The Leeds Teaching Hospitals NHS
NHS Trust

Focused Boost Treatments in HDR Prostate Brachytherapy

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UK and Ireland Prostate Brachytherapy Meeting, Belfast

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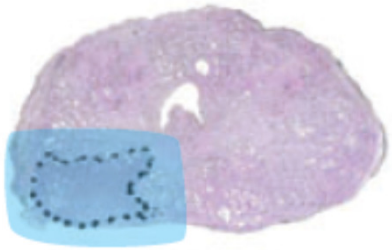
Defining the Approach

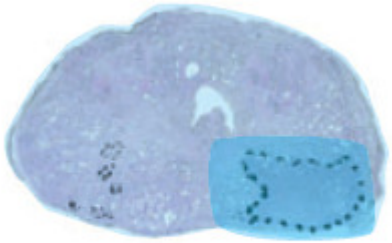


Ultra-Focal Therapy

- Target radiation to sub-volume containing tumour
- Unilateral disease

Focal Therapy

- Hemi-Gland Treatment
- Target radiation to half of gland containing tumour
- Unilateral disease



Focused Therapy

- Dose to index lesion higher than dose to whole gland
- Degree of clinically insignificant disease on contralateral side

Langley et al BJUI:109(1):2012 7-16

Background

Why Brachytherapy?

- Multiple RCTs using EBRT demonstrate dose escalation of order of 10Gy improves PSA control by 10-15%
- Prostate brachytherapy allows dose escalation beyond that achievable by any form of external beam
- Prostate Cancer is a multi-focal disease, so common practice to treat whole gland

Aims of Focused Boost Treatments

- Whole of Prostate Gland Treated – standard dose (15Gy in single #)
- Dose Escalate to dominant intra-prostatic lesion (DIL)
  - Improve local tumour control?
- Keep Toxicities to similar level

Study Investigations

1. Feasibility Study – mp-MRI delineation; dose optimisation
2. Patient FU of patients treated in pilot study – toxicity
3. F-PTV Boost v Sector Boost
4. Clinical Implementation

