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Consistency of cone beam CT-derived bladder volume and inflow during localized prostate cancer IMRT

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Purpose or Objective: Consistency of bladder volume (BV) during radiotherapy (RT) planning and treatment is important in maintaining the position of the prostate and the surrounding organs at risk, thus minimising RT-related tissue toxicity. This retrospective study evaluated the effectiveness of bladder-filling instructions in achieving a consistent and reproducible bladder volume at the time of planning CT and during the course of radical RT for prostate cancer. This study also assessed the rate of bladder filling (inflow) during the course of RT.

Material and Methods: 28 men with localized prostate cancer were instructed to void their bladder and then drink 500 ml of water before proceeding to RT planning scan 45 minutes later. This bladder filling process was repeated daily before each RT session. BV was assessed during planning CT and at four chronological phases of RT (fractions 1-9, 10-19, 20-29 and 30-37) via cone beam CT (CBCT). Each patient had between four to ten CBCTs taken during his RT sessions and the average BV at each phase was calculated. Inflow was assessed using delineated BV post-treatment in 20 patients. Inflow was calculated by taking the difference in BV between pre-RT CBCT and post-RT CBCT and dividing by the time between the scans. All patients were treated with 74 Gy in 37 fractions via intensity modulated radiotherapy (IMRT).

Results: The mean BV for all treatments (mean= 223.62 ml, range= 57.18– 871.85 ml, SD= 138.08 ml) was significantly lower (p=0.007) than the mean BV at the time of planning (mean= 318.88ml, range= 93.96 – 821.37 ml, SD= 165.10 ml). During RT, 68%, 50% and 38% of pre-treatment BV had >50ml, >100ml and >150 ml difference respectively when compared with their volume at the time of planning. When assessing the BV at different treatment time points, the mean BV for RT fractions 1-9 (239.31ml) was 25% lower than the mean planning volume (p= 0.025). The mean BV for RT sessions 30-37 (203.65 ml) was 36% lower than the mean planning volume (p<0.001).

Inflow over 128 fractions was significantly correlated (r=0.558, p<0.0001) with pre-RT BV. The mean inflow did not differ significantly over the course of RT. The mean inflow of RT sessions 1-9 (3.86 ml/min, SD= 2.50 ml/min) was not significantly higher (p=0.24) than that of RT sessions 30-37 (3.29 ml/min, SD=2.46 ml/min).

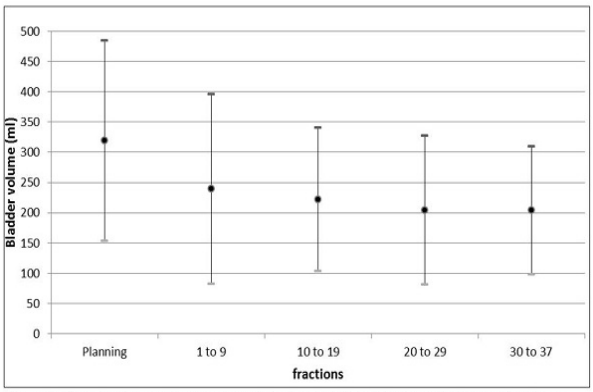

Figure 1: Mean bladder volume measured at planning CT and during radiotherapy fractions, with error bars indicating one standard deviation (SD).

	Planning	1 to 9	10 to 19	20 to 29	30 to 37
Mean bladder volume (ml)	318.88	239.31	222.31	203.93	203.65
SD (ml)	165.10	156.87	118.35	122.78	105.51
% volume difference to planning bladder volumes	0	-24.95	-30.28	-36.05	-36.14
Mean Inflow (ml/min)	-	3.86	4.00	4.02	3.29
SD (ml/min)	-	2.50	2.54	2.95	2.46

Table 1: Table summarizing the bladder volume (mean, SD and % volume differences to planning) and inflow (mean and SD) at planning and during radiotherapy.

Conclusion: A difference in BV was found between planning and during the course of radiotherapy. The mean BV decreased most during the first two weeks of radiotherapy. The large decrease in BV at the early phase of RT suggests a systematic difference in bladder filling at the time of planning compared with treatment. This process has been reviewed and a further analysis will be performed. Inflow from pre- and post-CBCT scans was found to be correlated with pre-RT BV. Inflow information may help to reduce bladder filling variations during treatment.

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Should pelvic radiotherapy be tailored to early patient-reported gastrointestinal toxicity?

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Purpose or Objective: Whole-pelvic radiotherapy (WPRT) is a cornerstone of the treatment of high-risk prostate cancer. However, late gastrointestinal (GI) toxicity is the major dose-limiting factor in this treatment. There are concerns that dose escalation and aggressive treatment regimens may result in increased acute toxicity, which may modulate long-term side-effects of radiotherapy, a phenomenon known as consequential late effects. The purpose of this work was to evaluate if late GI side-effects are related to acute toxicity using long-term patient-reported outcomes (PRO) of a previously unreported large, prospective phase I/II trial of IMRT for whole-pelvic treatment of prostate cancer.

