Role of Radiotherapy in Prostate Cancer

Recent advances

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Instructor, Duke-NUS Graduate Medical School, Singapore

ESMO GU Preceptorship Programme,
21 Nov 2018, Singapore
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Varian, AstraZeneca, Janssen

Advisory/Consultancy roles:
Varian
Outline

- **RT in the management of localised PCa**
  - Intermediate-risk vs High-risk vs M1 disease

- **Advancement in RT techniques**
  - Technological advances – SBRT; PSMA PET-fusion
  - Dose escalation and fractionation regimes
  - *HDR brachytherapy – more than just dose escalation?*
Treatment of Prostate Cancer in 2018

Options

- Active surveillance
- Surgery (Radical prostatectomy, RadP – open vs robotic)

- Radiotherapy
  - Image guidance
  - Brachytherapy
  - Stereotactic body ablative radiotherapy
  - Proton beam therapy

- Radiotherapy + hormonal therapy (novel anti-androgens)
Treatment of Prostate Cancer in 2018

**Low**
- cT1-T2a
- PSA <10
- GS ≤6
- Active surveillance

**Intermediate**
- cT2b-T2c
- PSA 10-20
- GS 7
- Favourable: RadP vs IGRT

**High**
- cT3-4
- PSA >20
- GS 8-10
- Unfavourable: IGRT + ADT

---

**NCCN Zumsteg-Spratt criteria (Eur Urol, 2013)**

Sub-stratification for IR-PCa
- ≥50% +ve biopsy cores
- Primary GG 4
- ≥2 NCCN IRF – cT2b,c; GS 7; PSA 10-20 ng/ml

ESMO GU Preceptorship, 21 Nov 2018, Singapore
Radiotherapy of Prostate Cancer in 2018

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Favourable RadP vs IGRT

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PSA >20
GS 8-10
Unfavourable IGRT + ADT

RadP +/- IGRT IGRT + LTAD

IGRT (image-guided RT)
- SBRT – 36.25 Gy/5#
- Mod hypofract – 60 Gy (3 Gy/#)
- Conv fract – 74-78 Gy (2 Gy/#)

Brachy – LDR (seeds) vs HDR mono

ESMO GU Preceptorship, 21 Nov 2018, Singapore
Radiotherapy of Prostate Cancer in 2018

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  over mod hypofract
- RT to Pelvis

Brachy – HDR boost
Radiotherapy of Prostate Cancer in 2018

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ESMO GU Preceptorship, 21 Nov 2018, Singapore
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Brachy – HDR boost

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Brachy – HDR boost

ESMO GU Preceptorship, 21 Nov 2018, Singapore
10-Year Outcomes after Monitoring, Surgery, or Radiotherapy for Localized Prostate Cancer


UK-wide clinical trial of 1,500 men, reported 2016
PROTECT cohort

10-Year Outcomes after Monitoring, Surgery, or Radiotherapy for Localized Prostate Cancer


