of the Yorkshire Cancer Network. PPM, an in-house electronic patient record, has recorded all cancer treatment delivered since 2003 and through links to local and national demographic services is able to relate this to patient outcome. PPM was therefore used to identify patients undergoing external beam radiotherapy in which treatment intent was recorded as radical, adjuvant or palliative. Median survival and cumulative mortality at 7, 14, 30, 60 and 90 days was calculated with comparisons made by year of treatment, treatment intent and the number of fractions of radiotherapy used.

Results: Between Jan 2004 and Dec 2010 a total of 40,607 courses of radiotherapy were delivered with validated survival data on 40,593 (99.9%). Treatment intent was recorded as radical, adjuvant and palliative in 12,045 (30%), 11,757 (29%) and palliative 16,791 (41%) respectively. Median survival and cumulative mortality for each subgroup is shown in the table.

Intent	Median survival (months)	Cumulative mortality (%) at time point (days)				
		7	14	30	60	90
Radical	58 months	0.1	0.3	1.1	3.0	4.8
Adjuvant	85.3 months	0.0	0.0	0.2	0.8	1.7
Palliative	5.1 months	1.3	4.4	12.0	24.5	34.2

No significant differences were observed between each treatment year. The observed 30 day mortality for palliative patients according to fractions received was 16.1% for a single, 9.0% for 2−5, 3.7% for 6−10 and 2.4% for 11−20 fractions respectively.

Conclusions: This large dataset demonstrates reassuringly low 90 day mortality for radical and adjuvant patient groups. The 30 day mortality for palliative patients and the subset analysis of mortality by fractions given, supports appropriate selection of patients for palliative radiotherapy.

2036 POSTER

Voxel Based Analysis of Dose for Prediction of Urinary and Rectal Toxicity in Prostate Cancer Radiotherapy

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Background: In prostate cancer radiotherapy the models for prediction of side effects on the ogans at risk (bladder, rectum) are traditionally based on the dose volume histograms (DVH), (NTCP) computed at an organ-basis during the planning step. However, since these models lack spatial accuracy, they may be inappropriate to explain toxicity events related with the local distribution of the dose.

Purpose: To investigate the relationship between toxicity events in bladder (GRAD>2 in two years) and rectum (bleeding in two years) and the dose spatial distribution in prostate cancer radiotherapy. We propose a new voxel based statistical analysis framework, including a non rigid mapping of 3D dose distributions to a common template.

Methods: We selected 121 prostate cancer patients treated with external radiotherapy. Clinical outcomes (rectal bleeding and urinary toxicity GRAD>2) within a two year follow up and 3D dose distributions were available. For each patient the dose was computed on the 512x512x256 pelvic CT scans, using the manual delineations, according to the standard clinical protocol. We first mapped the organs and the dose to a common template using a hybrid organ/intensity non rigid registration method, allowing to align barycentres and neighbouring structures across the population. Finally, two sample t-tests were performed at a voxel-basis leading to the computation of three dimensional maps for both, the dose differences and the p-values. Two comparisons were performed, namely rectal bleeding (20 individuals) vs non bleeding (44 individuals) and urinary toxicity(21 individuals) vs non toxicity (51 individuals). Anatomical regions were the differences were statistically significant were identified and correlated with the corresponding toxicty event.

Results: 3D Dose difference and p-values maps suggest that there is a strong correlation between a higher dose delivered to the organs at risk and the toxicity events. More importantly, the method allowed to highlight the specific regions where the dose was delivered and produced the organ damage. (81.99% of the voxels for the rectum and 50.24% for the bladder).

Conclusion: We proposed a new voxel wise statistical models of toxicity which allows to explain the risks associated with the dose spatial distribution in case of toxicity. The new model may help to find accurate relationships between local dose distribution and the damage to the and organs at risk.