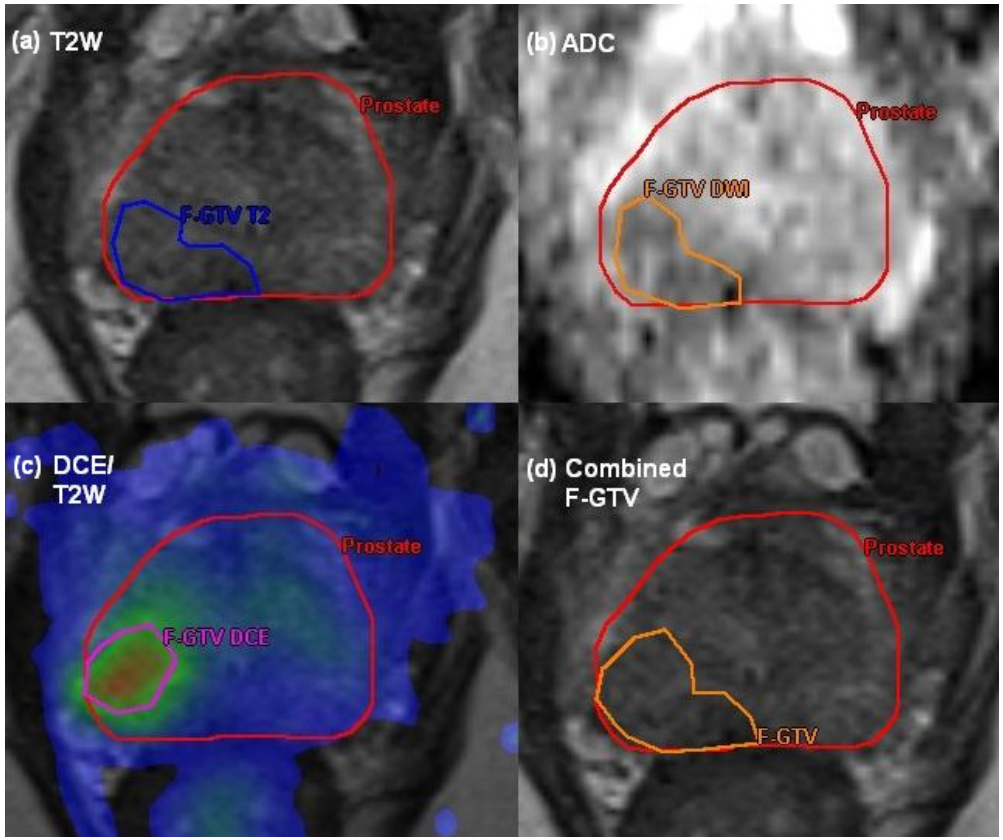
Pilot Study

- Primary End Points
  - Assess Feasibility of using functional MRI in the routine planning of HDR focused brachytherapy
  - Quantification of dose that can be delivered to F-GTV within the normal tissue constraints
- Secondary end points
  - Acute and late toxicity
  - PSA and disease control
- Brachy 15Gy mpd to prostate then 37.5 Gy in 15# EBRT
- 30 Patients
  - Cohort A: 15 Patients - retrospective plans
  - Cohort B: 15 Patients – focused boost plans delivered, if F-PTV identified
- mp-MRI performed week before HDR
- mp-MRI Fused to TRUS for planning

Defining Focal-GTV

- Manual Rigid Registration
  - DWI ADC and DCE Ktrans to T2W
- Transverse-oblique planes, aim to maintain consistent posterior edge of prostate.
- Delineated suspicious areas on each mp-MRI technique pre-MRI
- F-GTV generated by combining suspicious areas from (a), (b) and (c).

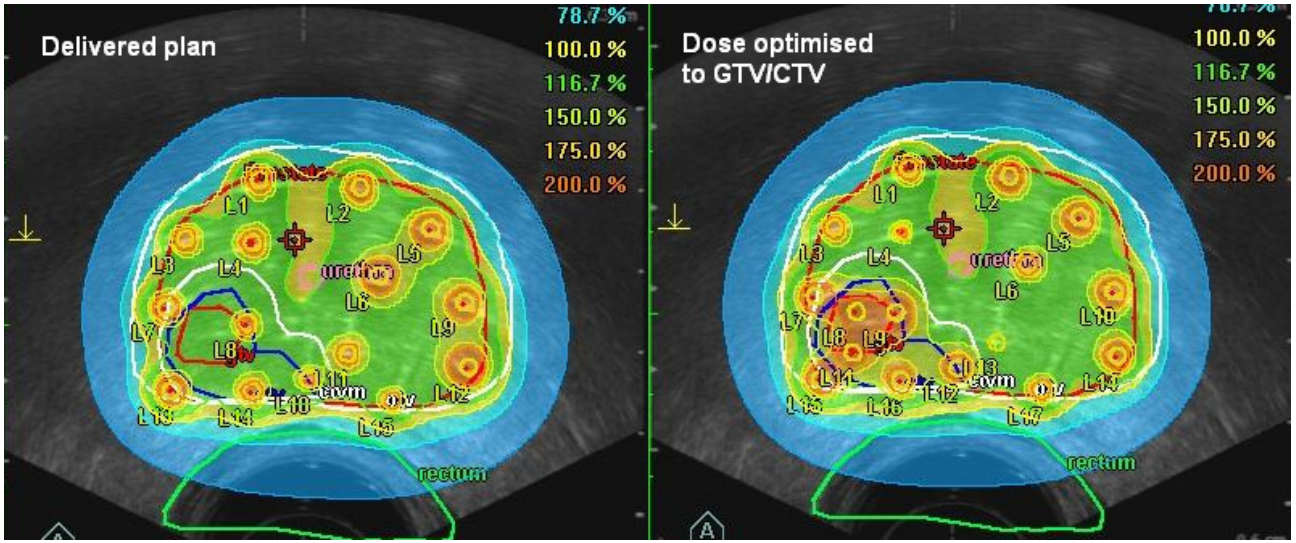
- F-PTV account for uncertainties
  - Tumour delineation
  - Image Registration
  - Treatment Delivery
  - Restricted to OAR contours



Mason et al Brachytherapy:2014:13(2) 137-145

Methods: Retrospective Planning Study

- 15 patients
- F-GTV defined on all patients
- F-PTV = F-GTV+4.5mm (margin includes delineation and registration uncertainties)
- Additional needles inserted into F-GTV (5mm spacing)
- Dose Escalate to F-PTV as much as possible, while adhering to
  - Standard 15Gy/single# whole gland objectives
  - Standard normal tissue dose constraints