2664 Patients with localized disease were eligible

1643 Underwent randomization

545 Were assigned to active monitoring

553 Were assigned to radical prostatectomy

545 Were assigned to radical radiotherapy

ESMO GU Preceptorship, 21 Nov 2018, Singapore
PROTECT cohort

Majority favourable-risk patients

<table>
<thead>
<tr>
<th></th>
<th>Active monitoring protocol (n=545)</th>
<th>Surgery (n=553)</th>
<th>Radiotherapy protocol (n=545)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median PSA² in ng/ml (IQR³)</td>
<td>4.7 (3.7, 6.7)</td>
<td>4.9 (3.7, 6.7)</td>
<td>4.8 (3.7, 6.7)</td>
</tr>
<tr>
<td>PSA² 10+ ng/ml (%)</td>
<td>57 (10)</td>
<td>57 (10)</td>
<td>58 (11)</td>
</tr>
<tr>
<td>Gleason score</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>421 (77)</td>
<td>422 (76)</td>
<td>423 (78)</td>
</tr>
<tr>
<td>7</td>
<td>111 (20)</td>
<td>120 (22)</td>
<td>108 (20)</td>
</tr>
<tr>
<td>8-10</td>
<td>13 (2)</td>
<td>10 (2)</td>
<td>14 (3)</td>
</tr>
<tr>
<td>Missing</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Clinical stage</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T1c</td>
<td>410 (75)</td>
<td>410 (74)</td>
<td>429 (79)</td>
</tr>
<tr>
<td>T2</td>
<td>135 (25)</td>
<td>143 (26)</td>
<td>116 (21)</td>
</tr>
</tbody>
</table>
Outcomes: *low-risk and favourable intermediate-risk prostate cancers*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Active Monitoring (N = 545)</th>
<th>Surgery (N = 553)</th>
<th>Radiotherapy (N = 545)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total person-yr in follow-up</td>
<td>5393</td>
<td>5422</td>
<td>5339</td>
</tr>
<tr>
<td>No. of deaths due to prostate cancer†</td>
<td>8</td>
<td>5</td>
<td>4</td>
</tr>
</tbody>
</table>

Hamdry et al. on behalf of *PROTECT* investigators, NEJM, 2016

ESMO GU Preceptorship, 21 Nov 2018, Singapore
PROTECT: QOL post-RT

- Incontinence
- Leakag e (Pads usage)
- Erectile function
- Sexual satisfaction

Donovan et al., NEJM, 2016

ESMO GU Preceptorship, 21 Nov 2018, Singapore
North Carolina Prospective Observational cohort
N = 1225; 2011-2013

Chen, et al., JAMA 2017

UK PROTECT

ESMO GU Preceptorship, 21 Nov 2018, Singapore
NC prospective: QOL post-RT

Contemporary data
Consistent with PROTECT
Highlights need for such high quality data

Chen, et al., JAMA, 2017

ESMO GU Preceptorship, 21 Nov 2018, Singapore
RT outcomes after AS

Curative Radiation Therapy at Time of Progression Under Active Surveillance Compared With Up-Front Radical Radiation Therapy for Prostate Cancer

Propensity-matched analysis
- LDR brachytherapy; N = 165
- IGRT-EBRT; N = 394
- 50% Unfavourable IR-PCa
Radiotherapy of Prostate Cancer in 2018

Low
- T1-T2a
- PSA < 10
- GS ≤ 6

Intermediate
- T2b-T2c
- PSA 10-20
- GS 7

High
- T3-4
- PSA > 20
- GS 8-10

What is the optimal dose??

Active surveillance

Favourable
- IGRT (image-guided RT)
  - SBRT – 36.25 Gy/5#
  - Mod hypofract – 60 Gy (3 Gy/#)
  - Conv fract – 74-78 Gy (2 Gy/#)
- Brachy – LDR (seeds) vs HDR mono

Unfavourable
- IGRT (image-guided RT)
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  - RT to Pelvis???
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RadP +/- IGRT
- IGRT + LTAD

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- Brachy – HDR boost

ESMO GU Preceptorship, 21 Nov 2018, Singapore
Defining the optimal dose in PCa

Biological Effective Dose

\[ \text{BED} = \text{Total Dose}(1 + \text{dose per } \#\alpha/\beta) \]

- Assumption: \( \alpha/\beta = 1.5 \text{ Gy for tumour} \) & \( 3.0 \text{ Gy for normal tissue} \)

**SBRT - 40 Gy/5#**
- \( \text{EQD2tumour} = 108.6 \text{ Gy} \)
- \( \text{EQD2normal} = 88 \text{ Gy} \)

**Conv fract 74-78 Gy/37-39# vs Pelvic RT (54 Gy) + Brachy boost (21 Gy/3#)**
- \( \text{EQD2tumour} = 101.9 \text{ Gy} \)
- \( \text{EQD2normal} = 93.8 \text{ Gy} \)

**Mod Hypofract - 60 Gy/20#**
- \( \text{EQD2tumour} = 77 \text{ Gy} \)
- \( \text{EQD2normal} = 72 \text{ Gy} \)

ESMO GU Preceptorship, 21 Nov 2018, Singapore
Contemporary moderate hypofractionation RCTs

**N = 6339**

**CHHIP (UK)**

N = 3216

60 Gy vs 74 Gy HR 0.84 (90% CI 0.68-1.03), log-rank p=0.16

57 Gy vs 74 Gy HR 1.20 (90% CI 0.99-1.46), log-rank p=0.11

**RTOG 0415 (US)**

N = 1115

**PROFIT (Canada/EU)**

N = 1206

**HYPRO (Dutch)**

N = 820

ESMO GU Preceptorship, 21 Nov 2018, Singapore
Contemporary moderate hypofractionation RCTs

\[ N = 6339 \]

CHHIP (UK)  
RTOG 0415 (US)

Caveat: >75% of patients are fav risk disease
What about unfav risk?

