Focused Boost Treatments in HDR Prostate Brachytherapy

Peter Bownes

On behalf of the Leeds Prostate Brachy Team

UK and Ireland Prostate Brachytherapy Meeting, Belfast
Defining the Approach

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

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

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

Langley et al BJU Int: 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

<table>
<thead>
<tr>
<th>Std Objectives</th>
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<tbody>
<tr>
<td>$V_{100}^{PTV} &gt; 95%$,</td>
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<tr>
<td>$V_{150}^{prostate} &lt; 45%$,</td>
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<tr>
<td>$V_{200}^{prostate} &lt; 15%$</td>
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</tbody>
</table>

Rectum: $V_{15Gy} = 0$, $D_{2cc} < 11.8Gy$.
Urethra:
$D_{10\%} < 17.5Gy$, $D_{0.1cc} < 17.5Gy$
Results: Retrospective Planning Study
Mason et al Brachytherapy:2014:13(2) 137-145

Median DVH Parameters (error bars = range)

- Standard Plan
- Focal boost - no additional needles
- Focal boost - additional needles

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 vs F-PTV Boost

<table>
<thead>
<tr>
<th>Plan</th>
<th>Plan</th>
<th>D\textsubscript{90} (Gy)</th>
<th>V\textsubscript{100} (%)</th>
<th>V\textsubscript{150} (%)</th>
<th>V\textsubscript{200} (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prostate</td>
<td>STD</td>
<td>17.2 (16.6–17.5)</td>
<td>99.9 (99.3–100)</td>
<td>33.3 (28.1–43.2)</td>
<td>10.1 (5.5–13.5)</td>
</tr>
<tr>
<td></td>
<td>FBOOST</td>
<td>17.3 (16.6–17.8)</td>
<td>99.9 (99.0–99.9)</td>
<td>42.1 (32.1–52.5)</td>
<td>12.1 (8.7–20.5)</td>
</tr>
<tr>
<td></td>
<td>SBOOST</td>
<td>17.3 (16.6–17.7)</td>
<td>99.8 (99.2–100)</td>
<td>43.4 (32.5–57.2)</td>
<td>12.3 (8.6–17.5)</td>
</tr>
<tr>
<td>PTV</td>
<td>STD</td>
<td>16.2 (15.5–16.6)</td>
<td>92.8 (87.3–97.2)</td>
<td>28.8 (26.2–36.7)</td>
<td>8.9 (5.4–11.5)</td>
</tr>
<tr>
<td></td>
<td>FBOOST</td>
<td>16.3 (15.3–16.8)</td>
<td>91.6 (87.4–97.1)</td>
<td>35.0 (28.0–44.5)</td>
<td>10.1 (7.6–16.4)</td>
</tr>
<tr>
<td></td>
<td>SBOOST</td>
<td>16.1 (15.3–16.8)</td>
<td>91.6 (87.4–97.1)</td>
<td>35.9 (28.5–45.3)</td>
<td>10.9 (8.0–13.7)</td>
</tr>
<tr>
<td>F-GTV</td>
<td>STD</td>
<td>18.3 (16.1–21.8)</td>
<td>100 (99.6–100)</td>
<td>35.8 (9.1–85.1)</td>
<td>6.1 (0.6–32.2)</td>
</tr>
<tr>
<td></td>
<td>FBOOST</td>
<td>24.3 (20.5–30.4)</td>
<td>100 (–)</td>
<td>95.4 (73.1–100)</td>
<td>46.9 (14.5–91.4)</td>
</tr>
<tr>
<td></td>
<td>SBOOST</td>
<td>22.3 (19.9–25.8)</td>
<td>100 (–)</td>
<td>88.7 (66.3–100)</td>
<td>29.9 (12.3–59.9)</td>
</tr>
<tr>
<td>F-PTV</td>
<td>STD</td>
<td>17.5 (15.8–19.3)</td>
<td>100 (97.5–100)</td>
<td>33.7 (16.0–56.5)</td>
<td>8.9 (2.5–16.7)</td>
</tr>
<tr>
<td></td>
<td>FBOOST</td>
<td>21.0 (18.8–24.1)</td>
<td>100 (–)</td>
<td>77.2 (64.7–96.9)</td>
<td>30.2 (12.3–54.1)</td>
</tr>
<tr>
<td></td>
<td>SBOOST</td>
<td>19.8 (18.9–24.2)</td>
<td>100 (–)</td>
<td>75.6 (49.7–96.7)</td>
<td>23.4 (10.1–48.1)</td>
</tr>
<tr>
<td>Involved sectors</td>
<td>STD</td>
<td>17.7 (16.8–18.1)</td>
<td>100 (98.0–100)</td>
<td>37.8 (14.4–49.4)</td>
<td>9.8 (3.3–18.6)</td>
</tr>
<tr>
<td></td>
<td>FBOOST</td>
<td>19.0 (18.0–21.5)</td>
<td>100 (98.6–100)</td>
<td>62.2 (53.1–82.7)</td>
<td>20.9 (14.4–31.7)</td>
</tr>
<tr>
<td></td>
<td>SBOOST</td>
<td>20.3 (18.7–22.8)</td>
<td>100 (–)</td>
<td>74.7 (56.9–91.1)</td>
<td>27.5 (16.1–38.7)</td>
</tr>
</tbody>
</table>