Mason et al Brachytherapy:2014:13(2) 137-145

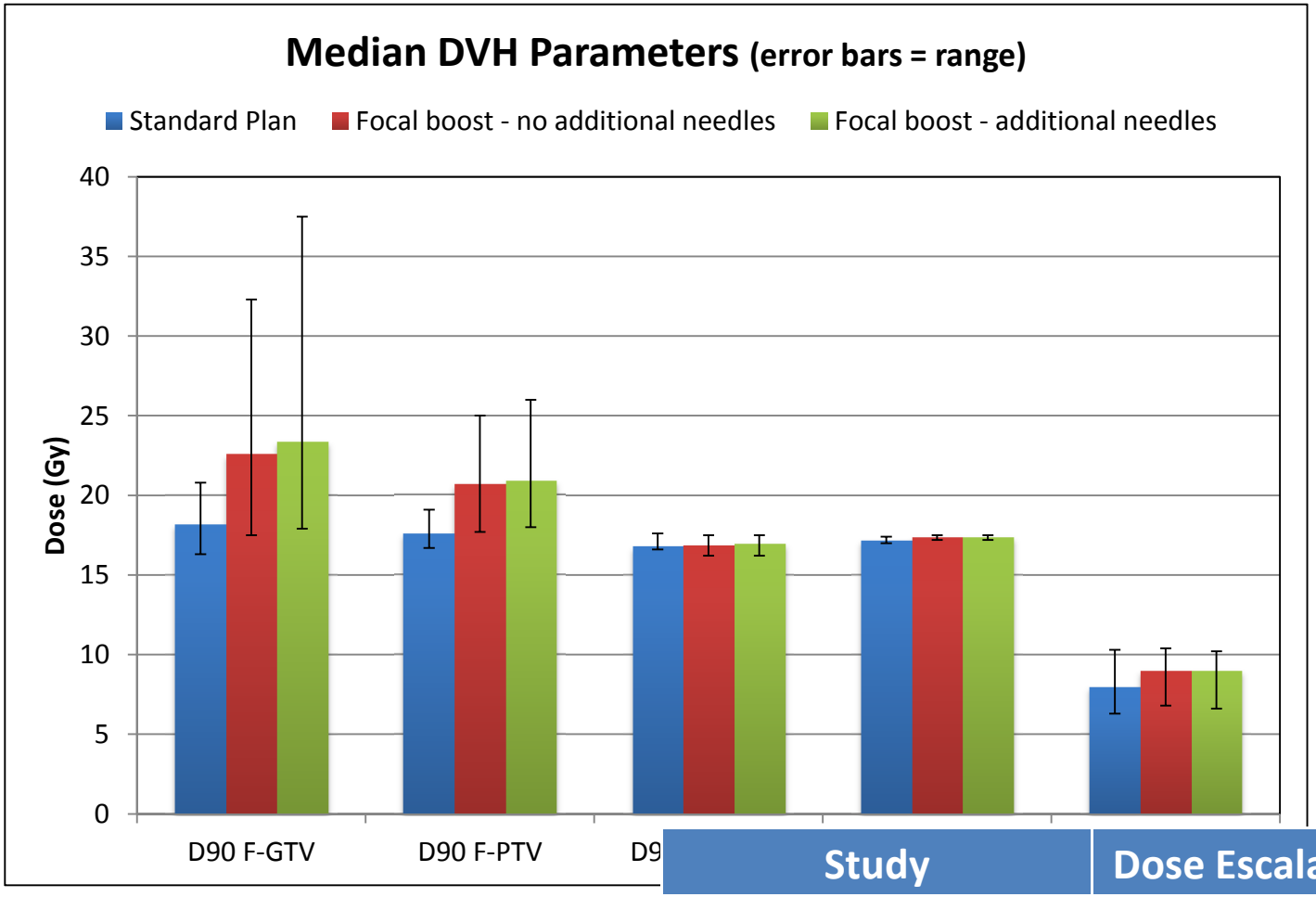
Std Objectives

V_{100}PTV >95%,
V_{150}prostate < 45%,
V_{200}prostate < 15%

Rectum: V15Gy = 0,
D2cc < 11.8Gy.
Urethra:
D10% < 17.5Gy,
D0.1cc < 17.5Gy

Results: Retrospective Planning Study

Mason et al Brachytherapy:2014:13(2) 137-145



Increased median F-PTV D90 from 17.6 to 20.9Gy (18.8%)
Increased median F-GTV D90 from 18.2 to 23.4Gy (28.6%)

Study	Dose Escalation
Crook et al Brachytherapy:2014:13 433-441	25-30% DIL
Pouliot et al IJROBP2004:59 1196-1207	20%

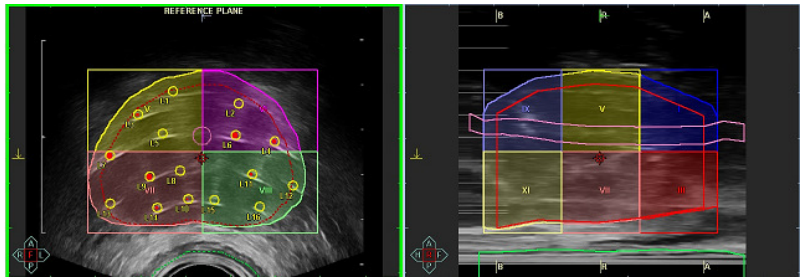
Prospective Cohort

- 8 patients received the focused boost treatment
  - 7 patients did not due to logistical reasons or no F-GTV
- Additional needles inserted into F-GTV (5mm spacing)
- Same methodology as retrospective cohort