ESMO GU Preceptorship, 21 Nov 2018, Singapore
Dose escalation in the unfavourable risk group?

Evidence for a dose response for PSA control

Zelefsky et al J Urol 2006
Dose escalation in the unfavourable risk group?

Evidence for a dose response for PSA control

Improved outcomes with dose escalation in localized prostate cancer treated with precision image-guided radiotherapy

Hamid Raziei, Fabio Y. Moraes, Jure Murgic, Melvin L.K. Chua, Melania Pintilie, Peter Chung, Cynthia Ménard, Andrew Bayley, Mary Gospodarowicz, Padraig Warde, Tim Craig, Charles Catton, Robert G. Bristow, David A. Jaffray, Alejandro Berlin

Radiation Medicine Program, Princess Margaret Cancer Centre, University Health Network, Department of Radiation Oncology, University of Toronto; Department of Biostatistics, Princess Margaret Cancer Centre, University Health Network, Toronto; and Département de radio-oncologie, Centre hospitalier de l’Université de Montréal (CHUM), Montréal, Canada

Gray's test p=1.4e-06
75.6 Gy, n=293, BCR at 8y=41.9%
79.0 Gy, n=313, BCR at 8y=31.9%
78.8 Gy, n=355, BCR at 8y=18.6%

Lower failures

Overall

IR-PCa

HR-PCa

ESMO GU Preceptorship, 21 Nov 2018, Singapore
Dose escalation in the unfavourable risk group?

**Evidence for a dose response for PSA control**

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**Graphs:**

- **Overall**
- **IR-PCa**
- **HR-PCa**
- **Fav IR-PCa**
- **Unfav IR-PCa**

*ESMO GU Preceptorship, 21 Nov 2018, Singapore*
## Randomised trials of dose escalation with Conventional Hyperfractionation

<table>
<thead>
<tr>
<th>Trial</th>
<th>n</th>
<th>Risk group(s)</th>
<th>Freedom from Biochemical Failure (5-10 year)</th>
<th>Subgroup benefit</th>
</tr>
</thead>
<tbody>
<tr>
<td>MD Anderson</td>
<td>301</td>
<td>All</td>
<td>73% v 50%</td>
<td>PSA&gt;10 or High-risk</td>
</tr>
<tr>
<td>GETUG 06</td>
<td>306</td>
<td>Intermediate, High</td>
<td>77% v 68%</td>
<td>PSA&gt;15</td>
</tr>
<tr>
<td>PROG</td>
<td>393</td>
<td>All</td>
<td>83% v 68%</td>
<td>Low</td>
</tr>
<tr>
<td>Dutch</td>
<td>664</td>
<td>All</td>
<td>54% v 47%</td>
<td>Intermediate</td>
</tr>
<tr>
<td>UK MRC RT01</td>
<td>843</td>
<td>All</td>
<td>55% v 43%</td>
<td>All</td>
</tr>
<tr>
<td>RTOG 0126</td>
<td>1499</td>
<td>Intermediate</td>
<td>70% v 55%</td>
<td>Intermediate</td>
</tr>
</tbody>
</table>
Randomised trials of dose escalation with Conventional Hyperfractionation