2037 POSTER

Principal Components Analysis of Dose Distribution for Characterizing Toxicity in Prostate Cancer Radiotherapy

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Background: Although image guided radiotherapy (IGRT) is one the most indicated treatment for prostate cancer, severe complications may appear as a consequence of high delivered doses to the neighboring organs at risk, namely the bladder and the rectum. The prediction of this toxicity events are commonly based on clinical data and dose volume histograms through the models such as the NTCP. However different spatial dose distributions may produce the same toxicity prediction using NTCP models and new models for analyzing dose distributions are needed.

The purpose of this work is to study the underlying characteristics of the 3D dose distributions, using a voxel based Principal Component Analysis (PCA), across a population of 120 patients treated for prostate cancer. This method allows to build appearance models of dose and to extract meaningful features that may be used in a further classification step in order to separate individuals with dose related toxicity events.

Data and Methods: 120 patients treated for prostate cancer with external radiotherapy were selected. Their 3D CT scans and planned doses were non-rigidly registered towards a single template based on a hybrid organ/intensity demons algorithm. Thus, all the doses corresponded voxel to voxel to the same anatomical structure. We then applied the PCA method across the whole population, considering each voxel of the warped dose as a feature. The PCA generative model of dose allowed us to decompose them into a new orthogonal space representing the directions where their variation was more significant, therefore reducing the representation of the whole dose distributions to only some features. Using the main eigenvalues, each individual was projected as a point into a new basis leading to a compact representation of the doses. A further classification method may be used to cluster the population into toxicity/non toxicity individuals based on the planned dose distribution.

Results: Reducing the voxel space from 5'954 625 features to only 75 main eigenvalues allowed us to represent the 90% of the dose variation across the whole population. Using these features, for example, we predicted rectal bleeding with a specificity of 62%, and urinary toxicity with 52% of specificity with a simple classifier such as k-means.

Conclusion: PCA Analysis allows to decompose dose distributions and to identify the most meaningful features to further classify individuals with toxicity. Further validation with different models is in progress as well as the implementation of better classifiers and non rigid registration methods to improve the specificity.

2038 POSTER

Investigating the Associations Between Late Rectal Morbidity and Simulated Rectal Motion

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Background: Rectum is the main dose-limiting organ in radiotherapy (RT) of prostate cancer (PC). The motion of this organ is extensive which leads to uncertainties in the rectum dose-volume histogram (DVH). This is likely to also influence the associations between rectal DVHs and morbidity. The aim of this study was to investigate the associations between motion-inclusive rectum DVHs and late rectal morbidity and compare to the static DVH as obtained from the treatment planning CT.

Method and Materials: Late rectal morbidity was defined as late gastro-intestinal (GI) toxicity according to the RTOG scoring system in 232 PC patients previously treated to 70 Gy with conformal RT. Rectal motion was simulated over the 35 treatment fractions assuming normally distributed translational random and/or systematic motion of different magnitude by changing the standard deviations (SDs) in steps of 0.1 cm (σ=0.1−1.0 cm). The motion was simulated in both isotropic and anisotropic (anterior-posterior) direction. The associations with dichotomized GI toxicity investigating patients with vs. without GI grade $\geqslant 2$ and the motion-inclusive DVHs as well as the static DVH was explored using Spearman's rank correlation coefficient.

Results: Overall, increased associations with rectal morbidity were obtained for intermediate doses (40−60 Gy) with the motion-inclusive DVHs over the static DVH. These associations peaked with randomly applied motion. For combined random and systematic motion the associations were

somewhat lower and much lower for systematic motion applied alone. In addition, anisotropic random motion provided stronger associations than the static DVH at high doses (70 Gy).
Conclusion: A simple model for rectal motion has been presented and the corresponding motion-inclusive DVHs have been investigated in relation to rectal morbidity. The motion-inclusive DVHs provided a stronger association with rectal morbidity as compared to the static DVH alone.