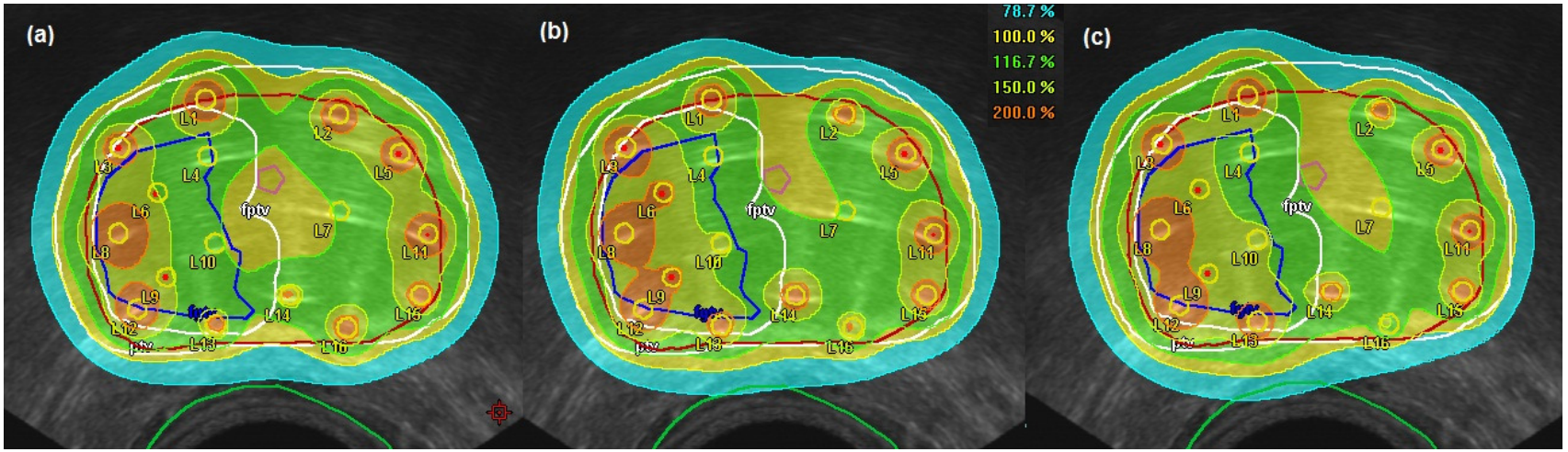
- Median F-PTV D90 of 22.5Gy
- Dose Escalation had minimal impact on OAR
  - All dose constraints met
  - Median Urethra D10% of 17.2Gy
  - Median Rectal D2cc increased from 8.5Gy to 9.0Gy
- GI & GU Toxicity in first 3 months (CTCAE 4.0)
  - No Grade 3
  - 3 out of 8 had Grade 2 or less

Method: Planning Strategy Comparison

Mason et al Radiother Oncol:2015:117(3) 521-524



- Two approaches to mitigate uncertainties
  - Apply margin to F-GTV
  - Boost sectors involved with F-GTV
- 15 patients from pilot study used ; 15Gy single fraction



Comparison of isodoses for a patient with F-PTV in the right anterior and right posterior mid-gland sectors. (a) no boost plan (b) F-PTV boost plan (c) sector boost plan.

Results: Sector Boost v F-PTV Boost

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 (–)

33%
22%

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.

Routine Clinical Implementation

- **Challenges**:
  - Limited MR capacity for pre-brachy mp-MRI
  - Image fusion uncertainties
  - Observer variability in contouring
  - Hormone effects - reduce prostate size and tumour conspicuity
  - Needles distorting gland
- **Option:**
  - Use staging scan instead of dedicated brachy scan
- **Added challenge:**
  - Changes in prostate size and morphology due to hormone therapy
- **Solution:**
  - Sector optimisation – boosting involved sectors seen on staging scan
  - Same objectives and dose constraints as the pilot/planning study
  - Improved efficiency in theatre

An Acceptable Compromise

Early Experience

- Clinical since Sept 2016
- Brachy MDT review staging scan prior to brachy (Oncologist, physics, radiologists) – define sectors if applicable
- Review period 1/9/16 to 5/4/16
- 60 patients received HDR prostate brachytherapy
- 11 patients received a sector focussed boost
- Inclusion criteria
  - HDR boost patients only
  - F-GTV visible on staging scan
  - Boost volume ≤ 50% of the prostate
  - Local referrals – ensure robust follow-up & staging scan requirements
- Initial implementation challenges
  - Trained staff availability
  - Theatre time restrictions

