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Comparison of focal boost high dose rate prostate brachytherapy optimisation methods

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ABSTRACT

For HDR prostate brachytherapy treatments of 15 Gy to the whole gland plus focal boost, optimisation to either tumour plus margin (F-PTV) or involved sectors was compared. For 15 patients median F-PTV D_{90} and V_{150} were 21.0 Gy and 77.2% for F-PTV optimisation and 19.8 Gy and 75.6% for sector optimisation.
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In radiotherapy for prostate cancer, it is common practice to prescribe one dose level to the whole prostate, as prostate cancer is known to be a multi-focal disease. Tumour control probability may be improved with a focal boost treatment where the whole gland is treated to the standard dose prescription and a focal boost dose is given to the dominant intra-prostatic lesion (DIL) [1,2] or other CTV sub-volume as described in GEC-ESTRO recommendations [3]. Focal boost treatments in high dose rate (HDR) prostate brachytherapy [4–7] typically use multi-parametric-MRI (mp-MRI) for tumour delineation; this is then fused to images acquired after needle insertion for treatment planning. Targeting of the focal boost dose is therefore impacted by uncertainties in tumour delineation and image fusion. Two approaches to mitigating these uncertainties are (i) applying a margin to the delineated tumour or (ii) dividing the prostate into sectors and boosting the sectors involved in the tumour. In this study dose optimisation is compared for the two approaches.

Many patients have several months of hormone therapy before HDR prostate brachytherapy and this can reduce prostate size and tumour conspicuity. Ideally treatment planning MRI scans are acquired after hormone therapy however pre-hormone therapy scans may be used if MRI capacity is limited. In the latter case due to prostate volume changes boosting based on involved prostate sectors may be the preferred approach to reducing image fusion uncertainties. In this study pre- and post-hormone therapy MRI scans are compared to determine whether or not the same prostate sectors are identified as being involved before and after hormone therapy.

Method

16 patients included in an mp-MRI guided focal boost prostate HDR brachytherapy pilot study [6] were retrospectively analysed for this investigation. The patients were aged 57–77 years, with biopsy proven prostate cancer, stages T1c–T3b, PSA at diagnosis 5–30 ng/ml, combined Gleason 7–9. All patients received 2–5 months (mean 3 months) hormone therapy before treatment with a single fraction of 15 Gy to the whole prostate planned using intra-operative trans-rectal ultrasound (TRUS), including focal boost to the visible tumour (detailed below), followed by 37.5 Gy in 15 fractions of external beam to the prostate and seminal vesicles [8].

Pre-hormone therapy staging mp-MRI scans were performed 3–6 months (mean 4 months) before brachytherapy and pre-treatment mp-MRI scans in the week before brachytherapy. The mp-MRI sequences are detailed in the Supplementary material and included T2-weighted (T2) MRI, diffusion weighted MRI (DWI) and dynamic-contrast enhanced MRI (DCE-MRI) (DCE-MRI was included in the pre-treatment scans but not the staging scans). Focal gross tumour volume (F-GTV) targets for focal boost were delineated on the MRI data by a consultant radiologist. This was done at the time of brachytherapy treatment for the pre-treatment MRI scans, with the delineated F-GTV fused to TRUS to perform focal boost treatments. F-GTVs were based on the

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Table 1
Median DVH values for the 15 patients in the optimisation study. For F-GTV, F-PTV and sectors, the values shown are the median (range) of the combined values (for both F-GTVs/F-PTVS or all sectors) for each patient.

	Plan	D_{90} (Gy)	V_{100} (%)	V_{150} (%)	V_{200} (%)
Prostate*	STD	17.2 (16.6–17.5)	99.9 (99.3–100)	33.3 (28.1–43.2)	10.1 (5.5–13.5)
	FBOOST	17.3 (16.6–17.8)	99.9 (99.0–99.9)	42.1 (32.1–52.5)	12.1 (8.7–20.5)
	SBOOST	17.3 (16.6–17.7)	99.8 (99.2–100)	43.4 (32.5–57.2)	12.3 (8.6–17.5)
PTV	STD	16.2 (15.5–16.6)	92.8 (87.3–97.2)	28.8 (26.2–36.7)	8.9 (5.4–11.5)
	FBOOST	16.3 (15.3–16.8)	91.6 (87.4–97.1)	35.0 (28.0–44.5)	10.1 (7.6–16.4)
	SBOOST	16.1 (15.3–16.8)	91.6 (87.4–97.1)	35.9 (28.5–45.3)	10.9 (8.0–13.7)
F-GTV	STD	18.3 (16.1–21.8)	100 (99.6–100)	35.8 (9.1–85.1)	6.1 (0.6–32.2)
	FBOOST	24.3 (20.5–30.4)	100 (–)	95.4 (73.1–100)	46.9 (14.5–91.4)
	SBOOST	22.3 (19.9–25.8)	100 (–)	88.7 (66.3–100)	29.9 (12.3–59.9)
F-PTV	STD	17.5 (15.8–19.3)	100 (97.5–100)	33.7 (16.0–56.5)	8.9 (2.5–16.7)
	FBOOST	21.0 (18.8–24.1)	100 (–)	77.2 (64.7–96.9)	30.2 (12.3–54.1)
	SBOOST	19.8 (18.9–24.2)	100 (–)	75.6 (49.7–96.7)	23.4 (10.1–48.1)
Involved sectors	STD	17.7 (16.8–18.3)	100 (99.0–100)	37.8 (14.4–49.4)	9.8 (3.3–18.6)
	FBOOST	19.0 (18.0–21.5)	100 (99.6–100)	62.2 (53.1–82.7)	20.9 (14.4–31.7)
	SBOOST	20.3 (18.7–22.8)	100 (–)	74.7 (56.9–91.1)	27.5 (16.1–38.7)
		D_{10} (Gy)	D_{2cm^3} (Gy)	V_{100} (cm^3)	
Urethra	STD	17.1 (17.1–17.2)	–	–	
	FBOOST	17.2 (17.1–17.5)	–	–	
	SBOOST	17.2 (17.1–17.5)	–	–	
Rectum	STD	–	8.4 (6.5–9.7)	0 (–)	
	FBOOST	–	8.9 (6.6–10.4)	0 (–)	
	SBOOST	–	8.9 (6.8–10.6)	0 (–)	

