PROSTATE CANCER
BRACHYTHERAPY

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## Risk categorization

<table>
<thead>
<tr>
<th>Risk Category</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very Low Risk</td>
<td>T1c</td>
</tr>
<tr>
<td></td>
<td>GS ≤ 6</td>
</tr>
<tr>
<td></td>
<td>PSA &lt; 10ng/ml</td>
</tr>
<tr>
<td></td>
<td>&lt; 3 Bx core +ve with ≤ 6 Cancer in each core</td>
</tr>
<tr>
<td></td>
<td>PSA Density &lt; 0.15ng/mL/g</td>
</tr>
<tr>
<td>Low Risk</td>
<td>T1-T2</td>
</tr>
<tr>
<td></td>
<td>GS ≤ 6</td>
</tr>
<tr>
<td></td>
<td>PSA &lt; 10ng/ml</td>
</tr>
<tr>
<td>Intermediate Risk</td>
<td>T2b – T2c or GS 7 or PSA 10-20 ng/mL</td>
</tr>
<tr>
<td>High Risk</td>
<td>T3a or GS 8-10 or PSA &gt; 20ng/mL</td>
</tr>
<tr>
<td>Very High Risk</td>
<td>T3b-T4 or Primary Gleason Pattern &gt; 5 or &gt; 4core with GS8-10</td>
</tr>
<tr>
<td>Metastatic</td>
<td>any T, N1 or any T, any N, M1 disease</td>
</tr>
</tbody>
</table>

NCCN 2016
Prostate cancer: Treatment Outlook

**Surgery**

**Radiation**

**Chemotherapy**

**Hormone**

**TABLE 66.1** RECOMMENDATIONS OF PELVIC RADIOThERAPy AND HORMONES

<table>
<thead>
<tr>
<th></th>
<th>Low Risk</th>
<th>Favorable Intermediate Risk</th>
<th>Unfavorable Intermediate Risk</th>
<th>High Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radiotherapy</td>
<td>PORT</td>
<td>PORT</td>
<td>WPRT</td>
<td>WPRT</td>
</tr>
<tr>
<td>Androgen suppression therapy</td>
<td>Not indicated</td>
<td>Neoadjuvant (2 mo) Concurrent</td>
<td>Neoadjuvant (2 mo) Concurrent ± Adjuvant (2 mo)</td>
<td>Neoadjuvant (2 mo) Concurrent Adjuvant (24–36 mo)</td>
</tr>
</tbody>
</table>

PORT, prostate-only radiotherapy; WPRT, whole-pelvic radiotherapy.

Perez 6th Edn p1319
Role Of Brachytherapy

Evolution

- Radium 226
- Gold
- Iodine 125
- TRUS guidance
- HDR BT
- GEC ESTRO & ABS guideline

1914 Desnos E et al.
1952 Flocks R et al.
1970 Whitemore et al.
1983 Holm HH et al.
1998-2002
2012
Why Brachytherapy?

- Escalation of Biological Effective Dose to much higher extent than External Beam RT (IMRT)
  Higher cure rate.
- Minimizing RT dose to nearby critical organ.
- Encompasses Prostate motion better than External RT.
- Overall Treatment time lesser than usual 8 weeks time for dose escalated External RT.
Role of Brachytherapy

- **BT Mono-therapy:**
  - Low Risk group
  - Favorable Intermediate group
    - (Low volume disease/Predominant pattern3/one adverse feature)

- **Brachytherapy Boost (after/before EBRT):**
  - Unfavorable Intermediate group
  - High risk group

- **Recurrence**
Types of Brachytherapy used

- **Low Dose Rate Brachytherapy (LDR BT)**
  - Permanent Prostate BT (PPB)

<table>
<thead>
<tr>
<th>Isotope</th>
<th>T 1/2</th>
<th>Mean Energy</th>
<th>Seed strength</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iodine 125</td>
<td>60 days</td>
<td>27 keV</td>
<td>0.3-0.6 mCi</td>
</tr>
<tr>
<td>Palladium 103</td>
<td>17 days</td>
<td>21 keV</td>
<td>1.2-2.2 mCi</td>
</tr>
<tr>
<td>Cesium 131</td>
<td>9.7 days</td>
<td>30.4 keV</td>
<td>2.5-3.9 mCi</td>
</tr>
</tbody>
</table>