Planning Aims

Primary Objectives (Std)

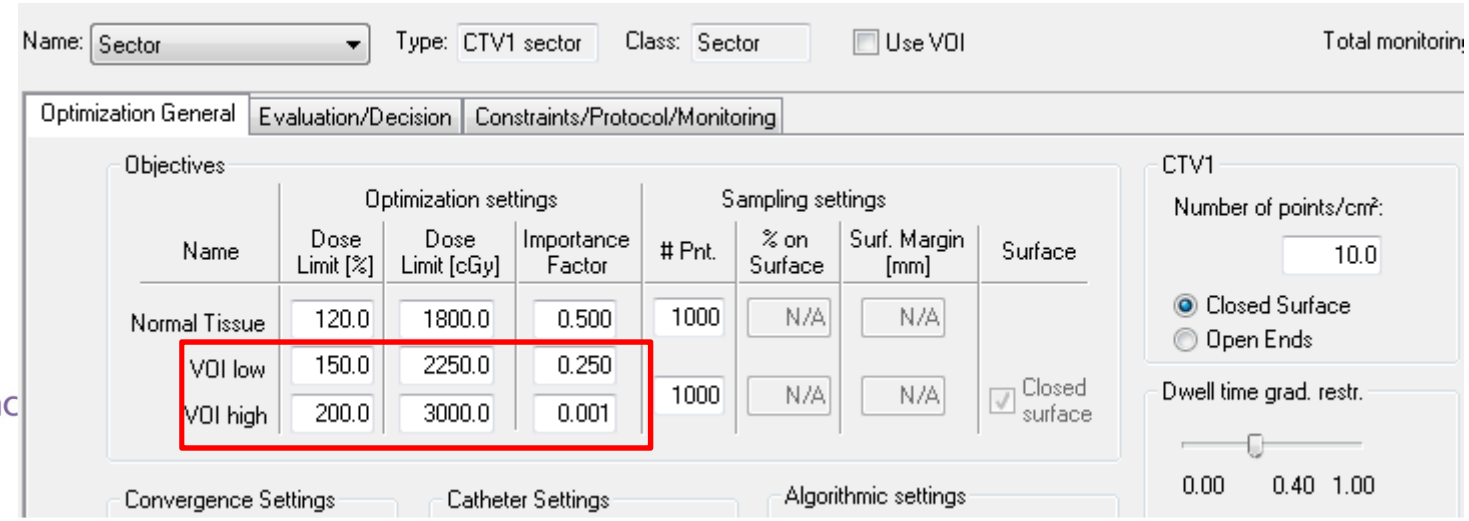
V_{100}PTV >95%,
D_{90}Prostate > 15Gy
V_{150}prostate < 45%,
V_{200}prostate < 15%

Rectum: V15Gy = 0, D2cc < 11.8Gy.
Urethra:
D10% < 17.5Gy, D0.1cc < 17.5Gy

Sector Boost Objectives

Dose Escalate to **involved sectors** as much as possible, while adhering to:

- Standard 15Gy/single# whole gland objectives
- Standard normal tissue dose constraints
- V150, V19Gy, D90, D98 of involved sectors



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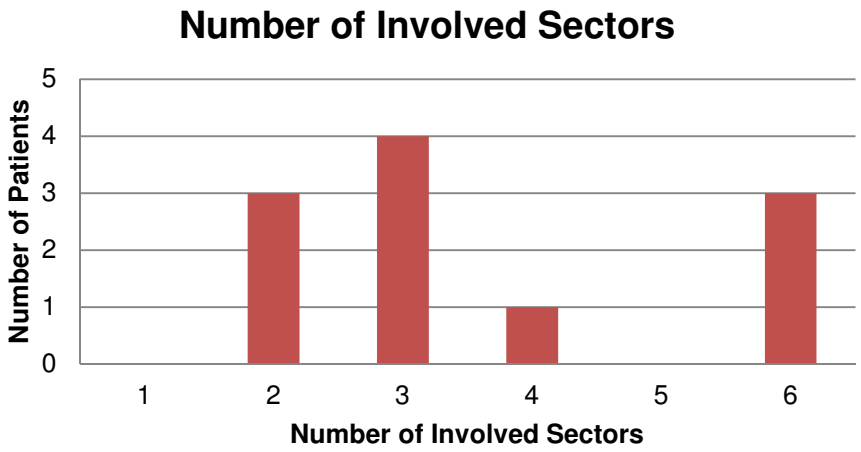
Results

