; the action level should instead dynamically reflect the uncertainty in the ICT calculation. Generally the uncertainty of a dose calculation is lower in geometries "close" to the reference geometry than in for example an IMRT treatment with the calculation point located off-axis.

Method: Using a large set of measured data we have developed an empirical method for estimation of the uncertainty in energy fluence per MU calculation performed with a published model. Also a semi-analytical method for estimation of uncertainty in the dose per energy fluence, for a pencil dose deposition model, has been developed. Both the calculations methods and the uncertainty estimation methods have been tested versus a set of 300 measurements in irregular MLC fields at three depths.

Result: A good agreement was found between calculated and measured doses. No deviation larger than 2% was observed. Predicted uncertainty and observed deviations was positively correlated.

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A comparison of dose escalation limits for intensity-modulated and three-dimensional conformal radiation therapy for the treatment of non small cell lung cancer

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Background: To compare the maximum level of dose escalation achievable using intensity-modulated and three-dimensional conformal radiation therapy (IMRT, 3DCRT) treatment planning for non-small cell lung cancer (NSCLC) patients, within the context of a dose intensification regime (i.e. 3 Gy per fraction).

Materials and Methods: A retrospective treatment planning study was performed on 20 patients to evaluate the potential of IMRT for achieving significantly enhanced dose intensification over conventional 3DCRT. Treatment plans were prepared for segmental multi-leaf collimated (SMLC) IMRT and compared to clinical 3DCRT plans. A set of pre-defined dose volume constraints (DVC) to the planning target

volume (PTV), spinal cord, combined lung and oesophagus were set and the maximum level of dose intensification defined as that point where further dose escalation would result in a breach of any one of the DVC's. Plans were assessed for a range of hypo-fractionated regimes from 45 Gy in 15 fractions (45/15) to 90/30. Secondary endpoints of the study included an evaluation of dose conformity and homogeneity within the PTV together with a calculation of Tumour Control Probability (TCP). Normal tissue toxicity was assessed using conventional dosimetric indices for spinal cord, oesophagus, combined lung and heart.

Results: The mean dose intensification level obtained for IMRT was 81/27 compared to 75/25 for 3DCRT (p=0.018). Dose intensification was achieved to 90/30 in 70% of patients using IMRT planning compared to 40% for 3DCRT. IMRT distributions were significantly more conformal than 3DCRT with a concomitant loss in homogeneity. TCP values were significantly enhanced for IMRT (47 vs 35% p=0.04). Equivalent dosimetric data was observed for spinal cord, oesophagus and heart despite increased dose intensification in the IMRT arm. Significant organ sparing was observed for 3DCRT in the combined lung but IMRT values obtained were below current clinical tolerances.

Conclusion: Significant dose intensification can be achieved using IMRT treatment planning. TCP's are improved and normal tissue toxicity is equivalent or below limits of current clinical acceptability.

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Registration of Megavoltage and Kilovoltage images for automated setup verification on Electronic Portal Imaging Device (EPID) Images

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Introduction: In radiotherapy accurate patient set-up is required for optimal treatment. Accurate set-up is realised by registration of images obtained during treatment (EPID) and treatment preparation (CT). Registration problems occur because of the different beam qualities used for EPID and CT (Megavoltage (MV) and Kilovoltage (KV), respectively), resulting in reduced visual contrast and signal-to-noise ratio with MV imaging during treatment. In practice the registration process at MAASTRO clinic is performed by a human expert (trained technician) by overlaying manually-contoured features of the DRR on the EPI. A fast and accurate method for automatic image registration will improve the quality of the procedure and decrease the workload.

Materials and methods: The automatic registration of KV and MV images is tested with two methods: normalized cross-correlation (NCC) and mutual information (MI). Images are pre-processed by means of several combinations of histogram equalization, unsharp masking (15x15 kernel), smoothing (Daubechies-4 wavelet), and edge enhancement (Haar wavelet). Either the pre-processed images or their wavelet spectrum representations are automatically registered using NCC or MI. For the experiments a database of 77 image pairs of the AP view of the pelvis is used. The performance is evaluated through a comparison with manual-registration data.

Results: As a measure of registration quality, we determine the Euclidian distance between the automatic and manual match. For every method the mean distance, sd, and outliers are calculated. Outliers are registrations with a distance ≥ 8 pixels (px). The wavelet method yields the best results. This method pre-processes the KV and MV images with smoothing and wavelet-based edge enhancement and automatic registration of the wavelet-spectrum representations by NCC, resulting in a mean distance of 5 px (SD 3, outlier percentage of 12 %). The second-best method uses pre-processing by histogram equalization followed by unsharp masking and again histogram equalization and registration

with MI in the image domain yielding a mean of 5 px (SD 3, outlier percentage 16 %).

Conclusion: We have obtained stable and reliable automatic registration using a wavelet approach. We expect further improvement of automatic-registration performance by employing alternative mother wavelets and/or thresholding in the wavelet domain. Rotation-invariant registration is currently implemented to improve performance.

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Requirements for the use of an atlas-based automatic segmentation for delineation of Organs at risk (OAR) in conformal radiotherapy (CRT): quality assurance (QA) and preliminary results for 22 adult patients with primary brain tumors.

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Introduction: In collaboration with the Dosisoft company, within the European project "MAESTRO", the assessment in clinical context of an anatomical atlas developed for the brain by INRIA (Institut National de Recherche en Informatique et en Automatique) was initiated. The principle of an atlas-based automatic segmentation (ABAS) is of great interest for OAR delineation in CRT: it provides an automatic segmentation of these OAR from registered multimodality images. Thus, numerous and complex processes are involved before the medical use for CRT. To ensure the reliability of the final result, the whole process must be assessed independently. We describe preliminary results for adult patients with brain tumors using the ABAS technique.

Description: Four steps are identified as crucial. Quality control of : (1) imaging devices: Computed Tomography (CT) scan, T1-weighted MRI with Gadolinium-contrast injection (2) data transfer integrity: image geometry, grayscale values, etc... (3) virtual simulation software: RT related parameters (4) brain multimodality image registration (CT, MRI). For steps (1) to (3), controls can be performed following the most relevant items of existing protocols (AAPM reports n°28, 62 and 83). In this work, we focus on the step (4) which is the initial stage of the ABAS technique. The controls of step (4) are performed on a suitable phantom. After that, the ABAS is assessed by expert clinicians on adult patients referred for CRT of their primary brain tumors.

Results: Results concerning the QA of brain image registration will be presented. Thus, the use of the ABAS will be presented for a series of 22 consecutive patients treated in the last 3 months: 11 high grade gliomas, 7 unfavourable low grade gliomas, 4 meningiomas, (either resected or biopsied). The feasibility was excellent: all the labelled structures were segmented within the T1 MRI images, the average time to perform the automatic segmentation of brain structures was 10 minutes (6 to 13 min). The evaluation of the quality of this automatic delineation is ongoing, based on the comparison of OAR volumes obtained by manual and automatic delineation.

Conclusion: the use of an ABAS needs to be accurately controlled following strict QA procedures. Preliminary results are encouraging for a large spectrum of adult primary brain tumors. Next step will consist in a detailed quantitative assessment of the accuracy of this automatic delineation.