<table>
<thead>
<tr>
<th>Trial</th>
<th>Local control</th>
<th>Salvage AST</th>
<th>Distant metastases</th>
<th>Prostate cancer mortality</th>
<th>Overall survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>MD Anderson</td>
<td></td>
<td></td>
<td></td>
<td>No</td>
<td>(8-year)</td>
</tr>
<tr>
<td>GETUG 06</td>
<td></td>
<td></td>
<td></td>
<td>No</td>
<td>(5-year)</td>
</tr>
<tr>
<td>PROG</td>
<td></td>
<td></td>
<td></td>
<td>No</td>
<td>(10-year)</td>
</tr>
<tr>
<td>Dutch</td>
<td></td>
<td></td>
<td></td>
<td>No</td>
<td>(7-year)</td>
</tr>
<tr>
<td>UK MRC RT01</td>
<td></td>
<td></td>
<td></td>
<td>No</td>
<td>(10-year)</td>
</tr>
<tr>
<td>RTOG 0126</td>
<td></td>
<td></td>
<td></td>
<td>No</td>
<td>(10-year)</td>
</tr>
</tbody>
</table>
RTOG 0126: Largest DE study with 10 Gy dose response

Effect of Standard vs Dose-escalated Radiation Therapy for Patients With Intermediate-Risk Prostate Cancer
The NRG Oncology RTOG 0126 Randomized Clinical Trial

No overall survival

Improved PSA control of 10-15%

ESMO GU Preceptorship, 21 Nov 2018, Singapore
Limited DE: Boost to DIL

Prostate Stereotactic Ablative Radiation Therapy Using Volumetric Modulated Arc Therapy to Dominant Intraprostatic Lesions

Standard whole prostate gland radiotherapy with and without lesion boost in prostate cancer: Toxicity in the FLAME randomized controlled trial

2014

MRI DIL  
DWI

Plan set B: Boost to DILs, prostate alone

<table>
<thead>
<tr>
<th>α/β (Gy)</th>
<th>Median</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>TCP: Prostate minus DIL (s)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>87.9*</td>
<td>82.2-89.9</td>
</tr>
<tr>
<td>3</td>
<td>95.5*</td>
<td>93.1-96.5</td>
</tr>
<tr>
<td>15</td>
<td>97.7*</td>
<td>96.3-98.4</td>
</tr>
</tbody>
</table>

2018

GU

GI

ESMO GU Preceptorship, 21 Nov 2018, Singapore
NCCS GU Radiation Oncology Program

Low-risk
- Active surveillance
- Offer SBRT trial – PROSTAR

Intermediate-risk
- Favourable – 60 Gy in 20# or PROSTAR
- Unfavourable – 74-78 Gy in 39# +/- 6-mo ADT (STAD)

High-risk
- 74-78 Gy in 39# + 3-y ADT (LTAD) +/- 1-2 y combination Zytiga??
- 46 Gy + HDR boost (15 Gy) + 1 to 3-y ADT (LTAD)
- ASCENDE-RT
Early data with Prostate SBRT

- **N = 67**
- **MFU = 2.7y**
- **36.25Gy in 5 fractions over 1.5 weeks**

King, et al, IJORB, 2012
“Comparable” outcomes with DE-EBRT

N = 1100

<table>
<thead>
<tr>
<th></th>
<th>35 Gy</th>
<th>36.25 Gy</th>
<th>38–40 Gy</th>
<th>ADT use</th>
<th>FU*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>641 (58%)</td>
<td>254 (40%)</td>
<td>319 (50%)</td>
<td>68 (11%)</td>
<td>50 (8%)</td>
</tr>
<tr>
<td>Intermediate</td>
<td>334 (30%)</td>
<td>108 (32%)</td>
<td>188 (56%)</td>
<td>38 (11%)</td>
<td>49 (15%)</td>
</tr>
<tr>
<td>High</td>
<td>125 (11%)</td>
<td>23 (17%)</td>
<td>82 (66%)</td>
<td>20 (16%)</td>
<td>48 (38%)</td>
</tr>
<tr>
<td>Total</td>
<td>1100</td>
<td>385 (35%)</td>
<td>589 (54%)</td>
<td>126 (11%)</td>
<td>147 (14%)</td>
</tr>
</tbody>
</table>
“Comparable” late toxicities with DE-EBRT

Table 3. Comparison of late urinary (GU) and rectal (GI) toxicity on the RTOG scale from the dose-escalation arm of randomized trials and intensity-modulated radiotherapy-based hypofractionated studies