- **High Dose Rate Brachytherapy (HDR BT)**

<table>
<thead>
<tr>
<th>Isotope</th>
<th>T 1/2</th>
<th>Mean Energy</th>
<th>T-AKR (µGy.m²/GBq.h)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iridium 192</td>
<td>73.8 days</td>
<td>0.38 MeV</td>
<td>108</td>
</tr>
<tr>
<td>Cobalt 60</td>
<td>5.26 years</td>
<td>1.25 MeV</td>
<td>308</td>
</tr>
</tbody>
</table>
Prostate BT applicators
Permanent Prostate Brachytherapy

Patient evaluation and work up:
- HP with GS
- Pre Treatment PSA
- DRE to access Clinical “T”
- Prostate Volume (TRUS)
- Access tolerability of patient for extended dorsal lithotomy position
- Pre anesthetic check up
Contraindications of PPB

<table>
<thead>
<tr>
<th>Absolute</th>
<th>Relative</th>
</tr>
</thead>
<tbody>
<tr>
<td>□ Limited life expectancy</td>
<td>□ IPSS &gt; 20</td>
</tr>
<tr>
<td>□ Ataxia Telangiectasia</td>
<td>□ Prior Pelvic RT</td>
</tr>
<tr>
<td>□ High Operative Risk</td>
<td>□ Volume &gt; 60cc</td>
</tr>
<tr>
<td>□ Absence of Rectum</td>
<td>□ Large median lobes</td>
</tr>
<tr>
<td>□ Large TURP defect</td>
<td>□ Inflammatory Bowel Disease</td>
</tr>
</tbody>
</table>
PPB Procedure

Pre Implant Planning

Imaging
(MRI > TRUS > CECT)

Target volume determination

Virtual planning

Mapping of seed positions in template
PPB procedure

Implantation Procedure

- Trans-perineal seed implantation
- TRUS and template guidance
- Seed positions as per preplanning sketch
## PPB dose to Planning Target Volume

<table>
<thead>
<tr>
<th>Iodine 125</th>
<th>Palladium 103</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mono therapy</td>
<td>Mono therapy</td>
</tr>
<tr>
<td>140-160 Gy</td>
<td>110-125 Gy</td>
</tr>
<tr>
<td>Combined</td>
<td>Combined</td>
</tr>
<tr>
<td>EBRT: 41.4-50.4 Gy</td>
<td>EBRT: 41.4-50.4 Gy</td>
</tr>
<tr>
<td>1.8 Gy/ per day</td>
<td>1.8 Gy/ per day</td>
</tr>
<tr>
<td>BT: 108-110 Gy</td>
<td>BT: 90-100 Gy</td>
</tr>
</tbody>
</table>

BJ Devis et al. Brachytherapy 2012
# Post implant Care

## Post operative care
- Check cystoscopy
- Analgesic
- Antibiotic
- Antispasmodic
- Tamsulosin
- CT scan at week 6
- Emergency care

## Radiation Protection
- No mandatory precaution
- Avoid contact with children and pregnant women
- Normal sexual life
# PPB Results: Mono-therapy

<table>
<thead>
<tr>
<th>Researcher</th>
<th>n</th>
<th>Follow up (Years)</th>
<th>Early Risk</th>
<th>Intermediate Risk</th>
<th>High Risk</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sylevester et al. 2011</td>
<td>215</td>
<td>15</td>
<td>86%</td>
<td>80%</td>
<td>62</td>
<td>PSARFS</td>
</tr>
<tr>
<td>Taira et al. 2011</td>
<td>1656</td>
<td>7</td>
<td>98.6%</td>
<td>-</td>
<td>-</td>
<td>7yr OS 77.5%</td>
</tr>
<tr>
<td>Zelefsky et al. (Multi Inst) 2007</td>
<td>2693</td>
<td>8</td>
<td>82%</td>
<td>80%</td>
<td>48%</td>
<td>PSA RFS</td>
</tr>
<tr>
<td>Stone et al. 2011</td>
<td>2111</td>
<td>12</td>
<td>88%</td>
<td>-</td>
<td>-</td>
<td>PSARFS</td>
</tr>
<tr>
<td>Zelefsky et al. 2012</td>
<td>1446</td>
<td>5</td>
<td>98%</td>
<td>95%</td>
<td>-</td>
<td>PSARFS</td>
</tr>
<tr>
<td>Potter et al. 2011</td>
<td>1449</td>
<td>12</td>
<td>89%</td>
<td>-</td>
<td>-</td>
<td>PSARFS</td>
</tr>
</tbody>
</table>
## PPB results: Boost (with EBRT)

