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Purpose/Objective: Gastrointestinal (GI) toxicity following radiotherapy (RT) for prostate cancer involves the interplay between various GI tract structures and symptoms. The purpose of this study was to further improve our understanding of the wider range of GI toxicity by studying the relationship between dose to various segments of the GI tract and patient-reported outcomes in four previously identified symptom groups, labelled *Leakage*, *Mucous*, *Pain*, and *Urgency*.

Materials and Methods: The three cohorts investigated in this study were previously treated for localized prostate cancer with primary or salvage external beam RT (EBRT or POSTOP) at two centres in 1993-2007 (N=681; time to follow-up: 1-14 years; average age at RT: 64-70 years). Prescribed dose was 70-78 Gy in 2Gy fractions. Relationships between maximum or mean absorbed dose (D_{max} or D_{mean}) to the most caudal 4 cm of the sigmoid colon (SC), the rectum (R), the anal sphincter region (AS), or combinations thereof (SC+R, SC+AS, R+AS, SC+R+AS), and single/joint symptoms in the previously identified symptom groups were investigated using logistic regression and the area under the receiver operating curve (A_z). The symptom groups were based on factor analysis results (59 symptoms in total, two centre-specific questionnaires (Q1 and Q2))[1].

[1] XX, et al. *Identifying groups of patient-reported gastrointestinal symptoms using factor analysis*, XX 2014.

Results: Among the statistically significant relationships identified between dose to single/joint structures and symptoms ($p \leq 0.05$; *Fig.1.*), *Leakage* was best predicted by AS D_{mean}, or AS+R and AS+R+SC D_{max} (A_z=0.68-0.73), and *Mucous* by AS D_{max} (A_z=0.67) or D_{mean} (A_z=0.62). *Pain* was best predicted by AS and AS+SC D_{max} (A_z=0.69), or AS+R, R+SC, and AS+R+SC D_{mean} (A_z=0.62) whereas *Urgency* was best predicted by AS and R D_{mean} (A_z=0.58-0.78), or R and R+SC D_{max} (A_z=0.62).

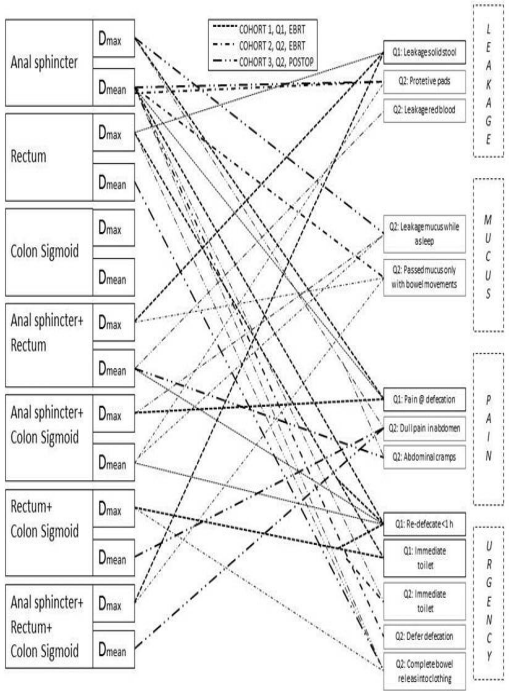

Fig.1. Significant relationships ($p \leq 0.05$) between dose to the GI tract and the four GI symptom groups in the three investigated cohorts with the stronger relationships in thicker lines (highest A_z symptom group and cohort. Abbreviations: D_{max}: maximum absorbed dose; D_{mean}: mean absorbed dose; Q1: data from questionnaire 1 (Centre 1); Q2: data from questionnaire 2 (Centre 2).

Conclusions: Our patient-reported outcome-based findings suggest that the anal sphincter, alone or in combination with other segments of the GI tract, is a key structure for a majority of the investigated GI symptoms. Sparing of the anal sphincter region, as defined separately from the rectum, has the potential to further reduce GI toxicity and increase the overall quality of life following RT for prostate cancer.

PO-0907

TCP modeling in a large cohort of NSCLC patients inclusive of geometric uncertainties

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Purpose/Objective: Tumor control probability (TCP) model parameters for NSCLC have been only obtained from outcome data of conventionally or SBRT regiments thus far. Moreover, TCP model parameters in the literature were typically derived using the CTV prescription dose or dose-volume histograms (DVHs) which do not reflect the presence of geometric uncertainties, especially in SBRT where the dose heterogeneity is often high. In this study, GTV and PTV DVHs and local control data of both conventional and SBRT treatments were used to derive optimal TCP model

parameters, including geometric uncertainties, from a large cohort of patients.