<table>
<thead>
<tr>
<th>Series</th>
<th>n</th>
<th>Dose/no. fx and median FU</th>
<th>GI Gr. 2</th>
<th>GI Gr. 3</th>
<th>GI Gr. 4</th>
<th>GU Gr. 2</th>
<th>GU Gr. 3</th>
<th>GU Gr. 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dutch†</td>
<td>333</td>
<td>78/39 and 4.2 yr</td>
<td>27%</td>
<td>5%</td>
<td>0%</td>
<td>26%</td>
<td>13%</td>
<td>0%</td>
</tr>
<tr>
<td>MDA‡</td>
<td>151</td>
<td>78/39 and 8.7 yr</td>
<td>19%</td>
<td>7%</td>
<td>0%</td>
<td>7%</td>
<td>3%</td>
<td>0%</td>
</tr>
<tr>
<td>MGH§</td>
<td>196</td>
<td>79.2/44 and 8.9 yr</td>
<td>24%</td>
<td>1%</td>
<td>0%</td>
<td>27%</td>
<td>2%</td>
<td>0%</td>
</tr>
<tr>
<td>RT01∥</td>
<td>422</td>
<td>74/37 and 5.2 yr</td>
<td>20%</td>
<td>6%</td>
<td>0%</td>
<td>4%</td>
<td>4%</td>
<td>0%</td>
</tr>
<tr>
<td>Kupelian¶</td>
<td>770</td>
<td>70/28 and 3.7 yr</td>
<td>3.1%</td>
<td>1.3%</td>
<td>0.1%</td>
<td>5.1%</td>
<td>0.1%</td>
<td>0%</td>
</tr>
<tr>
<td>Martin**</td>
<td>92</td>
<td>60/20 and 3.2 yr</td>
<td>4%</td>
<td>NR</td>
<td>0%</td>
<td>3%</td>
<td>NR</td>
<td>0%</td>
</tr>
<tr>
<td>Coote††</td>
<td>60</td>
<td>60/20 and 2 yr*</td>
<td>4%</td>
<td>NR</td>
<td>0%</td>
<td>4.2%</td>
<td>1.6%</td>
<td>0%</td>
</tr>
<tr>
<td>Lock‡‡</td>
<td>66</td>
<td>63.2/20 and 3 yr</td>
<td>25%</td>
<td>3.1%</td>
<td>1.5%</td>
<td>14.1%</td>
<td>4.7%</td>
<td>0%</td>
</tr>
</tbody>
</table>

ESMO GU Preceptorship, 21 Nov 2018, Singapore
**PROSTAR (PROstate STereotactic Ablative Radiotherapy)**

**NCCS prospective phase II trial**

- Single institution; Single-arm
- **NCCN Low-risk** or **single intermediate risk factor** (DRE T2b-c or Gleason 7 or PSA 10-20); organ-confined prostate adenocarcinoma, with no MRI evidence of ECE and SV invasion
- **36.25Gy in 5 fractions over 1.5 weeks (EOD)** delivered using LINAC-based treatment system
- No hormonal therapy
- **Primary end-point** - severe late GI and GU toxicities
- **Secondary end-points** – Patient-reported QOL, acute RT toxicities, biochemical relapse, prostate cancer specific mortality, overall survival
Precise targeting of **prostate & pelvis**

Contouring

**MRI**

**CT**

ESMO GU Preceptorship, 21 Nov 2018, Singapore
Small overlap

Small overlap
Target contouring
Accurate delineation of normal organs

- Rectum
- Bladder
- Fem heads
- Urethra
- Penile bulb
Plan optimisation for PTV coverage against OAR doses

ESMO GU Preceptorship, 21 Nov 2018, Singapore
Precise targeting of *prostate & pelvis*

**RT plan – Prostate + Pelvis**

- (L) Limitation of hotspot
- Ability to limit doses to rectum even if we RT the SVs
- (Top) SIB plan – 25 Gy to Pelvis; 35 Gy to Prostate