STD – standard plan delivering 15 Gy to the whole prostate.
FBOOST – plan delivering 15 Gy to the whole prostate and escalating dose to the F-PTV(s).
SBOOST – plan delivering 15 Gy to the whole prostate and escalating dose to the involved sector(s).
* Prostate is the whole prostate including F-GTV and F-PTV/sectors.

combination of all suspicious areas on the mp-MRI sequences with multiple separate F-GTVs per patient if appropriate. For the focal boost treatments a 4.5 mm margin in all directions (constrained to avoid the urethra and remain inside the prostate capsule) was applied to the F-GTV to generate an F-PTV, on the TRUS images, to allow for tumour delineation and image registration uncertainties [6]. Staging scans were delineated more than one year after the last patient treatment for this retrospective planning study. For consistency of MRI scan parameters, only staging scans performed at the same centre as pre-treatment scans were analysed, which restricted this part of the study to 10 patients. For both sets of MRI data, the prostate volume was determined to assess the effects of hormone therapy. 12 prostate sectors were defined by first dividing into three base, mid-gland and apex segments, and then dividing each of these into four sectors: right anterior, left anterior, right posterior and left posterior. The sectors intersected by the F-GTV/F-PTVs were manually determined for each scan.

Treatment plans were generated using DVH-based inverse optimisation in Oncentra Prostate™ v4.0 [9], with minor manual adjustments to dwell times applied if necessary to meet plan objectives and constraints: prostate $V_{100} > 95\%$, PTV $V_{100} > 95\%$, urethra $D_{10} < 17.5$ Gy and rectum $D_{2cm^3} < 11.8$ Gy, $V_{rect,100} = 0$ (PTV = prostate + 3 mm, 0 mm posteriorly, 100% dose = 15 Gy). 2 mm spaced dwell positions were activated throughout the PTV. Three optimisation strategies were compared for each patient.

- Standard plans with optimisation objectives set to give 100% dose to the whole prostate.
- F-PTV boost plans with optimisation objectives set to give 150% dose to as much of the F-PTV as possible while giving 100% dose to the remainder of the prostate and maintaining the plan objectives and constraints listed above.
- Sector boost plans with optimisation objectives set to give 150% dose to as much as possible of the prostate sectors intersected by the F-PTV, while giving 100% dose to the other sectors and maintaining the plan objectives and constraints listed above.

All treatment plans were based on the pre-treatment mp-MRI data fused to planning TRUS. Plans used the same needle positions except that up to two additional needles were inserted to target the F-GTV if required for focal boost plans. Note that the involved sectors boosted in sector boost plans were determined from the TRUS F-PTVs to allow direct comparison of optimisation to the F-PTV boost plans. If implementing sector boost in clinical practice it would not be necessary to generate F-PTVs so that the tumour delineation and image fusion steps would not be required.

Results

One patient had no visible tumour in the pre-treatment MRI scan so was excluded from the optimisation study. Of the remaining fifteen patients, five had bi-lateral disease and ten had unilateral disease. Table 1 summarises the DVH values achieved in the optimisation study. The per-patient median (and range) of the boosted volume was 5.8 cm^3 (1.6–13.4 cm^3) in F-PTV-based and 9.8 cm^3 (2.2–14.2 cm^3) in sector-based focal boost plans. Median prostate conformal index [10] values were 0.62, 0.62 and 0.61 in standard, F-PTV boost and sector boost plans respectively. Median PTV conformal index [10] values were 0.87, 0.85 and 0.84 in standard, F-PTV boost and sector boost plans respectively. The number of involved sectors per patient was one (one patient), two (five patients), three (three patients), four (four patients), five (one patient) and six (one patient). In almost all cases the involved sectors were adjacent. Across all patients 47 sectors were boosted, with 37 posterior and 10 anterior, and 6, 23 and 18 in apex, mid-gland and base segments respectively. Suppl Fig. 1 (in Supplementary material) shows an isodose comparison for one patient in the study. Higher doses and better coverage were achieved for posterior sectors compared to anterior sectors due to the position of the urethra. The median D_{90} and V_{150} were 18.4 Gy and 53.3% for anterior sectors and 21.0 Gy and 80.6% for posterior sectors.