Prostate CyberKnife® SBRT Tips and Tricks
“Heterogeneous” (HDR-like) Treatment Method

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“Heterogeneous” (HDR-like) Treatment Method

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–Topics:
  –•Rationale/Indications
  –•Outcomes (brief)
  –•Contouring
    –Image Interpretation and Fusion
    –Low-risk versus Intermediate-risk
  –•Dosimetry
  –•Conclusions
Rationale

- Working Concept:
  - CyberKnife® is a non-invasive HDR delivery tool
- Basic Dosimetry Goal:
  - Recapitulate HDR Brachytherapy
  - Based on “Real HDR”
    - 38Gy/4 fx (has peer reviewed efficacy documentation)
      » Demanes DJ, Martinez, AA, et al; Int J Radiat Oncol, Biol, Physics, 81(5); 1286-1292: Dec 2011
    - 97% PSA-based DFS at 8 yrs (low- and int-risk)
Prostate Cancer Scenarios we treat with CyberKnife® System SBRT:

- Low- and Intermediate-risk (Gleason <7, PSA <20, ≤T2b)
  - Two IRB approved clinical trials: 3,800cGy/4 fx
    » Accuray-sponsored multi-institutional: 18 institutions
    - Completed – n=261
    » Local San Diego trial
    - Ongoing – n= 258

- Localized High-risk (Gleason ≥8; PSA ≥20; ≥T3)
  - Third IRB-approved trial (“UCLA Study”): 4,000cGy/5 fx
    - Ongoing – n= ?? (UCLA project)(San Diego has enrolled n = 36)

- Post-RT local recurrence (Biopsy proven; r/o metastases)
  - Fourth IRB-approved trial: 3,400cGy/5 fx; Zero GTV to PTV margin expansion
    - Ongoing – n= 51

- Oligometastases (Newest project; no specific clinical trial as yet)
  - Selected cases w focal metastatic lesions, usually identified by newer PET/CT techniques
    » (SBRT “Hunt and destroy” - Defer the need for ADT for PSA relapses after primary tx)
CyberKnife® System as a Noninvasive Prostate HDR Dosimetry Delivery Mechanism: Feasibility and Preliminary Clinical Results

Virtual HDR CyberKnife treatment for and preliminary clinical observations. localized prostatic carcinoma: dosimetry comparison with HDR brachytherapy

Fuller DB; Naitoh J; Lee C; Hardy S; Jin H

CyberKnife® System as a Noninvasive Prostate HDR Dosimetry Delivery Mechanism: Feasibility and Preliminary Clinical Results

Virtual HDR CyberKnife Treatment for Localized Prostatic Carcinoma: Dosimetry Comparison With HDR Brachytherapy and Preliminary Clinical Observations
Donald B. Fuller, John Naitoh, Charles Lee, Steven Hardy, Haoran Jin
International Journal of Radiation Oncology • Biology • Physics, Vol. 70, Issue 5, p1588–1597; Published in issue: April 01, 2008
CyberKnife® System as a Noninvasive Prostate HDR Dosimetry Delivery Mechanism: Feasibility and Preliminary Clinical Results

Hypofractionation Dose Equivalents:
2 current studies (PTV)

<table>
<thead>
<tr>
<th>α/β</th>
<th>36.25 Gy/5 fx</th>
<th>2 Gy/fx dose equivalent</th>
<th>38 Gy/4 fx</th>
<th>2 Gy/fx dose equivalent</th>
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<tr>
<td>1.2</td>
<td>BED</td>
<td>2 Gy/fx dose equivalent</td>
<td>BED</td>
<td>2 Gy/fx dose equivalent</td>
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<tr>
<td>255</td>
<td>96 Gy/48 fx</td>
<td>339</td>
<td>126 Gy/63 fx</td>
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<td>124</td>
<td>74 Gy/37 fx</td>
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<tr>
<td>89</td>
<td>64 Gy/32 fx</td>
<td>110</td>
<td>78 Gy/39 fx</td>
<td></td>
</tr>
<tr>
<td>63</td>
<td>52 Gy/26 fx</td>
<td>74</td>
<td>62 Gy/31 fx</td>
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</tbody>
</table>
CyberKnife® System as a Noninvasive Prostate HDR Dosimetry Delivery Mechanism: Feasibility and Preliminary Clinical Results

