CyberKnife® Monotherapy for Low-Risk Prostate Cancer: High Dose-Rate Brachytherapy Fractionation and Dose Gradients

CyberKnife® Centers of San Diego CyberKnife Team:
Radiation Oncologist: Donald B. Fuller, M.D.
Medical Physicist: Haoran Jin, Ph.D.
CyberKnife Center: CyberKnife Centers of San Diego San Diego, CA
Case History
This 76-year-old man presented during a routine check-up with a PSA of 7.7 ng/ml. A biopsy four months later revealed adenocarcinoma involving 30% of the submitted tissue with a Gleason score of 3+3=6. A subsequent bone scan and CT of the abdomen and pelvis showed no evidence of metastatic disease. PSA analysis was repeated two months later, and measured 9.4 ng/ml. In his initial evaluation, he had an International Prostate Symptom Score (IPSS) of 4 and Sexual Health Inventory for Men (SHIM) score of 23; the lesion was staged as T2a at the right base. The patient was diagnosed as having low-risk, organ confined prostate cancer.

CyberKnife® Treatment Rationale
Several treatment options were discussed with the patient, including radical prostatectomy, external beam radiotherapy, and brachytherapy. The unique radiobiology of prostate cancer suggests that the disease is particularly sensitive to large-dose-per-fraction (hypofractionated) radiation treatment regimens. In support of this, good biochemical disease control with few serious side effects has recently been reported for the hypofractionated approach referred to as high dose rate (HDR) brachytherapy. The CyberKnife® Centers of San Diego developed a CyberKnife-based hypofractionated prostate treatment that effectively reproduces the dose, dose distribution, and fractionation of HDR brachytherapy. This approach has been designed to escalate the dose to the peripheral zone of the prostate, which typically harbors the majority of cancer cells. This treatment option allows patients to benefit from HDR brachytherapy dose sculpting while avoiding the invasive aspect of of indwelling catheter placement required of the HDR brachytherapy procedure.

T1-weighted, gadolinium-enhanced MRI treatment planning image; GTV (prostate) defined by white line; planning target volume (PTV) defined by blue line; rectal mucosa defined by yellow and turquoise lines. Note that the 1.5T MRI renders the neurovascular bundle (NVB) visible (red arrow) so that a treatment plan can be constructed that limits dose to this structure.
Planning Process
CT and MRI imaging were used for the planning process. The MRI images were fused to the CT image set to better define the prostate capsule, rectal mucosa, neurovascular bundle (NVB) and the penile bulb. For both image sets, a Foley catheter was used to fill the bladder with 100 ml of H₂O, to aid in identifying the urethra and bladder. The rectum was emptied by administration of a Fleet Enema®. The planning treatment volume was created by expanding the prostate volume in all directions by 2 mm, except posteriorly where the prostate abutted the rectum. In this region the margin expansion was reduced to zero. Constraints provided by the radiation oncologist resulted in the following doses to critical structures:

<table>
<thead>
<tr>
<th>Structure</th>
<th>Dose parameters</th>
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<tbody>
<tr>
<td>Urethra</td>
<td>(D_{\text{max}} = 44 \text{ Gy (116%)}}; \quad \text{Median} = 38.4 \text{ Gy (101%)}</td>
</tr>
<tr>
<td>Rectum Outer Wall</td>
<td>(D_{\text{max}} = 34.7 \text{ Gy (91%)}}</td>
</tr>
<tr>
<td>Rectum Mucosa</td>
<td>(D_{\text{max}} = 25.3 \text{ Gy (67%)}}</td>
</tr>
<tr>
<td>Penile Bulb</td>
<td>(D_{\text{max}} = 22.7 \text{ Gy (60%)}}; \quad \text{D}_{50} = 7.3 \text{ Gy (19%)}</td>
</tr>
<tr>
<td>Neurovascular Bundles</td>
<td>Steep gradient: (48 \text{ Gy (126%)} - 26.8 \text{ Gy (71%)} )</td>
</tr>
</tbody>
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Treatment Delivery
Four fiducials were implanted transperineally into the prostate prior to the planning CT scan. A treatment plan was constructed based on co-registered CT/MRI scans. The patient was treated with a total dose of 38 Gy delivered in 4 equal fractions occurring on consecutive days.
Outcome and Follow-Up

- Two weeks post-treatment, the patient experienced increased frequency of bowel movements (BM) and acute dysuria, and was prescribed Flomax®.
- One month after the treatment, the patient’s dysuria and increased BM frequency improved; PSA dropped to 4.7 ng/ml from a pretreatment level of 9.4 ng/ml.
- At the 2-month follow-up, the patient’s dysuria and increased BM frequency had resolved; patient’s IPSS and SHIM score were at baseline levels; PSA continued to decline, measured at 2.5 ng/ml.
- During the 18-month follow-up period, the patient’s PSA level continued to decline steadily, reaching 0.5 ng/ml (see figure); the patient’s iPS was 5 and his SHIM score was 16.

Conclusion

- The CyberKnife® System successfully reproduced an HDR-like dose distribution, delivering treatment in a minimally invasive fashion.
- Treatment-related toxicity was mild (grade I - II urinary symptoms) and resolved over time in this first 18 months of follow up; further follow-up is required to assess chronic toxicity in this patient.
- A significant reduction in PSA levels followed treatment throughout the first 18 months of follow-up.

References