Virtual HDR® Prostate CyberKnife Radiosurgery: PSA-response, Toxicity and Quality of Life Evaluation

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Typically, prostate cancer is a **peripheral** zone disease.

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HDR Brachytherapy preferentially treats the peripheral zone

High dose-rate afterloading $^{192}$iridium prostate brachytherapy: feasibility report

Mate TP, Gottesman JE, Hatton J, Gribble M, Van Hollebeke L

International Journal of Radiation Oncology*Biology*Physics

01 June 1998 (Vol. 41, Issue 3, Pages 525-533)
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• **CK Dosimetry Model:** HDR **Brachytherapy:** 38Gy/4 fx
  – This has peer reviewed documentation
    • Grills, IS, Martinez, AA, et al; J Urol 2004; 171(3); 1098-1104
      – 98% PSA-based DFS at 35 mo. median f/u
      – HDR brachytherapy had lower grade 2 GU toxicity incidence than $^{103}$Pd seed brachytherapy in this series
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We like everything about HDR brachytherapy except this . . .
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- **Virtual HDR® CyberKnife**
- **Working Concept:**
  - CK is a **non-invasive** HDR delivery tool
- **Basic Dosimetry Goal:**
  - Recapitulate HDR Brachytherapy
VIRTUAL HDR CYBERKNIFE RADIOSURGERY FOR LOCALIZED PROSTATIC CARCINOMA:
A PHASE II STUDY

- **Principal Investigator**
  - Donald B. Fuller, M. D.
- **Accrual Goal:**
  - 100 patients/4 years
    - 40 accrued to date (+ 60 on subsequent Accuray-sponsored study)
- **IRB approval?**
  - Yes – Approved through Scripps Health IRB, San Diego
- **Primary Objective**
  - Toxicity and quality of life evaluation
- **Secondary Objective**
  - PSA response and PSA-based DFS evaluation
- **Tertiary Objective**
  - Compare Virtual HDR® CyberKnife Dosimetry with simulated HDR Dosimetry – Accomplished
VIRTUAL HDR CYBERKNIFE RADIOSURGERY FOR LOCALIZED PROSTATIC CARCINOMA: A PHASE II STUDY

• **Methods:**
  – **Eligibility**
    • 40 Patients
    • Median F/U 12 mo; Max F/U 2 years
    • Favorable and Intermediate prognosis cases
      – Favorable: <=T2b, Gleason <=6, PSA < 10 ng/ml – 28 cases
      – Intermediate: <=T2b, Gleason 7 or PSA 10.1- 20 ng/ml – 12 cases
    • PSA-based relapse-free survival
    • CTCAE Toxicity evaluation
    • Full Scale EPIC QOL evaluation
VIRTUAL HDR CYBERKNIFE RADIOSURGERY FOR LOCALIZED PROSTATIC CARCINOMA: A PHASE II STUDY

**Methods:**

- **Treatment**
  - **38 Gy/4 fx**
    - Favorable: Prostate + 2 mm (shaved to 0 mm at rectal interface)
    - Intermediate: Prostate + 5 mm (shaved to 0 mm at rectal interface)
  - HDR-like dose molding; >95% PTV
    - At least 1% of PTV gets >150% of prescription dose
    - EUD = approximately 48Gy/4fx
  - HDR-like OAR dose constraints
    - Outer rectal wall $D_{\text{max}} = 38\text{Gy}$ (100% Rx dose)
    - Rectal mucosa $D_{\text{max}} = 28.5\text{Gy}$ (75% Rx dose)
    - Bladder $D_{\text{max}} = 45.6\text{ Gy}$ (120% Rx dose)
    - Urethra $D_{\text{max}} = 45.6\text{ Gy}$ (120% Rx dose)
    - Urethra $D_{50} = 39.9\text{ Gy}$ (105% Rx dose)
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“Low risk” PTV “Intermediate risk”

“Low risk” PTV PTV PTV PTV “Intermediate risk” NVB NVB NVB NVB
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“Low risk”

“Intermediate risk”

SV coverage
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• Speaking of Extreme Heterogeneity

Assume alpha/beta = 3

47.5Gy/4fx; BED = 234 (140Gy/70fx)

38Gy/4fx; BED = 158 (94Gy/47fx)

28.5Gy/4fx; BED = 96 (58Gy/29fx)
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• Clinical Results:

PSA Response

Median PSA (ng/ml)

+/- 1 standard deviation

[Graph showing PSA response over time with median values and standard deviations]
## PSA nadir: Percent of pts w PSA <= 0.5ng/ml

<table>
<thead>
<tr>
<th>PSA nadir: % &lt;= 0.5 ng/ml</th>
<th>12 mo</th>
<th>18 mo</th>
<th>24 mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>40%</td>
<td>60%</td>
<td>100%</td>
<td></td>
</tr>
</tbody>
</table>
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Post-CK PSA Bounce: 3 Case Examples
10/24 patients followed >= 12 months have at least one PSA bounce
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Post-CK Urinary Morbidity

Alpha Blocker Incidence

IPSS score

34% 40-67% 27%

27% 27% 34%

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A MULTIDISCIPLINARY APPROACH
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Sexual function: SHIM Score

- Low
- Median
- High

Pre 1 mo 3-4 mo 6 mo 12 mo 18 mo 24 mo
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<table>
<thead>
<tr>
<th>n</th>
<th>Urinary</th>
<th>Bowel</th>
<th>Sexual</th>
<th>Hormonal</th>
</tr>
</thead>
<tbody>
<tr>
<td>40</td>
<td>Baseline</td>
<td>85.17</td>
<td>94.73</td>
<td>51.93</td>
</tr>
<tr>
<td>33</td>
<td>2 mo</td>
<td>81.81</td>
<td>93.07</td>
<td>48.25</td>
</tr>
<tr>
<td>28</td>
<td>6 mo</td>
<td>86.18</td>
<td>92.73</td>
<td>44.78</td>
</tr>
<tr>
<td>20</td>
<td>12 mo</td>
<td>83.03</td>
<td>92.05</td>
<td>39.1</td>
</tr>
<tr>
<td>10</td>
<td>18 mo</td>
<td>88.85</td>
<td>91.61</td>
<td>50.0</td>
</tr>
</tbody>
</table>
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• **Summary of Results:**
  - 40 patients
    • Median f/u 1 yr; Max 2 yrs
  - PSA-based DFS
    • 100% (ASTRO and Phoenix)
  - Median PSA
    • 1 year - 1.1 ng/ml
    • 1.5 yr - 0.45 ng/ml
    • 2 yr – 0.25 ng/ml
  - Toxicity
    • Grade III or higher - Zero
    • CTCAE Grade 1-2 delayed GU – 10% (all Grade 2)
    • CTCAE Grade 1-2 delayed GI -10% (7% Grade 1; 3% Grade 2)
  - EPIC Quality of Life Summary to 18 months
    • Bladder Domain – Minimal decrease at 2 months w subsequent recovery
    • Bowel Domain – No significant change
    • Sexual Domain – Decrease to 12 months followed by Recovery
    • Hormonal Domain – No significant change
Conclusions

Virtual HDR® CyberKnife Monotherapy Protocol:
• Very encouraging PSA response
  – Pending longer-term confirmation it looks like brachytherapy
  – PSA bounces are common within the first 18 months
• Favorable toxicity profile with typically rapid resolution
  – Zero incidence of grade 3 toxicity to date
  – Some patients require protracted use of alpha blockers
• QOL outcome is favorable