Materials and Methods: Multi-institutional data of 693 NSCLC patients of which 530 SBRT (stage-I) , and 163 treated with concurrent chemoradiation (CCRT) with volumetric image guidance in all fractions with DVHs of PTV and GTV and their corresponding local control rates at two year were available for this analysis. The prescription dose in the CCRT regiment was 24x2.75Gy with daily low-dose Cisplatin. The sensitizing effect of chemotherapy was accounted for in the TCP model by using a correction factor of 1.17 to total surviving fraction of cells at the end of treatment. In the SBRT patients, doses varying from 37.5 to 60 Gy were delivered in two to 10 fractions. The median follow-up was 1.13 and 1.5 years respectively in the CCRT and SBRT regiments. In method one of this study, the DVH and volume of the GTV is used to estimate the population average radiosensitivity ($\bar{\alpha}$),its standard deviation (σ_α) and equivalent uniform dose (EUD) 'a' parameters in the 'Marsden TCP' model. In method two, the dose of the PTV and the volume of the GTV (to calculate the total clonogens in the GTV) were used to account for day-to-day geometric uncertainties. The α/ß value and clonogen density was fixed to 10 Gy and 1e7 cells/cc respectively in both methods. The two methods were compared with the Akaike information criterion (AIC). To test the validity of the combined SBRT+CCRT TCP modeling, these two regiments were also modelled with separate $\bar{\alpha}$, σ_α and 'a' parameters. The likelihood-ratio test was used to calculate the p-value between the separate and combined models.

Results: The best-fit parameters are given in table 1 along with their 95% confidence intervals calculated with profile-likelihood method for both methods. The $\bar{\alpha}$, σ_α are almost equal in both methods while the EUD 'a' parameter approaching PTV mean dose and GTV minimum dose. The PTV based model was superior to the GTV based model with an AIC difference of 32.8 units. Separate analysis of SBRT and CCRT did not yield a superior TCP model (p=0.28).

Table 1: Best-fit TCP model parameters and their corresponding NML & AIC with 95% CIs

Parameter	GTV Vol + PTV Dose	GTV Vol + GTV Dose
$\bar{\alpha}$ (Gy^{-1})	0.38(0.32-0.45)	0.38(0.33-0.39)
σ_α (Gy^{-1})	0.18(0.14-0.26)	0.18(0.15-0.19)
a (EUD)	-0.3(-1.1-∞)	-17.0 (-35- 10)
NML	-0.27	-0.29
AIC	375.9	408.7

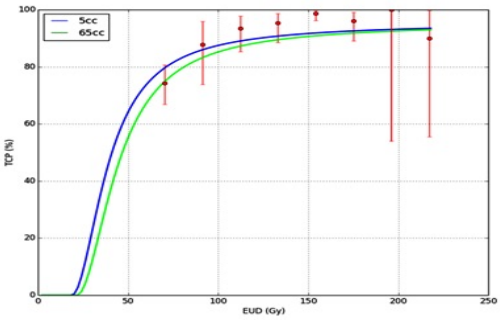

Figure 1. Dose-response curves with the obtained TCP model parameters and the actual clinical outcomes with 95% confidence intervals in conventional and SBRT treatments with a small (SBRT) and a large (conventional) tumour volume

Conclusions: The tumor control probability of chemoradiation and SBRT regiments were successfully described by a single model. Separate analysis of chemoradiation and SBRT regiments did not improve the model. An EUD approaching the PTV mean dose best described the TCP indicating that geometric uncertainties play a role despite accurate image guidance.

PO-0908

Corpora cavernosa dose and patient-reported sexual dysfunction in prostate cancer radiotherapy

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Purpose/Objective: Dose-response modelling of sexual dysfunction after radiotherapy (RT) for prostate cancer has so far mainly focused on relationships between dose to the penile bulb (*PB*) and erectile dysfunction. However, radiation-induced sexual dysfunction involves the interplay between various symptoms and critical structures. In this study we hypothesized that dose to the corpora cavernosa (*CC*), alone or in combination with the *PB* (*CC*+*PB*), better explains the occurrence of interacting symptoms on sexual dysfunction than dose to the *PB* exclusively.

Materials and Methods: To identify interacting symptoms, i.e. symptom groups, we applied factor analysis (FA) to 16 patient-reported symptoms on sexual dysfunction in three cohorts (N=372). The investigated subjects were previously treated for localized prostate cancer either with primary or salvage external beam RT (EBRT or POSTOP), or EBRT combined with brachytherapy in 1993-2006 (time to follow-up: 1-14 years; average age at RT: 64-70 years). Prescribed dose was 70 Gy@2.0 Gy/fraction. The ability of maximum and mean absorbed dose (D_{max} or D_{mean}; population median of D_{mean}: *CC*=50 Gy, *PB*=67 Gy, *CC*+*PB*=51 Gy) in *CC*, *PB*, and *CC*+*PB* to predict single/joint symptoms in identified symptom groups was studied for EBRT and POSTOP (logistic