<table>
<thead>
<tr>
<th>Authors</th>
<th>n</th>
<th>Follow up (years)</th>
<th>Intermediate Risk</th>
<th>High Risk</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sylvester et al. 2007</td>
<td>232</td>
<td>15</td>
<td>80%</td>
<td>68%</td>
<td>PSA RFS</td>
</tr>
<tr>
<td>RTOG P - 0019</td>
<td>130</td>
<td>4</td>
<td>86%</td>
<td>-</td>
<td>PSA RFS</td>
</tr>
<tr>
<td>McMaster University</td>
<td>104</td>
<td>8.2</td>
<td>24%</td>
<td>-</td>
<td>Prostate biopsy rate</td>
</tr>
</tbody>
</table>
High Dose Rate Brachytherapy (HDR BT)
High Dose Rate BT

- Advantages:
  - Radiobiological advantage
  - Image guided accurate needles placement
  - Individualized source position and optimization facility.
  - Rapid delivery nullifies the influence of organ motion.
  - Cost effective.
  - Better radiation protection for personnel.
High Dose Rate BT

- **Disadvantages:**
  - Fractionated radiation
  - Increased work load per patient
  - Logistic issues (TRUS guidance)
  - Quality assurance
**HDR BT : Results**

Published outcome data for temporary high-dose-rate brachytherapy (HDR) with external beam radiotherapy in prostate cancer (most recent data cited where recurrent publications from the same group).

<table>
<thead>
<tr>
<th>First author</th>
<th>Patient numbers</th>
<th>HDR dose</th>
<th>bRFS (%)</th>
<th>G3/4 toxicity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Low</td>
<td>Inter</td>
</tr>
<tr>
<td>Borghede 1997</td>
<td>50</td>
<td>10 Gy x 2</td>
<td>84%</td>
<td>45 mo</td>
</tr>
<tr>
<td>Degr 2002</td>
<td>230</td>
<td>9-10 Gy x 2</td>
<td>100%</td>
<td>70%</td>
</tr>
<tr>
<td>Pellizon 2003</td>
<td>209</td>
<td>4-6 Gy x 4</td>
<td>91%</td>
<td>40 mo</td>
</tr>
<tr>
<td>Hiratsuka 2004</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chiang 2004</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Astron 2005</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Martinez 2005</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yamada 2006</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vargas 2006</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chin 2006</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Phan 2007</td>
<td></td>
<td></td>
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<tr>
<td>Chen 2007</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kalkner 2007</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sato 2008</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Demanes 2009</td>
<td>209</td>
<td>5.5-6 Gy x 4</td>
<td>90%</td>
<td>87%</td>
</tr>
<tr>
<td>Zwahlen 2010</td>
<td>196</td>
<td>4-5 Gy x 4</td>
<td>94%</td>
<td>83%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wilder 2010</td>
<td>284</td>
<td>5.5 Gy x 4</td>
<td>92%</td>
<td>79%</td>
</tr>
<tr>
<td>Morton 2011</td>
<td>125</td>
<td>15 Gy x 1</td>
<td>97.9%</td>
<td>97.9%</td>
</tr>
<tr>
<td>Ktreatian 2012</td>
<td>165</td>
<td>6 Gy x 3</td>
<td>92%</td>
<td>79%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>9.5 Gy x 2</td>
<td>95%</td>
<td>81%</td>
</tr>
</tbody>
</table>

**HDR BT as Boost with EBRT is effective dose escalation strategy with good bRFS, Local Control and Survival**

Hoskin PJ. Radiotherapy and Oncology 2013
## HDR BT + EBRT: Patient selection

### Inclusion criteria
- Stages T1b–T3b
- Any Gleason score
- Any PSA level

### Exclusion criteria
- TURP within 3–6 months
- Maximum urinary flow rate (Qmax) < 10 ml/s
- IPSS > 20
- Pubic arch interference
- Lithotomy position or anaesthesia not possible
- Rectal fistula

GEC- ESTRO 2013 guideline
Requirement for HDR BT

- Remote after loader
- Modern Planning system
- Prostate Template
- The Team Effort