- Compared Sector Boost Plan (treated) to No Boost
- 11 Patients

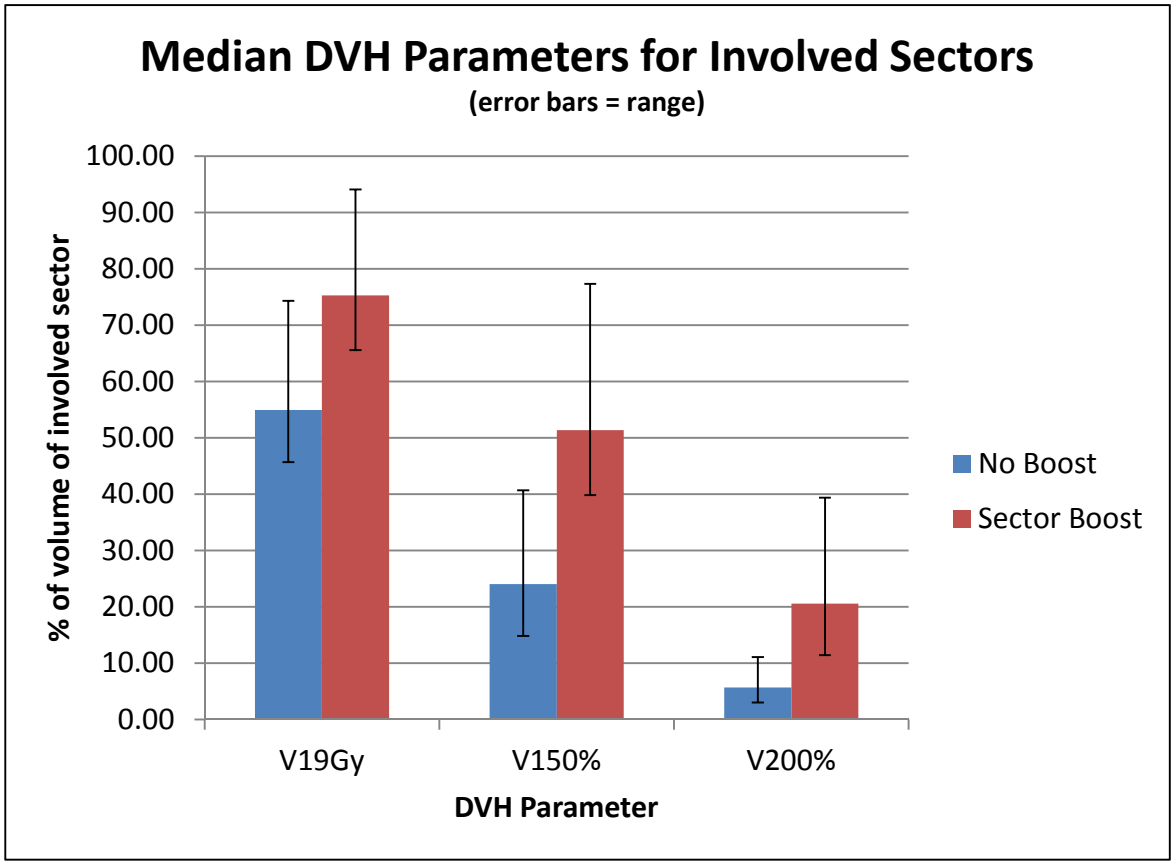


Standard Dosimetric Parameter	Aim / Constraint	Median DVH Values (range)	
		No Boost	Sector boost
V100 PTV (%)	>95%	96.0 (94.5–98.0)	96.9 (95.4 -98.2)
D90 PTV (Gy)	> 15Gy	16.3 (16.0-16.6)	16.3 (15.8-16.6)
V100 Prostate (%)	>95%	99.8 (99.3-99.96)	99.8 (99.0-99.96)
V150 Prostate (%)	< 45%	30.8 (24.1-39.4)	38.8 (25.8-43.6)
D90 Prostate (Gy)	> 15Gy	17.2 (16.8–17.6)	16.8 (16.2-17.3)
D2cc Rectum (Gy)	< 11.8Gy	8.7 (7.7-10.5)	9.4 (7.8-10.1)
D10 Urethra (Gy)	< 17.5Gy	17.1 (17.1-17.2)	17.2 (16.9-17.47)