2039 POSTER

Clinical Validation in Phantoms and Patients of a 4D-CT Based Method for Lung Ventilation Measurement

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Background: Lung cancer patients referred to radiotherapy (RT) often present with regional lung function deficits, and it is therefore of interest to image their lung function prior to treatment. In this study a method was developed that uses a deformable image registration (DIR) between the peak-inhale and peak-exhale phases of a thoracic four-dimensional CT (4D-CT) scan to extract ventilation information. The method calculates the displacement vector fields (DVFs) resulting from the DIR using the so-called Jacobian map approach and applies this to extract information regarding regional lung volume change.
Materials and Methods: The DVFs resulting from DIRs were analysed to compute the Jacobian determinant of vectors in the field, thus obtaining a map of the vector gradients of the entire registered CT image, i.e. voxel-wise local volume change. Geometric and quantitative validation was achieved using images of both phantoms and patients. In the phantom studies, translations and deformations of known size and direction were introduced to validate both the DIR algorithm and the method as a whole. Furthermore, five patients referred to receive stereotactic body RT (SBRT) underwent two 4D-CT scans while immobilised in a stereotactic body frame (SBF): One scan was acquired with respiration restricted by an abdominal compression plate and the other scan under free breathing.
Results: In the phantom studies deformation errors were found to be of the order of the expected precision of 3 mm, corresponding to the image slice distance, in lateral and vertical directions. For the longitudinal direction a more pronounced discrepancy was observed, with the algorithm predicting displacement lengths of less than half of the physically introduced deformation. Qualitatively the method performed as expected. In the patient study an inverse consistency test showed deviations of up to 6 mm, i.e. almost twice the image slice separation. Jacobian maps of the patient images indicated well-ventilated areas as anatomically expected.
Conclusion: The established method provides a means of using a (commercially available) DIR algorithm to obtain a quantitative measure of local lung volume change. With further phantom and patient validation studies, quantitative maps of specific ventilation should be possible to produce and use in a clinical setting.

2040 POSTER

Adequacy Evaluation of GyE Using the Incidence of Late Skin Damage After Proton or Carbon Ion Radiotherapy for Patients Received With Total Prescribed Doses of 52.8 GyE/4fr or 64 GyE/8fr

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Purpose: Particle radiotherapy using proton and carbon-ion beams can theoretically produce a superior dose distribution to the target using the sharp distal falloff of the Bragg peaks. In addition, proton and carbon-ion beams have moderate (RBE = 1.1 in proton) or high relative biological effectiveness (RBE = 2−3.7 in carbon-ion beams depending on the depth in the spread-out Bragg peak), so a therapeutic advantage can be expected. But, in clinical situation, prescribed dose is identified as gray equivalent (GyE), which is the physical dose multiplied by the RBE of carbon ions or protons. And the RBE was determined by in vivo study using regenerating jejunal crypts of mice and in vitro study using colony formation assay of human salivary gland cancer cells. We irradiate patients by prescribed doses expressed in GyE that are directly related to photon doses under the assumption that all tissues are judged to have approximately the same RBE for carbon ions or protons.
Hyogo Ion Beam Medical Center (HIBMC) is the only medical institution where both proton (PRT) and carbon-ion radiotherapy (CiRT) are available. Skin is one of organ at risk in the treatment of particle radiotherapy. The purpose of this study is to investigate the incidence of late skin damages after PRT and CiRT limiting the same protocols of 52.8 GyE/4fr or 64 GyE/8fr and to evaluate the adequacy of GyE to the skin.
Methods: From June 2005 to July 2008, 179 skin regions of 158 patients received PRT in 50 or CiRT in 129. These patients, 118 males and 61 female, aged 36−91 (median 71) with various tumours including liver cancer in 84 (47%), lung cancer in 70 (39%), bone & soft tissue sarcoma in 17 (10%), others in 8 (4%), were followed after the therapy at least for more than a year.
One hundred thirty-four regions received a total prescribed dose of 52.8 GyE/4fr (PRT in 27 or CiRT in 107), and 45 received 64 GyE/8fr (PRT in 23 or CiRT in 22). Maximum skin doses were ranging from 5.3 to 64.0 GyE (31.7 GyE), and percent maximum skin doses to prescribed doses (%MAX_SKD) were 10–105% (60%). In spite of the retrospective study, there was no difference between PRT and CiRT regarding age, sex, PS, PTV, %MAX_SKD, fraction doses to the skin, biologically effective dose at an α/β ratio of 3 GyE at skin (BED3(skin)), and skin region except for the number of ports. Late skin damage was assessed by RTOG late morbidity scoring system. The median duration of follow-up was 25 months (range, 12−51 months).
Results: The incidence of late skin damage of grade 3 was in 8 regions (4.5%) and of grade 4 in 7 (3.9%) in all cases. In 52.8 GyE/4fr group, there was no difference ($p = 0.3073$) of the incidence of severe grade 3−4 late skin damage between PRT in 3 regions (11.1%) and CiRT in 6 (5.6%). In patients with 64 GyE/8fr, there was also no difference ($p = 0.9534$) between PRT in 3 regions (13.0%) and CiRT in 3 (13.6%).
Conclusion: These analyses showed no significant difference in the late skin reactions between PRT and CiRT in the same treatment protocols of 52.8 GyE/4fr or 64 GyE/8fr and concluded that it is adequate to use the GyE to the human skin for either PRT or CiRT.