OT and Brachytherapy Suit with Anesthesia support
Steps of HDR BT

- Patient preparation
- Pre BT MRI
- Pre Planning
- Anesthesia (Spinal)
- Procedure
- Imaging
- Planning
- Evaluation
- Treatment
- Post Radiation Care
Pre Procedure works

- Patient Preparation
- PAC Check up
- Pelvic MRI
- Bowel Preparation
Pre planning
Application
Application
Imaging

- CT or MR images obtained following recovery from anesthetics.
- CT Slice thickness $\leq$ 3mm
- MRI:
  - T2: Optimal anatomical definition
  - T1: Accurate catheter reconstruction
- Image fusion may maximize image accuracy
Contouring

- **Target:**
  - Clinical Target Volume

- **Organ At Risk:**
  - Urinary Bladder
  - Rectum
  - Sigmoid Colon
  - Urethra
  - Penile Bulb

**Clinical Target Volume (CTV):**
Prostate + extra prostatic extension + SV
3mm margin to cover macroscopic spread
Planning
Plan evaluation

Dose reporting

- External beam dose
- Implant technique; number of catheters;
- CTV: D90, V100, V150, V200
- PTV (if defined): D90, V100, V150, V200
- Organs at risk:
  - a. Rectum: D2 cc, D0.1 cc
  - b. Urethra: D0.1 cc, D10, D30

Dose Volume Histogram Parameters

OAR dose constraints:
- Rectum: D2 cc ≤ 75 Gy EQD2
- Urethra:
  - D0.1 cc = 6120 Gy EQD2
  - D10 ≤ 120 Gy EQD2
  - D30 ≤ 105 Gy EQD2
### Dose: Planning aim dose

#### EBRT + HDR BT

- EBRT dose: 45-50 Gy
- BT Dose:
  - 15 Gy in 3 #
  - 11–22 Gy in 2 #
  - 12–15 Gy in 1 #

#### HDR BT Mono-therapy

- 34 Gy in 4 #
- 36–38 Gy in 4 #
- 31.5 Gy in 3 #
- 26 Gy in 2 #

#### HDR BT in recurrence

- 36 Gy in 6 fractions
- 21 Gy in 3 fractions

---

**Golden Rule**

- D90 > Planning aim (100%)
- PTV V100 ≥ 95%

---

GEC ESTRO guideline 2013
## Dose fractionation evidences

<table>
<thead>
<tr>
<th>Institution</th>
<th>Dose fractionation</th>
<th>Bladder</th>
<th>Urethra</th>
<th>Rectum</th>
</tr>
</thead>
<tbody>
<tr>
<td>MSKCC</td>
<td>Boost 7Gyx3, Mono 9.5Gyx4, Salvage 8Gyx4</td>
<td></td>
<td>$V_{75} &lt; 1$ cc</td>
<td></td>
</tr>
<tr>
<td>UCSF</td>
<td>Boost 15Gyx1, Mono 10.5Gyx3, Salvage 8Gyx4*</td>
<td></td>
<td>$V_{125} &lt; 1$ cc, $V_{150} = 0$ cc</td>
<td></td>
</tr>
<tr>
<td>WBH</td>
<td>Boost 10.5Gyx2, Mono 4 $\times$ 9.5 Gy (historical), 12–13.5Gyx2 (current), Salvage 7Gyx4 combined with hyperthermia</td>
<td>No constraint (intra-op TRUS-based dosi)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TCC</td>
<td>Boost 6Gyx2 $\times$ 2 implants</td>
<td>$&lt;80%$ of Rx</td>
<td>$&lt;125%$ of prescription</td>
<td>$&lt;80%$ of Rx to outer wall</td>
</tr>
<tr>
<td>GW</td>
<td>Boost 6.5Gyx3, Mono two sessions of 6.5Gyx3</td>
<td>$&lt;100%$ prescription</td>
<td>$&lt;110%$ prescription</td>
<td>mucosa $&lt;60%$, outer wall $&lt;100%$</td>
</tr>
<tr>
<td>Toronto</td>
<td>Boost 15Gyx1</td>
<td>n/a</td>
<td>$D_{10} &lt; 118%$, Max $&lt; 125%$</td>
<td>$V_{80} &lt; 0.5$ cc</td>
</tr>
<tr>
<td>UCLA-CET</td>
<td>Boost 6Gyx4, Mono 7.25Gyx6</td>
<td>90–100% wall, 80% balloon</td>
<td>120% combo, 105% any TUR, 110% mono</td>
<td>Rectal wall 80%</td>
</tr>
</tbody>
</table>

* (dose tunnel whenever possible)
Treatment

Using transrectal ultrasound and a template as a guide, metal needles are inserted into the prostate.