Material and Methods: 496 patients were recruited between August 2001 and September 2013. Treatment consisted of

WPRT with intensity modulation techniques and long-term androgen-deprivation therapy. Strict radiotherapy dose-volume constraints were used for treatment planning to minimize the risk of serious toxicity.
PRO data (UCLA-Prostate Cancer Index scale) was available for 450 patients. Patients with less than 2 year follow-up data and any patients without acute (10 week after RT initiation) data were excluded, giving 251 patients for analysis. Median follow-up was 5 years. Only bowel habit outcomes were included for this analysis (questions 17 to 21). Data from patients with positive toxicity scores at baseline was excluded on an endpoint-by-endpoint basis.
We separated patients according to acute toxicity into two groups using question-specific toxicity grade cut-offs which differed between each PRO question. We then assessed if the group with acute toxicity had more toxicity in the late setting by calculating the odds-ratios (OR); we also computed p-values using Fisher's exact test. seline was excluded on an endpoint-by-endpoint basis.

Results: We found that patients with positive self-reported acute GI toxicity at 10 weeks have an increased risk of developing serious late GI problems, while patients without toxicity are more likely to be free of chronic toxicity (table 1). as excluded on an endpoint-by-endpoint basis.

UCLA-PCI bowel habit item *Grade cut-off*	OR	95% CI	p-value
Rectal urgency *More than once a week or higher*	2.0	1.1 - 3.6	0.0163
Loose stools *Half the time or higher*	4.6	2.7 - 8.1	<0.0001
Bowel distress *Moderate/Severe*	3.8	2.1 - 7.1	<0.0001
Crampy abdominal pain *Several times a week or higher*	6.9	3.5 - 14.1	<0.0001
Bowel problem *Moderate/Severe*	6.0	3.2- 12.1	<0.0001

Table 1: Odds ratios for late patient-reported gastrointestinal toxicity according to early toxicity.
Equal cut-off points were used for early and late outcomes.

Conclusion: Patients with moderate to severe acute bowel toxicity are at increased risk of serious late GI problems which impact quality of life, potentially reflecting a consequential late effect. Tailoring treatment with the modification of treatment planning according to early clinical outcomes may prove to be necessary to tackle this problem.

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SBRT in the treatment of bone metastases in hormone refractary prostate cancer

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Purpose or Objective: Evaluate the utility of SBRT in terms of local control (LC), global survival (OS), compliance to the treatment and toxicity in patient with oligometastatic and hormone refractary prostate cancer, limited to the skeletal structures.

Material and Methods: 46 patients with bone metastases from prostate cancer, were treated with SBRT between January 2009 and August 2015. At diagnosis 15/46 patients presented bone metastases. Bone lesions irradiate were 131 (range 1-4). Median age was 68 years (range 54-85). Median PSA pre-treatment was 168,1 ng/ml (range 0,23 -1.470). Patients received a median dose of 30 Gy (range 8-40 Giy) in 3 fractions (range 1 -5). The treatment was delivery by LINAC 6 MeV (Elekta Synergy-S) using technical IGRT-VMAT. All patients received some form of androgen-deprivation therapy (ADT) after completing SBRT. 18/46 patients was submitted systemic chemotherapy treatment.

Results: Median follow-up was 22 months (range 1-78). LC was 100% and OS 50,2% at 5 years. 22/46 patients were died for progression disease, 24/46 patient were still alive, of these 14 were disease free and 10 were in progressione disease. The first post-SBRT PSA was lower than pre-treatment levels in 30 patients (65,2%) and continued to decline or remain undetectable in 23 patients (50%) at follow-up of 6 months. Median PSA post-treatment was 32,4 (range 0,29-196). No severe acute or late toxicity of grade >2 was observed.

Conclusion: SBRT is a safe and effective treatment for prostate cancer metastases, presenting excellent LC and an acceptable toxicity profile in selected patient with hormone refractary disease. More importantly, half the patient achieving reductions in serum PSA values.

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Primary focal prostate radiotherapy: do all patients really need whole-prostate irradiation?

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Purpose or Objective: Primary focal therapy has been explored for 20 years now, and more than 2000 patients have been treated so far with several techniques but only limited data have been published on the primary focal radiotherapy (FRT). From the technical point of view, primary FRT can be performed through either focal brachytherapy or external beam radiotherapy. The majority of series include both low-dose-rate (LDR) and high-dose-rate (HDR) brachytherapy, and only recently the feasibility of primary FRT by external beam irradiation has been reported. The current review aims to assess the available evidence for primary FRT performed either by the means of brachytherapy or external beam radiotherapy.

Material and Methods: Inclusion criteria were: Medline search for full paper in English language on primary FRT for early prostate cancer including review articles, planning studies or patient series (clinical outcome available) published before May 31, 2015.

Results: Twenty-two papers have been found: 11 review articles, 4 planning studies and 7 patient series. Eleven review articles were dedicated to all types of focal therapy including FRT and 2 to FRT only. All planning studies were performed on cohort of 5-10 patients and included brachytherapy both HDR (24 patients overall), and LDR (9 patients). All studies underline the significant organs-at-risk dose reduction as well as the higher sensitivity to systematic set-up error as target volume decreases from whole-gland to hemi-gland and to ultra-focal target. Patient series included together 715 patients (range 8-318, 99% treated with brachytherapy). Median follow-up period was 33.6 months (range 2-61 months). Promising tumour control was highlighted in low-risk cancer. In intermediate-risk tumours, FRT might be suboptimal (see Table 1). Moreover, some reports on consensus criteria are already available in literature.