2041 POSTER

The Impact of Metabolic Tumour Volume Parameters in Predicting the Treatment Outcomes of the Patients With Locally Advanced Pharyngo-laryngeal Cancer

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Background: To evaluate the impact of metabolic tumour volume parameters in tumour control of locally advanced pharyngo-laryngeal cancer (PLC) received radiotherapy and chemotherapy.
Material and Methods: Between June 2006 and December 2007, 60 newly-diagnosed non-metastatic PLC patients, who completed definitive intensity modulation radiotherapy, chemotherapy, and pre-treatment PET-CT scans. Metabolically active tumour regions were delineated based on pre-treatment PET-CT scans and CT simulation images. The optimal cutoff values of SUV_{max} and total lesion glycolysis (TLG) were determined by receiver operating characteristic (ROC) analysis.
Results: There were 97% males with median age of 39 years old and 65% of the patients were in Stage IV (Stage IVa:45% and IVb: 20%). The 2-year overall survival (OS) rate was 62.7% in stage III, 27.6% in stage IVa, and 25% in stage IVb ($p = 0.033$). The 2-year disease free survival (DFS): stage III 87.7%, stage IVa 33.9%, and IVb 33.3% ($p = 0.004$). The optimal cutoff values were 126 for the TLG of primary tumour (TLG-T), 19 for TLG of largest lymph node (TLG-N), 13.6 for SUV_{max} of primary tumour (SUV_{max}-T), and 7.1 for SUV_{max} of the largest lymph node (SUV_{max}-N). Patients with lower TLG-T and TLG-N were with significantly better 2-year DFS rate (69.5% vs. 31.5%, $p = 0.000$; 62.1% vs. 33.3%, $p = 0.004$, respectively), but there were no significant difference in OS ($p = 0.067$; $p = 0.463$). SUV_{max}-T did not influence the OS ($p = 0.463$) or DFS ($p = 0.062$). Primary tumour size was also analyzed for the DFS ($p = 0.001$) and OS ($p = 0.08$). On multivariate analysis, the independent predictive factors for DFS were the TLG-T ($p = 0.004$), SUV_{max}-N ($p = 0.016$), and stage ($p = 0.058$).
Conclusions: TLG-T and SUV_{max}-N were the significant predictors of disease free survival. Before entering definitive CCRT, the stage IVa and IVb group with lower TLG-T could be identified as a good candidate for the larynx preservation. Comparing to stage and SUV_{max}, TLG serves as a better reference in predicting the treatment response.