### Dose constraints

<table>
<thead>
<tr>
<th>Target</th>
<th>Parameter</th>
<th>Required Value</th>
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</thead>
<tbody>
<tr>
<td>PTV</td>
<td>D95% (Gy)</td>
<td>&gt;=35.00 Gy</td>
</tr>
<tr>
<td>PTV Dmin</td>
<td>Dmin (Gy)</td>
<td>&gt;=33.25 Gy</td>
</tr>
<tr>
<td>PTV Dmin (Major)</td>
<td>Dmin (Gy)</td>
<td>&gt;=32.55 Gy</td>
</tr>
<tr>
<td>PTV</td>
<td>D1cc (Gy)</td>
<td>&lt;=37.45 Gy</td>
</tr>
<tr>
<td>PTV</td>
<td>Dmax (Gy)</td>
<td>&lt;=37.45 Gy</td>
</tr>
<tr>
<td>PTV Volume</td>
<td>V0 Gy (cc)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Organ at Risk</th>
<th>Parameter</th>
<th>Required Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rectum</td>
<td>D1cc (Gy)</td>
<td>&lt;=36.75 Gy</td>
</tr>
<tr>
<td>Rectum</td>
<td>D3cc (Gy)</td>
<td>&lt;=33.25 Gy</td>
</tr>
<tr>
<td>Rectum</td>
<td>D10% (Gy)</td>
<td>&lt;=31.50 Gy</td>
</tr>
<tr>
<td>Rectum</td>
<td>D20% (Gy)</td>
<td>&lt;=28.00 Gy</td>
</tr>
<tr>
<td>Rectum</td>
<td>D50% (Gy)</td>
<td>&lt;=17.50 Gy</td>
</tr>
<tr>
<td>Bladder</td>
<td>D1cc (Gy)</td>
<td>&lt;=36.75 Gy</td>
</tr>
<tr>
<td>Bladder</td>
<td>D10% (Gy)</td>
<td>&lt;=31.50 Gy</td>
</tr>
<tr>
<td>Bladder</td>
<td>D50% (Gy)</td>
<td>&lt;=17.50 Gy</td>
</tr>
<tr>
<td>Femur L</td>
<td>Dmax (Gy)</td>
<td>&lt;=19.25 Gy</td>
</tr>
<tr>
<td>Femur L</td>
<td>D10cc (Gy)</td>
<td>&lt;=19.25 Gy</td>
</tr>
<tr>
<td>Femur R</td>
<td>Dmax (Gy)</td>
<td>&lt;=19.25 Gy</td>
</tr>
<tr>
<td>Femur R</td>
<td>D10cc (Gy)</td>
<td>&lt;=19.25 Gy</td>
</tr>
<tr>
<td>Femur Both</td>
<td>Dmax (Gy)</td>
<td>&lt;=19.25 Gy</td>
</tr>
<tr>
<td>Femur Both</td>
<td>D10cc (Gy)</td>
<td>&lt;=19.25 Gy</td>
</tr>
<tr>
<td>Urethra</td>
<td>Dmax (Gy)</td>
<td>&lt;=37.45 Gy</td>
</tr>
<tr>
<td>Penile Bulb</td>
<td>Dmax (Gy)</td>
<td>&lt;=35.00 Gy</td>
</tr>
<tr>
<td>Penile Bulb</td>
<td>D3cc (Gy)</td>
<td>&lt;=19.25 Gy</td>
</tr>
<tr>
<td>Small Bowel</td>
<td>Dmax (Gy)</td>
<td>&lt;=30.00 Gy</td>
</tr>
<tr>
<td>Small Bowel</td>
<td>D1cc (Gy)</td>
<td>&lt;=27.50 Gy</td>
</tr>
<tr>
<td>Large Bowel</td>
<td>Dmax (Gy)</td>
<td>&lt;=30.00 Gy</td>
</tr>
<tr>
<td>Large Bowel</td>
<td>D1cc (Gy)</td>
<td>&lt;=27.50 Gy</td>
</tr>
<tr>
<td>Skin</td>
<td>Dmax (Gy)</td>
<td>&lt;=29.05 Gy</td>
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</table>

