symptomatic pseudo-progression after SRT of brain metastases needs to be considered as a serious radiation induced toxicity. Reduction of the high dose volume of normal brain tissue may prevent this toxicity.

OC-0056

FLAME: Influence of dose escalation to 95Gy for prostate cancer on urethra-related toxicity and QOL

J. Van Loon[1], M. Van Vulpen[1], F. Pos[2], K. Haustermans[3], R. Smeenk[4], L. Van den Bergh[3], S. Isebaert[3], G. McColl[4], M. Kunze-Busch[4], B. Doodeman[2], J. Noteboom[1], E. Monninkhof[5], U.A. Van der Heide[2]

[1]*UMC Utrecht, Radiation Oncology, Utrecht, The Netherlands*
[2]*The Netherlands Cancer Institute, Radiation Oncology, Amsterdam, The Netherlands*
[3]*University Hospital Leuven, Radiation Oncology, Leuven, Belgium*
[4]*University Medical Center Radboud, Radiation Oncology, Nijmegen, The Netherlands*
[5]*UMC Utrecht, Julius Center for methodology, Utrecht, The Netherlands*

Purpose or Objective: Following EBRT for prostate cancer, patients can develop aggravation of urinary symptoms mostly due to urethral dose. With dose-escalated EBRT it is suggested that genitourinary toxicity increases with increasing dose. In the experimental arm of the FLAME-trial (284 patients) a dose of 77Gy to the entire prostate gland in 35 fractions was administered, with an integrated boost up to 95Gy to the macroscopic lesions. No dose constraints for the urethra were set during the trial. The objective of this study is to evaluate urethral dose parameters, urethra-related toxicity and prostate-specific QoL scores for patients treated with and without dose-escalated EBRT.

Material and Methods: Between 2009 and 2015, 571 intermediate and high risk prostate cancer patients were enrolled in the FLAME trial, a phase 3, single blind, multi-center randomized controlled trial (NCT01168479). The control arm (287 patients) received a dose of 77Gy to the entire prostate gland in 35 fractions. The experimental arm (284 patients) received the same dose, but with an integrated boost up to 95Gy to the multi-parametric MRI-based intraprostatic lesion. For this study, the urethra was delineated retrospectively on T2 weighted MRI, using a circle shape with a diameter of 3 mm, to obtain dose parameters. These dose parameters, the Genitourinary Toxicity scores(CTCAE v3.0) and the urinary symptoms scale of the EORTC QLQ-PR25, were compared for both treatment arms. The physician in attendance scored toxicity at baseline, weekly during treatment, 4 weeks after treatment and every 6 months up to 10 years. QoL was filled out 1 week before treatment and the next questionnaires were sent to the patient every 6 months up to 10 years. Mean differences between groups at 1 year of follow-up were calculated using an independent samples t-test (dosimetry and QoL), Chi-square test or Fisher's exact test (toxicity). Statistical significance was considered P<0.01.

Results: Results after analysis of 100 patients (50 patients in each treatment arm) with a median follow-up of 22 months show for the control arm an average Dmean (mean dose to the urethra) of 77.3 ± 0.5 Gy (range 75.9-78.0 Gy), with an average Dmax (maximum dose to the urethra) of 79.6 ± 0.8 Gy (range 78.0-81.3). In the experimental arm, average Dmean was 82.0 ± 2.8 Gy (range 77.4-89.0 Gy) and average Dmax was 89.7 ± 0.6 Gy (range 80.7-97.7 Gy). For both Dmean and Dmax the difference between treatment arms was significant (p=0.000). Grade 3 GU toxicity did not occur, grade 2 GU toxicity occurred in a subset of patients, although no significant difference was found between both treatment arms for the separate GU items (table 1). Urinary symptoms-related QOL was not significantly different across treatment arms.

Time of follow-up	1 year		Difference
Treatment group	77Gy	95Gy	P-value
Urinary frequency/urgency - ≥ grade 2 toxicity	15 (30%)	14 (28%)	0.83 (Chi-Square)
Urinary retention - ≥ grade 2 toxicity	4 (8%)	2 (4%)	0.68 (Fisher's exact)
Bladder spasms - ≥ grade 2 toxicity	0 (0%)	0 (0%)	-
Incontinence, urinary - ≥ grade 2 toxicity	3 (6%)	2 (4%)	1.0 (Fisher's exact)
Hemorrhage - ≥ grade 2 toxicity	0 (0%)	1 (2%)	1.0 (Fisher's exact)
Dysuria - ≥ grade 2 toxicity	5 (10%)	5 (10%)	1.0 (Fisher's exact)

Table 1. Incidence of GU toxicity at 1 year after radiation treatment.

Conclusion: Results showed a significant difference in urethral dose, but no significant differences in toxicity or quality of life when comparing both treatment arms of the FLAME trial.

OC-0057

Cardiotoxicity and cardiac substructure dosimetry in dose-escalated lung radiotherapy

S. Vivekanandan[1], N. Counsell[2], A. Khwanda[3], S. Rosen[3], E. Parsons[4], Y. Ngai[2], L. Farrelly[2], L. Hughes[2], M. Hawkins[1], D. Landau[5], J. Fenwcik[1]

[1]*University of Oxford, Oncology, Oxford, United Kingdom*
[2]*University College London Clinical Trials Unit, Clinical Trials Unit, London, United Kingdom*
[3]*Imperial College London, Cardiology, London, United Kingdom*
[4]*RTTQA, Mount Vernon, London, United Kingdom*
[5]*Guy's and St Thomas' Hospital, Oncology, London, United Kingdom*

Purpose or Objective: Radiotherapy of lung cancer delivers quite high doses of radiation to the heart. We explored associations between overall survival (OS) and radiation dose to heart and its substructures and electrocardiographic (ECG) changes.

Material and Methods: We analysed data from 79 patients in IDEAL CRT, a phase I/II trial of isotoxic radiotherapy (RT) dose escalation trial, sponsored by University College London (C13530/A10424). Mean and maximum prescribed doses were 69 and 75.6Gy calculated as 2Gy fractionation equivalents (EQD2, α/ß=10Gy). Whole heart, left ventricle (LV), right ventricle (RV), right atrium (RA), left atrium (LA) and AV node (AVN) were outlined on RT planning scans and differential dose volume histograms (DVHs) extracted, converting physical DVHs to EQD2s (α/ß=3). Patient-to-patient DVH variability was represented using a small number of Varimax-rotated principal components (PCs) explaining 95% of total variance. ECGs were analysed at baseline, 6 and 12 months (mo) after treatment, and changes in heart rate (HR) recorded, with patients dichotomised according to presence or absence of 'any ECG rhythm change' (conduction abnormalities or ischaemia). OS was modelled using Cox regression from the start of treatment. Univariate analysis (UVA) and multivariate analysis (MVA) of clinical factors included 'any rhythm ECG change' at 6 and 12 months, change in HR at 6 or 12 months, planning target volume (PTV), and prescribed dose (PD). MVA of whole heart dosimetric factors included all 7 Heart PCs, PTV, and PD. MVA of heart substructures included heart substructure PCs with p < 0.2 on UVA having similar dosimetric distributions to significant Heart PCs, PTV and PD.