Novel Radiotherapy Approaches for Prostate Cancer

Bridget Koontz MD
Associate Professor of Radiation Oncology
Duke Cancer Institute
Disclosures

• Research Funding: Janssen Pharmaceuticals

• Advisory Board: BlueEarth Diagnostics

• Committee Member: ASTRO, NRG, SMSNA
Technology in Radiation Oncology

1915
Superficial XR unit

1950s
Betatron

1970s
Therac-20

https://www.mskcc.org/timeline/msk-radiation-therapy-timeline-progress
External Beam Radiotherapy

http://www.varian.com
3D Conformal RT
Intensity Modulated Radiotherapy
Intensity Modulated Radiotherapy

IMRT

3D
IMRT – 10 year Outcomes

*30% high risk received 3mo ADT

New Technologies

- Radium-223
- SBRT
- HDR Brachy
- IGRT
- Hypofx
Prostate is a moving target!!
Image-guided Radiation Therapy

“OBI”

“CBCT”
Protons Physically Different
Proton Radiotherapy

7-field IMRT

2-field Proton

IMRT spared bladder in high dose region, rectal dose equivalent. IMRT included more normal tissue to low doses.

Trofimov IJROBP 2006.
5 year Proton Results - UF

*High Risk used concurrent docetaxel/STADT

Bryant IJROBP 2016; 95:422-434.
5 year Proton Results - UF

*All Treated to 81 Gy
*High Risk 50% 3mo ADT

Int Risk ~25% received ADT
*High Risk used concurrent docetaxel/STADT

Bryant IJROBP 2016; 95:422-434.
Rationale for Hypofractionation

• Improved planning technology – tighter “margin” around target
• Improved targeting technology – “on-board imaging”, GPS devices
• Prostate slow-growing and therefore relatively radioresistant

HYPOFRACTIONATION Hypothesis:
A few carefully targeted large dose fractions can provide similar results as many small dose fractions
## Moderate Hypofractionation Randomized Trials

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Risk Group</th>
<th>Regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>RTOG</td>
<td>1115</td>
<td>Low</td>
<td>73.8/1.8 vs 70/2.5</td>
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<tr>
<td>HYPRO</td>
<td>820</td>
<td>Int/High</td>
<td>79/2 vs 64.6/3.4</td>
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<tr>
<td>CHHiP</td>
<td>3163</td>
<td>Low/Int</td>
<td>74/2 vs 60/3 vs 57/3</td>
</tr>
<tr>
<td>PROFIT</td>
<td>1206</td>
<td>Int</td>
<td>78/2 vs 60/3</td>
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</table>
## Moderate Hypofractionation Randomized Trials

<table>
<thead>
<tr>
<th>Group</th>
<th>Median FU</th>
<th>Results</th>
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<tbody>
<tr>
<td>RTOG</td>
<td>71mo</td>
<td>5yDFS 85% vs 86%</td>
</tr>
<tr>
<td>HYPRO</td>
<td>60mo</td>
<td>5yRFS 77% vs 80%</td>
</tr>
<tr>
<td>CHHiP</td>
<td>62mo</td>
<td>5yPFS 88% vs 90% vs 86%</td>
</tr>
<tr>
<td>PROFIT</td>
<td>66mo</td>
<td>5yFFBF 79% vs 79%</td>
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HDR Brachytherapy

- Temporary catheters placed using same technique
- Iridium-192 source robotically loads each catheter sequentially
- Procedure repeated twice a day for 4-5 treatments

www.prostate-cancer.com
www.seradiotherapy.com
 HDR Monotherapy

Krauss IJROBP, Volume 97, Issue 1, 2017, 98–106
HDR Monotherapy

3-yr rate = 93.2% [95% CI: 79.8%-97.9%]

Krauss IJROBP, Volume 97, Issue 1, 2017, 98–106
DR Monotherapy for Intermediate Risk Prostate Cancer

≤ clinical T2c and PSA 10–19.9 ng/mL or Gleason score 7

7.25 Gy x 6 in two implants 7 days apart

Patel Brachytherapy 2017 in press.
HDR monotherapy toxicity

• Grade 2 toxicities:
  – dysuria (2.1%), hematuria (1.1%), urgency (8.9%), incontinence (7.4%), stricture (5.3%), penile pain (1.6%), and frequency (5.3%)
  – GI (1.1%)