- 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.

**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-PTV/sectors) for each patient.

**33% 22%**
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 focused 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)

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

Rectum: \( V_{15\text{Gy}} = 0 \), \( D_{2\text{cc}} < 11.8\text{Gy} \).
Urethra:
\( D_{10\%} < 17.5\text{Gy} \), \( D_{0.1\text{cc}} < 17.5\text{Gy} \)

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
- \( V_{150}, V_{19\text{Gy}}, D_{90}, D_{98} \) of involved sectors
Results

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

<table>
<thead>
<tr>
<th>Standard Dosimetric Parameter</th>
<th>Aim / Constraint</th>
<th>Median DVH Values (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>No Boost</td>
</tr>
<tr>
<td>V100 PTV (%)</td>
<td>&gt;95%</td>
<td>96.0 (94.5–98.0)</td>
</tr>
<tr>
<td>D90 PTV (Gy)</td>
<td>&gt; 15Gy</td>
<td>16.3 (16.0-16.6)</td>
</tr>
<tr>
<td>V100 Prostate (%)</td>
<td>&gt;95%</td>
<td>99.8 (99.3-99.96)</td>
</tr>
<tr>
<td>V150 Prostate (%)</td>
<td>&lt; 45%</td>
<td>30.8 (24.1-39.4)</td>
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<td>D90 Prostate (Gy)</td>
<td>&gt; 15Gy</td>
<td>17.2 (16.8–17.6)</td>
</tr>
<tr>
<td>D2cc Rectum (Gy)</td>
<td>&lt; 11.8Gy</td>
<td>8.7 (7.7-10.5)</td>
</tr>
<tr>
<td>D10 Urethra (Gy)</td>
<td>&lt; 17.5Gy</td>
<td>17.1 (17.1-17.2)</td>
</tr>
</tbody>
</table>

All aims/constraints met
Sector Results

- Mean PTV Volume = 47.2 cm$^3$ (range 32.5 to 84.8 cm$^3$)
- Mean Volume of involved sectors = 13.8 cm$^3$ (range 7.7 to 20.9 cm$^3$)
- 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

![Median DVH Parameters for Involved Sectors](image)

(error bars = range)
### 3 Sectors

#### Sector DVH Parameter

<table>
<thead>
<tr>
<th>Parameter</th>
<th>No Boost</th>
<th>Sector Boost</th>
<th>Sector Boost (treated)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mean D90</strong></td>
<td>16.7Gy (16.5-17.0Gy)</td>
<td>20.6Gy</td>
<td>20.6Gy (18.4-21.5Gy)</td>
</tr>
<tr>
<td><strong>V19Gy</strong></td>
<td>66.4%</td>
<td>92.0%</td>
<td></td>
</tr>
<tr>
<td><strong>V150</strong></td>
<td>33.3%</td>
<td>73.3%</td>
<td></td>
</tr>
</tbody>
</table>
### 6 Sectors

<table>
<thead>
<tr>
<th>Sector DVH Parameter</th>
<th>No Boost</th>
<th>Sector Boost (treated)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean D90 (range)</td>
<td>15.7Gy (14.4-16.7Gy)</td>
<td>16.4Gy (15.3-19.7Gy)</td>
</tr>
<tr>
<td>V19Gy</td>
<td>54.9%</td>
<td>72.3%</td>
</tr>
<tr>
<td>V150</td>
<td>24.4%</td>
<td>51.4%</td>
</tr>
</tbody>
</table>
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.