ESMO GU Preceptorship, 21 Nov 2018, Singapore
Post-SBRT *Late effects*

<table>
<thead>
<tr>
<th>Late GI Toxicities</th>
<th>Number of Patients (%) N=47</th>
</tr>
</thead>
<tbody>
<tr>
<td>G0</td>
<td>30(63.8%)</td>
</tr>
<tr>
<td>G1</td>
<td>16(34.1%)</td>
</tr>
<tr>
<td>G2</td>
<td>1(2.1%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Late GU Toxicities</th>
<th>Number of Patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>G0</td>
<td>26(27.6%)</td>
</tr>
<tr>
<td>G1</td>
<td>17(69.8%)</td>
</tr>
<tr>
<td>G2</td>
<td>4(8.4%)</td>
</tr>
</tbody>
</table>

GI – 1 case of bleed  
GU – 4 cases of urine frequency
Post-SBRT QOL change over time

Mean Score for each domain

Mean Score for each domain for Top 50th percentile

Mean Score for each domain for Bottom 50th percentile

GI
GU
Sexual

Baseline 12 months Post RT FU 24 months Post RT FU
Time after SBRT (months)

Baseline 12 months Post RT FU 24 months Post RT FU
Time after SBRT (months)

Baseline 12 months Post RT FU 24 months Post RT FU
Time after SBRT (months)

ESMO GU Preceptorship, 21 Nov 2018, Singapore
Post-SBRT Sexual dissatisfaction

ESMO GU Preceptorship, 21 Nov 2018, Singapore
PROSTAR vs other SBRT studies

- 230 low-risk treated with Cyber-knife;
- 35Gy & 36.25Gy in 5 consecutive days;
- 10 yr DFS 93%;
- 10% G2-3 GU; 4% G2 GI;
- EPIC sexual score declined by 40%

ESMO GU Preceptorship, 21 Nov 2018, Singapore
HDR brachytherapy boost as an effective dose intensification strategy

ASCENDE-RT
Ph III trial
(Morris et al., IJORBP, 2017)

Control arm
46 Gy EBRT to Pelvis
+ 32 Gy to Prostate
+ 12-mo ADT

Experimental arm
46 Gy EBRT to Pelvis
+ LDR 110 Gy to Prostate
+ 12-mo ADT
HDR brachytherapy boost as an effective dose intensification strategy

Biochemical Progression Free survival

• Primary Endpoint: By Intent to treat

Kaplan-Meier (95% CI)

Randomization

(N=398)

DE-EBRT (N=200)  LDR-PB (N=198)

PFS

5 yr  83.8 (±5.6)  88.7 (±4.8)

7 yr  75.0 (±7.2)  86.2 (±5.4)

9 yr  62.4 (±9.8)  83.3 (±6.6)

Log rank P = 0.001

DE-EBRT ARM

Intermediate-risk

High-risk
Contemporary data with HDR brachy boost

UK MVCC Ph III *(Hoskin et al., 2012)*
Int-high-risk Prostate Cancers
55 Gy/20# vs
37.5 Gy/15# + 8.5 Gy x 2 HDR

Beaumont *(Martinez et al., 2011)*
Int-high-risk Prostate Cancers
46 Gy/23# to Pelvis ->
<8.5 Gy x 2 HDR vs >9 Gy x 2 HDR
Radiotherapy to the primary tumour for newly diagnosed, metastatic prostate cancer (STAMPEDE): a randomised controlled phase 3 trial

N = 2061, 117 centres, 2018

[Graphs showing failure-free survival and overall survival with and without radiotherapy]
Radiotherapy to the primary tumour for newly diagnosed, metastatic prostate cancer (STAMPEDE): a randomised controlled phase 3 trial

N = 2061, 117 centres, 2018
Radiotherapy to the primary tumour for newly diagnosed, metastatic prostate cancer (STAMPEDE): a randomised controlled phase 3 trial

N = 2061, 117 centres, 2018

HORRAD trial, Boeve, Eur Urol, 2018
Summary

- Contemporary techniques have resulted in optimal local control and favourable toxicity profiles in localised prostate cancer.

- Dose escalation and fractionation require a risk-adapted approach.

- Modern technologies from imaging to enhance target contouring; precision matching and dose escalation permit novel RT strategies in high-risk disease.
Thank you!

Questions