• Grade 3 toxicities
  – Urethral stricture (3.2%), incontinence (1.6%)

Patel Brachytherapy 2017 in press.
ASCENDE-RT: An Analysis of Survival Endpoints for a Randomized Trial Comparing a Low-Dose-Rate Brachytherapy Boost to a Dose-Escalated External Beam Boost for High- And Intermediate-Risk Prostate Cancer

- Cumulative late Gr3+ GU: 19 vs 5% (p<=.0001)
- 5y actuarial gr3+ GU = 9 vs 2% (p=.06) (50% urethral strictures)
- Late Gr3+ GI toxicity: 9 vs 4% (p=.12)
- 5y actuarial gr3+ GI = 2 v 1% (p=.5)

Stereotactic Body Radiotherapy

Standard fractionation: 35-40 treatments in 8-9 weeks

HYPOfractionation: 4-5 treatments in 2 weeks!!

www.cyberknife.com
# SBRT – Example Studies

<table>
<thead>
<tr>
<th>Study</th>
<th>FU</th>
<th>Schedule</th>
<th>Outcome</th>
<th>Toxicity</th>
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<tbody>
<tr>
<td>Aluwini</td>
<td>28</td>
<td>38 Gy/4 fx</td>
<td>3 yr BC 98%</td>
<td>Gr 2 GU 15%</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Gr 2 GI 3%</td>
</tr>
<tr>
<td>Chen</td>
<td>28</td>
<td>35–36.25 Gy/5 fx</td>
<td>2 yr BRFS 99%</td>
<td>2 yr Gr ≥2 GU 31%</td>
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<tr>
<td></td>
<td></td>
<td>11% ADT</td>
<td></td>
<td>2 yr Gr ≥2 GI 1%</td>
</tr>
<tr>
<td>Fuller</td>
<td>20</td>
<td>38 Gy/4 fx</td>
<td>3 yr BRFS 98%</td>
<td>any Gr GU 44%</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>any Gr GI 11%</td>
</tr>
<tr>
<td>Katz</td>
<td>54</td>
<td>35–36.25 Gy/5 fx</td>
<td>6 yr FFBF 97%</td>
<td>Gr ≥2 GU 9%</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Gr ≥2 GI 4%</td>
</tr>
<tr>
<td>King</td>
<td>32</td>
<td>36.25 Gy/5 fx</td>
<td>4 yr BRFS 94%</td>
<td>Gr ≥2 GU 7%</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Gr ≥2 GI 12%</td>
</tr>
<tr>
<td>Loblaw</td>
<td>55</td>
<td>35 Gy/5 fx</td>
<td>5 yr BC 98%</td>
<td>5 yr Gr ≥2 GU 5%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>5 yr Gr ≥2 GI 7%</td>
</tr>
<tr>
<td>Meier</td>
<td>30</td>
<td>40 Gy/5 fx</td>
<td>3 yr BRFS 99%</td>
<td>Gr 2 GU 10%</td>
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<tr>
<td></td>
<td></td>
<td>No ADT</td>
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<td>Gr 2 GI 2%</td>
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<tr>
<td>Menkarios</td>
<td>33</td>
<td>45 Gy/5 fx</td>
<td>3 yr BC 97%</td>
<td>Gr ≥2 GU 14%</td>
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<tr>
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<td></td>
<td>Gr ≥2 GI 16%</td>
</tr>
</tbody>
</table>
Radium-223

ALS YMPCA Trial

A Overall Survival

Hazard ratio, 0.70 (95% CI, 0.58–0.83)
P<0.001

Radium-223
(median overall survival, 14.9 mo)

Placebo
(median overall survival, 11.3 mo)

No. at Risk
Radium-223
Placebo

614 578 504 369 274 178 105 60 41 18 7 1 0 0
307 288 228 157 103 67 39 24 14 7 4 2 1 0

Parker C, NEJM 2013; 369, 213
Radium-223

• Current Utilization:
  – Symptomatic Bone Predominant Metastatic CRPC

• Currently in Trials:
  – Metastatic CRPC +/- Abi, Enza, Docetaxel
    • (PEACE-III with enza)

?? Role in very high risk non-metastatic??
Thank you