Template is sutured to the skin between the scrotum and the anus and metal needles are replaced with hollow plastic ones.

Thin cable from HDR unit is passed through needles to deliver high-intensity radiation directly into the prostate.

High-intensity radiation delivered directly into the prostate.
**HDR BT**

- **Post Implant care**
  - Analgesia: Epidural preferred
  - If multiple fraction: give 2# < 24hrs
    - > 2# repeat implantation
  - Antispasmodic
  - Antibiotic
  - Bladder irrigation if needed
  - Check catheter displacement
Follow up

- 4-6 monthly for first 2 years
- Annually > 2 years

To do list:
- DRE
- Serum PSA
- Other investigations as per clinical need
- Evaluate GU/rectal/Sexual toxicities
Toxicity

Genitourinary

- Acute:
  - Reversible urgency and frequency
  - Acute urinary retention (<5%)

- Late:
  - Urinary stricture (<15%)
  - Prolonged urinary incontinence (Rare)
# Toxicity

## Grade 3 late GU complications

<table>
<thead>
<tr>
<th>Author</th>
<th>N</th>
<th>Followup (mo)</th>
<th>Dose</th>
<th>Type of treatment</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Astrom (60)</td>
<td>214</td>
<td>48</td>
<td>10Gy×2</td>
<td>Boost</td>
<td>13 patients experienced urethral strictures</td>
</tr>
<tr>
<td>Demanes (17)</td>
<td>209</td>
<td>86</td>
<td>5.5 Gy−6.0Gy×4</td>
<td>Boost</td>
<td>6.7% late Grade 3 and 1% Grade 4 GU toxicity (TUR related)</td>
</tr>
<tr>
<td>Hsu (7)</td>
<td>112</td>
<td>30</td>
<td>9.5Gy×2</td>
<td>Boost</td>
<td>Less than 3% Grade 3 toxicity at 18 mo</td>
</tr>
<tr>
<td>Phan (49)</td>
<td>309</td>
<td>59</td>
<td>6Gy×4</td>
<td>Boost</td>
<td>4% late Grade 3 GU</td>
</tr>
<tr>
<td>Deger (50)</td>
<td>442</td>
<td>60</td>
<td>9−10 Gy×2</td>
<td>Boost</td>
<td>9% late Grade 3 GU toxicity</td>
</tr>
<tr>
<td>Martinez (77)</td>
<td>207</td>
<td>66</td>
<td>5.5−11Gy×2</td>
<td>Boost</td>
<td>8% late Grade 3 GU toxicity</td>
</tr>
<tr>
<td>Sullivan (52)</td>
<td>425</td>
<td>41</td>
<td>4−5Gy×46.5 Gy×3</td>
<td>Boost</td>
<td>8% late Grade 3 GU toxicity</td>
</tr>
<tr>
<td>Zwahlen (73)</td>
<td>587</td>
<td>66</td>
<td>5Gy×4−6Gy×3</td>
<td>Boost</td>
<td>7% late Grade 3 GU toxicity</td>
</tr>
<tr>
<td>Demanes (57)</td>
<td>298</td>
<td>62</td>
<td>7Gy×6</td>
<td>Mono</td>
<td>3% late Grade 3 GU toxicity</td>
</tr>
<tr>
<td>Ghilizan (51)</td>
<td>173</td>
<td>17</td>
<td>9.5Gy×4</td>
<td>Mono</td>
<td>1% late GU Grade 3 toxicity</td>
</tr>
<tr>
<td>Hoskin (78)</td>
<td>197</td>
<td>37</td>
<td>12−13.5Gy×2</td>
<td>Mono</td>
<td>3−7% strictures</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>8.5Gy×4</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>9Gy×4</td>
<td></td>
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</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>10.5Gy×3</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>13Gy×2</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

GU = genitourinary; TUR = transurethral resection.
Toxicity

Rectal toxicity

- Acute:
  - Proctitis
  - Transient urgency and frequency

- Late:
  - Rectal telangeiectasia (4-11%)
  - Rectal Ulcer (<2%)
  - Rectal fistula (<1%)

Sexual

- Erectile dysfunction (40% cases)
  - Reversible (PD 5 Inhibitors)

Perez and Brady 2013