• Back-up: Extreme Heterogeneity

Assume alpha/beta = 3

- 47.5 Gy/4 fx; BED = 234 (140 Gy/70 fx)
- 38 Gy/4 fx; BED = 158 (94 Gy/47 fx)
- 28.5 Gy/4 fx; BED = 96 (58 Gy/29 fx)

Not a scalpel . . .
CyberKnife® System as a Noninvasive Prostate HDR Dosimetry Delivery Mechanism: Feasibility and Preliminary Clinical Results

Which treatment is “better?”

Brachy PSA Nadir: 0.1 ng/mL
EBRT PSA Nadir: 0.6 ng/mL

Zelefsky, et al. Urology (77); 986-993; 2011
Which treatment is “better?”

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Figure 1. PSA relapse-free survival for favorable risk patients for brachytherapy versus EBRT. 10-year RFS was 89%, respectively ($P =$ 0.0001).

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**Figure 1.** PSA relapse-free survival for favorable risk patients. PSA relapse-free survival rate for brachytherapy versus IMRT at 7 years was 95% and 89%, respectively ($P = .004$).
5-year efficacy and quality of life outcomes of a multi-institutional HDR-like prostate SBRT trial - ESTRO 2018

![Graph showing PSA levels over time with time points at 0, 12, 24, 36, 48, 60, 72, 84, and 96 months.]

- Median PSA (ng/mL)
  - 0.1 ng/mL
  - < 0.1 ng/mL

N=259  N=160  N=130  N=35
5-year efficacy and quality of life outcomes of a multi-institutional HDR-Like prostate SBRT trial - ESTRO 2018

NOTE: One single additional biochemical relapse after 5 years thus far (max f/u = 10 years and n >100 at 6 years . . .)
SBRT for Post-Radiotherapy **Locally Recurrent** Prostatic Carcinoma: Evaluation of Toxicity, PSA Response and Disease-free survival

- 3800cGy/4 fx – De Novo
- 3400cGy/5 fx – Salvage
  – Side by Side

De Novo: 38Gy/4 fx

Salvage: 34Gy/5 fx
High-dose-rate stereotactic body radiation therapy for post-radiation therapy locally recurrent prostatic carcinoma: Preliminary prostate-specific antigen response, disease-free survival, and toxicity assessment

• PRO; 2015; 5(6); e615
  N = 29

0.16 ng/mL at 2 years
High-dose-rate stereotactic body radiation therapy for post-radiation therapy locally recurrent prostatic carcinoma: Preliminary prostate-specific antigen response, disease-free survival, and toxicity assessment

- **PRO; 2015; 5(6); e615**
  - Result updated Nov 1, 2017
  - N = 29

- N = 18

- N = 8

- 82%
- 67%

Result appears comparable to HDR brachytherapy salvage

- Efficacy
- Toxicity
  - UCSF
  - Memorial Sloan Kettering
- But its NON-invasive

N = 49 (Unpublished)
Prostate CyberKnife® System Training
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• Contouring
  – Image Fusion
Prostate CyberKnife® System Training
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• Contouring
  – Image Interpretation – Prostate Contouring
    • McLaughlin P.W., et al, IJROPB, 76(2), 369-378, Feb 2010
      – A) Raw Image
      – B) Normal Anatomy
      – C) Apex Overdone
      – D) Apex Overdone
      – E) Apex Overdone
      – F) SV Included
      – G) Bladder Beak
      – H) Base Shaved
      – I) Summated issues
Contouring

- Low-risk versus Intermediate-risk versus Local recurrence

Low-risk

Intermediate bilateral

Intermediate unilateral

Local Recurrence

e.g. – bilateral Gleason 7

e.g. – R sided Gleason 7

(Lower Dose)
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Low-risk

Intermediate-risk
Robotic Prostate SRS: Emulating HDR Brachytherapy – Not just dose schedule but also dosimetry morphology

- Peripheral Zone Tuning Structure:
Robotic Prostate SRS: Emulating HDR Brachytherapy – Not just dose schedule but also dosimetry morphology

