Purpose/Objective: To assess clinical and dosimetric factors affecting acute urinary toxicities on a large cohort of patients treated with external beam radiotherapy (RT) for prostate cancer with radical intent.

Materials and Methods: The final dataset of a prospective multicentre study was considered. It included 542 patients treated with conventionally (74-80 Gy at 1.8-2 Gy/fr) or (GEE) models. Dosimetric-symptom correlates were contrasted for the different analytic methods.

Results: For dysuria and haematuria, stronger relationships were found to the dose indices using peak and Cox models compared to mean symptom, AG and GEE models. Despite the different strength of relationship, dose-surface of the bladder receiving higher than 65 Gy (S65) and S70 consistently show strong relationship to dysuria. S60 to S65 are the most significant for Hpeak, H(GEE), HCox and Hmean. None of the dosimetric indices satisfy the proportional hazard assumption for HAG. For urinary incontinence and frequency, stronger relationships for dosimetric indices were found for AG, GEE and to lesser extent mean score model while both peak and Cox models do not result in significant or show trend towards significance. S35 to S40 were found to be the most significant for F(GEE), Fmean and FAG while S20 to S25 for IAG and Imean.

Conclusions: The use of peak or time-to-event model alone is not optimal in assessing dose-volume correlates for certain urinary symptoms endpoints. Dosimetric-symptom correlates analysis should be supplemented by longitudinally-defined endpoints and/or using recurrent event models to account for multiple events per patient.

OC-0255
Multi-variable models of acute urinary toxicity: final results of a large prospective study
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Purpose/Objective: As urinary symptoms tend to recur throughout follow-up, conventional method of analysis using cumulative peak event and time-to-event may not be optimal to uncover the dosimetric-symptom correlates. We assessed the bladder dosimetry and urinary symptom correlates using longitudinally-defined endpoints and using recurrent event models which are contrasted to the conventional analysis methods.

Materials and Methods: In this study, 754 dose-surface information and their corresponding specific urinary symptoms (dysuria (D), haematuria (H), incontinence (I) and frequency (F)) from a cohort of patients who received prostate radiotherapy in the RADAR TROG 03.04 trial were analysed. The dosimetric-symptom correlates were analysed using: 1) conventional methods (cumulative incidence/peak and time-to-event Cox analysis), 2) longitudinally-defined endpoint (mean symptoms), 3) recurrent event models using the Andersen-Gill extension of the Cox regression model for counting process (AG) & generalised estimating equation (GEE) models. Dosimetric-symptom correlates were contrasted for the different analytic methods.
moderately hypofractionated RT (65-75.2 Gy at 2.2-2.7 Gy/fr) in 5 fractions per week.

Relevant clinical factors were collected for each patient: T stage, concomitant morbidities and drugs, androgen deprivation (AD), previous surgery, smoking, alcohol, age and BMI. Urinary symptoms were self-reported by each patient through the International Prostate Symptom Score (IPSS) before and after RT; based on previous results, absolute (cm²) weekly dose-surface histograms (DSH_w) were chosen as dosimetry descriptors.

A multivariate logistic regression (MVR) was performed for two endpoints: 1) the onset of moderate-severe urinary toxicities at RT end (IPSSend ≥ 15) for a subgroup of patients with none/mild symptoms before RT (IPSSbefore<15); 2) the worsening of urinary symptoms after RT described by an IPSS increase of at least 10 points after RT (DIPSS ≥ 10).

The choice of relevant factors to be included in the MVR had been previously carried out through an in silico methodology combining a bootstrap resampling, a backward feature selection based on minimization of residuals and a basket and network analysis of bootstrapped models. Features with the greatest percentage of occurrences (OCC) in the bootstrapped models were included in the MVR. A dedicated software for data mining (KNIME) was used.

Results: IPSS scores before and after RT were available for 429 patients. 97 out of 385 patients (25%) with none/mild symptoms before RT showed IPSSend≥15; while DIPSS≥10 was found in 85/429 (20%) patients. Results of variable selection and MVR are reported in Figure and Table: models with six (AUC=0.70) and five variables (AUC=0.66) were considered for the IPSSend≥15 (1) and DIPSS≥10 (2) endpoints, respectively.

The most robustly predictive clinical variables were: IPSS before RT (OR=1.17, OCC=92%) in model 1); and AD (OR=0.63, OCC=78% and OR=0.49, OCC=72%) as a risk factor. The medium-high weekly doses and the use of anti-hypertensives were found as risk predictors, while AD was protective in both analyses.

Conclusions: Correlations between clinical/dosimetric parameters and the onset or worsening of urinary symptoms were studied.

The role of pre-treatment urinary symptoms was confirmed as a risk factor. The medium-high weekly doses and the use of anti-hypertensives were found as risk predictors, while AD was protective in both analyses.

OC-0256

Dose-surface maps to explore acute gastrointestinal toxicity following prostate radiotherapy

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Purpose/Objective: The dose delivered to organs at risk differs between patients due to differences in their personal anatomies. Such differences may correlate with variations in toxicity. For several acute gastrointestinal toxicity endpoints we constructed average dose difference maps on the rectal surface between the groups of patients with and without event. The significance of dose differences was tested.

Materials and Methods: RTOG (grade ≥1, ≥2) toxicity endpoints derived from identical questionnaires were available for prostate cancer patients treated to 78Gy in 39 fractions within two prospective trials, one using 3D-CRT and bony set-up correction (n=215), the other using image-guided (IG) IMRT with gold markers and reduced PTV margins (n=260). Two mappings of the treatment planning dose distribution on the delineated rectum surface were defined using regular intervals along the central rectum axis. The first (rectum) mapping intersects the rectum surface with planes perpendicular to this axis, and places the axis origin at the half-height of the delineated prostate. The second (anus) mapping uses horizontal intersection planes, and places the origin at the lowest delineated contour. Dose maps were constructed and averaged over patients with and without each endpoint, and dose difference maps were generated.

Significance was tested by normalizing the dose difference to the local standard deviation, and calculating p values for the maximum normalized difference based on a permutation method. Contours were drawn around regions with p<0.05.

Results: Tighter margins and increased conformity led to smaller high dose regions on the anal and rectal surface for IG-IMRT patients (Fig. 1a-d), and to lower grade ≥2 GI toxicity (29% vs. 49% for 3D-CRT). Significantly higher (p<0.05) local dose was found for 3D-CRT patients with proctitis, mucus loss, and stool frequency ≥6 in the anus mapping, and for