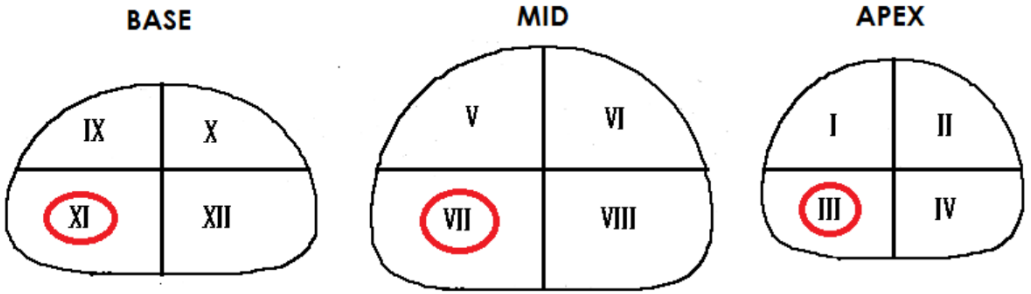
All aims/constraints met

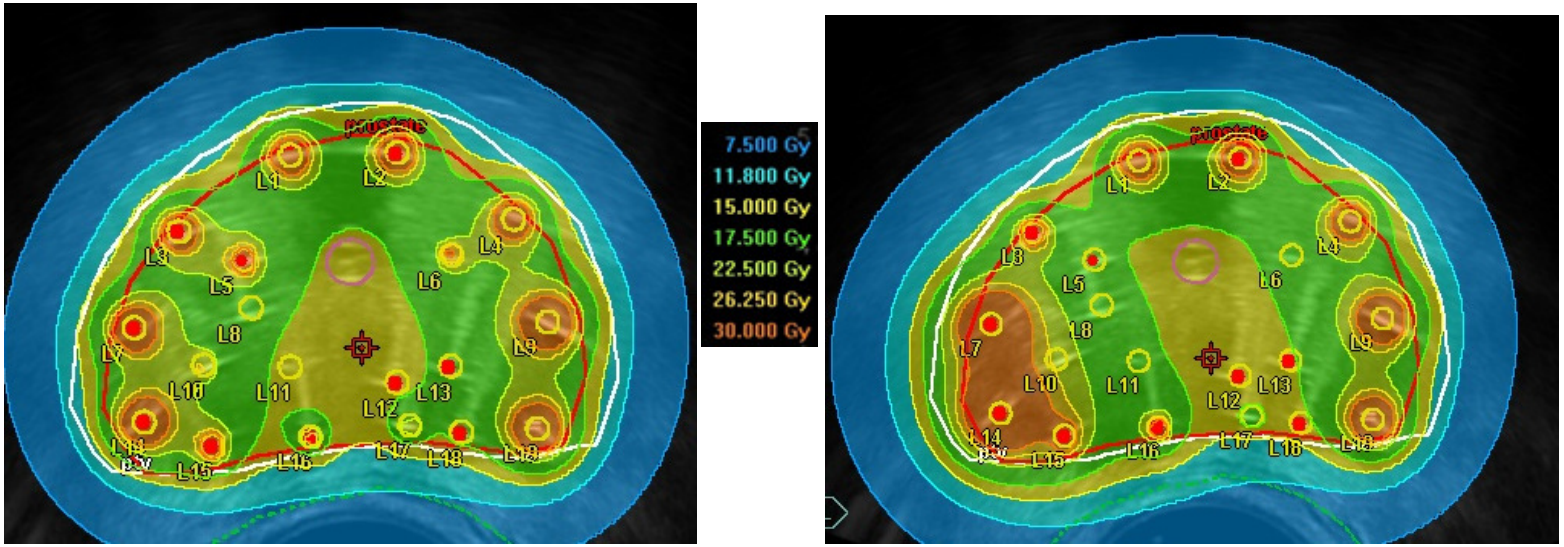
Sector Results

- Mean PTV Volume = 47.2cm^3 (range 32.5 to 84.8cm^3)
- Mean Volume of involved sectors = 13.8cm^3 (range 7.7 to 20.9cm^3)
- Mean ratio involved sector vol/PTV = 0.31 (range 0.14 to 0.5)
- **V* are combined for all the involved sectors**
  - OCP only computes individual sector results. Composite calculated manually