• Cancer Coverage and Dosing:
  – 2 mm vs 5 mm margin
    • Wider coverage beyond the prostate
    • Hotter dose within the prostate
Robotic Prostate SRS: Emulating HDR Brachytherapy – Not just dose schedule but also dosimetry morphology

- NVB:
  - 2 mm vs 5 mm margin

NOTE: No effect on potency preservation outcome
In our multi-institutional series
Robotic Prostate SRS: Emulating HDR Brachytherapy – Not just dose schedule but also dosimetry morphology

**PTV:**
- Rx: 9.5 Gy x 4 = 38 Gy (Wm Beaumont HDR protocol)
- Coverage: $V_{100} \geq 95\%$
- Rx isodose: 50% - 67% ($V_{150\%} \geq 1\%$ of PTV volume)
  - **NOTE:** Rx isodose < 50% permitted as minor violation

**Rectum**
- $D_{\text{max}} \leq 38$ Gy

**Rectal Mucosa**
- $D_{\text{max}} \leq 28.5$ Gy (75% Rx dose)
Robotic Prostate SRS: Emulating HDR Brachytherapy: Prostate-Rectum interface

HDR: Borrowed from Alvaro Martinez
Robotic Prostate SRS: Emulating HDR Brachytherapy – Not just dose schedule but also dosimetry morphology

*Urethra:
  – $D_{\text{max}} \leq 45.6 \text{ Gy (120\% Rx dose)}$
  – $D_{50} \leq 39.9 \text{ Gy (105\% Rx dose)}$
  – $D_{10} \leq 41.8 \text{ Gy (110\% Rx dose)}$

*Bladder
  – $D_{\text{max}} \leq 45.6 \text{ Gy (120\% Rx dose) (NOTE: now try for 100-110\%)}$

* CI & nCI $< 1.5$ (Most plans achieve nCl $\leq 1.2$)
Robotic Prostate SRS: Emulating HDR Brachytherapy – Not just dose schedule but also dosimetry morphology

• HDR-like vs Homogeneous
Robotic Prostate SRS:
Emulating HDR Brachytherapy – Not just dose schedule but also dosimetry morphology

• Summary Dosimetry Slide: Low-risk Case

PTV:
3800 cGy
nCl < 1.2

Urethra:
Median ~ 3990 cGy (105% of Rx dose)

Rectal Wall:
3800 cGy (Dmax)

Rectal Mucosa:
2850 cGy (75% of Rx dose) (1%)

NVB:
~3800 cGy (D50) (~1000 cGy higher w/ 5 mm PTV)

Peripheral Zone:
Mostly > 4750 cGy (125%)
Prostate CyberKnife® System Training
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– Fiducials
  • We currently use 5 –
    – (Method is not specified in protocol)
  • 2 strands of 2 fiducials per strand (2 cm spacer) –
    – L post/lat and R post/lat
  • Single seed R or L anterior
  • Placed transperineally - Local anesthetic +/- Ativan
Robotic Prostate SRS: Emulating HDR Brachytherapy – Not just dose schedule but also dosimetry morphology

- NON-Coplanar . . .
  - We need to consider all OAR above and below the imaging plane that contains the PTV!!
Robotic Prostate SRS: Emulating HDR Brachytherapy: Prostate-Rectum interface

Bowel prep and constant bladder filling protocol

Rotated Fiducials
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• Conclusions:
  → We are able to reasonably “clone” intra/peri-prostatic HDR dosimetry with this SBRT technique
    • Moderately larger “low dose bladder bath” – Anterior-weighted non-coplanar geometry
    • No specific clinical consequence to this

  → PSA response, Efficacy and toxicity of this technique appear non-inferior versus HDR or other methods; PSA nadir eventually reaches “surgical”

  → HDR-like dosimetry versus Homogeneous
    • Higher dose (EUD ~125% of prescribed; Dmax > 150%)
    • Smaller Margins (2-5 mm peripherally; 0 mm against rectum)
    • A bit more labor intensive to contour
    • Attention to bladder filling and bowel prep
    • No obvious toxicity differences
    • PSA nadir appears to be lower w this technique
      – A little more like a radical prostatectomy-like . .
Thank You