Are mean lung dose and changes in respiration during RT predictive for pulmonary function changes after RT?

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Purpose/Objective: Radiotherapy (RT) of lung cancer patients could be improved if patient specific dose tolerances can be estimated during the first weeks of a fractionated treatment course. Such tolerances may be estimated from the delivered dose distribution and changes in ventilation and respiration patterns extracted from frequently recorded 4D-Cone Beam CT.

Materials and Methods: This is a study of 140 non-small-cell lung cancer (NSCLC) patients, which were treated with 60-66 Gy in 30-33 fractions. Measures of ventilation were generated by the freeware tool elastix (http://elastix.isi.uu.nl/), which was used for deformable registrations between inspiration phases and expiratory phases as well as calculation of Jacobian determinant images of Elekta XVI 4D-CBCT reconstructions. Approximately 3000 recorded XVI scans were available for this study group. The mean of the Jacobian determinant (MJD) within the healthy lung region was used as a measure of the overall lung ventilation during the treatment course. Amsterdam Shrouds of the 4D-CBCT projections were generated by RTK-software, and the respiratory period (ReP) was estimated from the extracted respiratory signal. For each patient the slope of linear fits of MJD and ReP values vs. fraction number for the first 10 fractions as well as for the full number of fractions were used as measures for ventilation and respiration changes during RT. Relative changes (after/before-1) in forced expiratory volume in 1 second (FEV1) and forced expiratory vital capacity (FVC) before and after the treatment course were chosen as clinical endpoints ($\Delta$FEV1 REL and $\Delta$FVC REL) respectively as dependent variables with the co-variables MJD-slope, ReP-slope and mean lung dose (MLD).

Results: The deformable registrations and calculating MJDs as well as estimating RePs from Amsterdam Shrouds were carried out successfully for all the 140 patients. In the multivariable analysis only MLD was significant in relation to $\Delta$FEV1 REL and $\Delta$FVC REL respectively. Plots of $\Delta$FEV1 REL and $\Delta$FVC REL as a function of MLD are shown in the figure. Both plots show a declining tendency, indicating that higher MLD corresponds to larger decrease in clinically measured lung function tests. Spearman correlation coefficient between $\Delta$FEV1 REL and $\Delta$FVC REL versus mean lung dose were -0.249 (p=0.003) and -0.252 (p=0.003), respectively.

Conclusions: In this study it was possible to carry out the deformable registrations on the 4D-CBCT-scans, but for the current 4D-CBCT image quality, it was not possible to show an association between changes in mean Jacobian or respiration period during RT with changes in FEV1 and FVC.

PO-0917
Predicting radiation-induced patient-reported genitourinary toxicity in four prostate cancer cohorts

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Purpose/Objective: Genitourinary (GU) toxicity following radiotherapy (RT) for prostate cancer involves the interplay between various symptoms. Commonly used toxicity scoring systems capture a subset of GU symptoms only. The purpose of this study was to investigate the wider range of GU toxicity as reported by patients (atomized patient-reported outcomes), how such symptoms interact, and to what extent their occurrence can be explained by the urinary bladder dose.

Materials and Methods: We applied factor analysis (FA) to group 35 patient-reported GU symptoms in four prostate cancer cohorts (N=1009). The investigated cohorts included patients that were previously treated for localized prostate cancer with either primary or salvage external beam RT (EBRT), or EBRT combined with brachytherapy at two centres during 1993-2007 (time to follow-up: 1-14 years; average age at RT: 64-70 years). Prescribed dose was 70-78 Gy in 2 Gy fractions. Relationships between maximum or mean absorbed dose (Dmax or Dmean; population median of D mean: 49-54 Gy) to the urinary bladder and single/joint symptoms in the identified symptom groups were investigated for patients treated with primary EBRT using logistic regression and receiver operating curve analysis, quantifying the area under the curve (AUC).

Results: Three distinct symptom groups, labelled Incontinence, Obstruction, and Urgency were consistently identified across all cohorts. For patients treated with primary EBRT, Dmax predicted multiple joint symptoms of Urgency (p=0.02; AUC=0.73), and one single or two joint
symptoms of Incontinence (p≤0.04; A<sub>z</sub>=0.59, 0.61). D<sub>mean</sub> predicted one single or two joint symptoms of Urgency (p=0.05; A<sub>z</sub>=0.57, 0.63).

Conclusions: Based on a large number of atomized GU symptoms and a large number of patients treated at two centres, our results suggest that bladder maximum dose is particularly critical for patient-reported urinary incontinence and urgency after primary EBRT for localized prostate cancer. These findings together with a more comprehensive modelling approach have the potential to further improve our understanding of the complex dose-response of the GU tract.

PO-0918
Interruptions management in radiotherapy treatments: three years of experience
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Purpose/Objective: The prolongation of the overall treatment time (OTT) has influence in the control probability for certain type of tumours [1,2]. We develop a program to register interruptions that occur during the treatments and a protocol to compensate them with the help of a database. In this work we show the main results of applying these procedures during 42 months.

Materials and Methods: We use Microsoft Access 2007© software to create a database of the treated patient. The more important fields are: demographic data, the ICD code of the disease, number of fractions and the dose per fraction, starting treatment date, the date in which the treatment should finish and the real ending date. If an interruption occurs, we register: the reason, the starting date and the ending date of it. The treatments were classified in three growing categories of prioritising according to the need to manage interruptions, using the criteria of [3]. In our protocol we try to keep the OTT for category one and prostate cancer according to [2] with the use of compensatory measures, these are mainly: give two sessions in the same day or one fraction with an equivalent dose of two fractions. The category two is compensated with increased total dose. We made a general analysis of the results of the interruptions management with the protocol described previously. In addition we categorized the treatments by their duration (CD): [0-10], [11-15], [16-28] and [29-40] treatment days and we obtained the average prolongation days (APD). Finally we studied the benefits of applying this protocol to different tumor sites: head and neck (HN), lung, cervix and breast (local control rate), and prostate (biochemical failure) using the data of [1] and [2].

Results: We analyzed 1893 treatments, 82.3% suffered an interruption with APD = 4.58, (4.37, 4.79) days, CI(95%). 31% of the interruptions had some kind of compensatory measure. The upper panel of the figure shows the APD for each one of the CD categories, the x-axis represents the treatment days median value of the category. The graphic shows a linear behavior with the total treatment days. This fact, and the high percentage of treatments that are interrupted, make necessary to take preventive actions for category 1 cases.

The table show the absolute increase in TCP for each tumor site if we only include the compensatory measure to keep the OTT, column 1, and the column 2 is the result including all compensatory measures. In parentheses is the quantile of patients who have a benefit bigger than 4%. The HN and prostate treatments have a high APD because their highest duration (upper panel of figure), therefore the protocol pays special attention to these pathologies and the benefits are greater. The contrary occurs to breast cancer. The lower panel of the figure shows the histogram of the benefit in local control rate for HN patients.

Conclusions: A compensatory measures program implementation improves the output of the treatments, especially in the HN.