3 Sectors



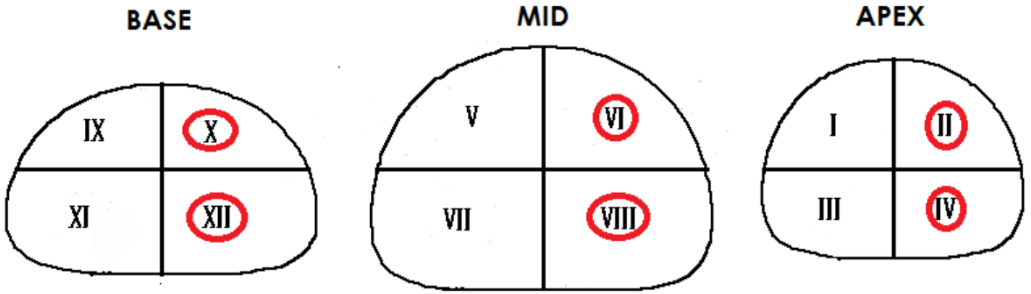


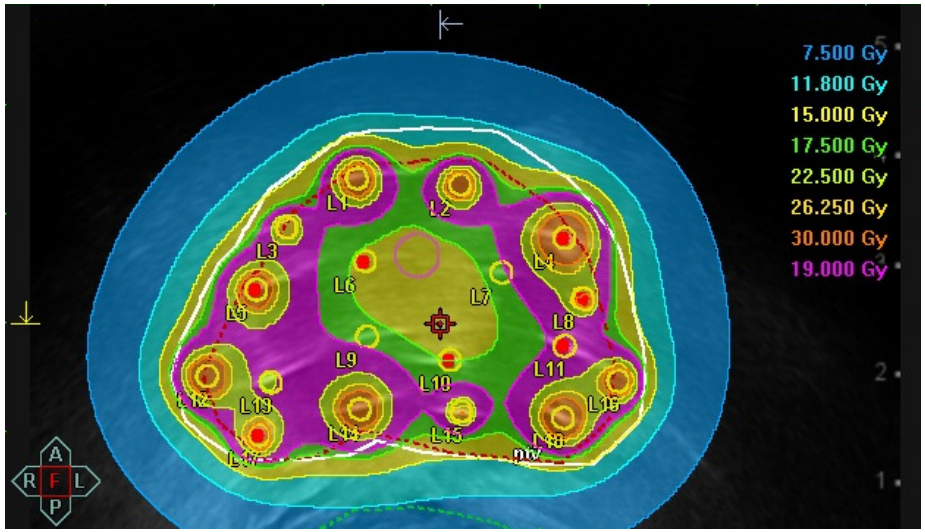
No Boost

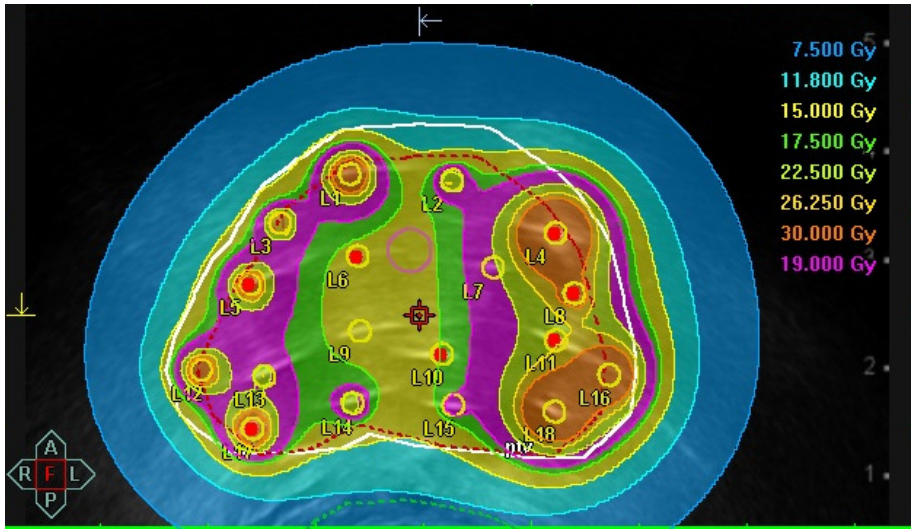
Sector Boost (treated)

Sector DVH Parameter	No Boost	Sector Boost
Mean D90 (range)	16.7Gy (16.5-17.0Gy)	20.6Gy (18.4-21.5Gy)
V19Gy	66.4%	92.0%
V150	33.3%	73.3%

6 Sectors







	No Boost	Sector Boost (treated)
Sector DVH Parameter	**No Boost**	**Sector Boost**
Mean D90 (range)	15.7Gy (14.4-16.7Gy)	16.4Gy (15.3-19.7Gy)
V19Gy	54.9%	72.3%
V150	24.4%	51.4%

Conclusions

- HDR Focused Boost to DIL is feasible while treating remaining prostate to standard dose
  - Typical dose escalation to F-GTV 110 -135%
  - Same OAR dose constraints used
- Sector boosting is an alternative efficient optimisation approach to dose escalate involved sectors.
  - Produces similar focal boost doses
  - Allows the option to use staging MRI scans
  - Successful implementation into routine clinical practice
  - Add minimal additional time to procedure
  - Currently TPS reports parameters for each sector only. Require combined sector information.