Early-stage prostate cancer treatment alternatives

Background

The American Cancer Society estimates that 217,730 new prostate cancer cases occurred in the United States during 2010, making it the most frequently diagnosed cancer in men. Prostate cancer is one of the leading causes of cancer death in men, but mortality is only 15% of incidence due to slow tumor growth and an older population, with 32,050 deaths in 2010.

Over the past 20 years, the annual age-adjusted incidence of prostate cancer has increased, likely due to prostate-specific antigen (PSA) screening and increased use of transurethral prostate resection for the relief of urinary obstruction. Risk factors include age and family history with incidence significantly higher for African Americans.

Early detection is recommended with a digital rectal exam and a PSA test in all men over the age of 50. Opinions differ regarding the importance of absolute PSA, PSA velocity, and the optimal frequency of repeating the PSA. About 38% of men will die with unsuspected prostate cancer, which highlights the chronicity of the cancer.

Treatment options

Treatment options for early stage disease vary depending upon the patient’s age, cancer stage, and confounding medical conditions. These include surgery, brachytherapy (BT), external beam radiation, and stereotactic body radiation therapy (SBRT).

Another option is “active surveillance,” or careful observation, which may be appropriate for older men with small, non-aggressive tumors, low Gleason scores and low PSA levels.

Given the multiple therapeutic options, patients have a choice of therapy which requires informed consent with an understanding of the PSA control, toxicity, and cost. Higher radiation doses yield better tumor control. Intensity-modulated radiation therapy (IMRT) and brachytherapy reduce normal tissue toxicity. Acute toxicities and quality-of-life related issues from surgery—such as pain, blood loss, infection, hospital stay, and surgical recovery—are not included in the table on the back. Also not included are the important toxicities of erectile dysfunction and penile shortening.

Image-guided radiation therapy (IGRT) has a role as imaging technologies to detect and compensate for organ motion have become more widely available. Favorable data exist from several SBRT studies with small patient numbers and short to medium follow-up. The American Society for Radiation Oncology (ASTRO) recommends that these SBRT treatments be performed under Institutional Review Board (IRB)-approved clinical trials until the data matures. Twelve SBRT prostate clinical trials involving 1,477 patients (average 123; range 10 to 300) are ongoing, according to the NIH, and include a wide range of technologies.

The table on the back shows relative uniformity of results independent of treatment. The data also point to improving biochemical control with increasing biological effective dose (BED), which is a measure of normalized dose based on the tissue. As the incidence of prostate cancer increases, it is expected that refinements of therapy will give better results. Direct comparisons between treatment options are not fully valid as the data are not derived from randomized studies. Most of the chronic toxicities listed for external beam are Grade 2, which can be treated with steroids. Grade 3 toxicities represent a small fraction (0-6% urinary and 0-7% rectal) of chronic toxicities.

Conclusion

Evidence is developing in support of a wide range of treatment therapies for early stage prostate cancer. Varian Medical Systems provides solutions for three radiotherapy options (BT, external beam, and SBRT), including RapidArc radiotherapy technology, backed by years of clinical research at centers using these options.
### PSA Response: IMRT, IMRT+ BT, and SBRT Treatments

3 independent groups: 25 consecutive early-stage prostate patients

![Graph showing PSA response over time for IMRT, IMRT+BT, and SBRT treatments](image)

Data courtesy of 21st Century Oncology, Plantation, FL

---

### Treatment Techniques for Early Stage Prostate Cancer

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Author</th>
<th>Center</th>
<th>Year Pub.</th>
<th># of Patients</th>
<th>Median Follow-Up (months)</th>
<th>Dose (Gy)</th>
<th># of Fx</th>
<th>Prostate BED [α/β=1.5]</th>
<th>% PSA Relapse</th>
<th>Late Normal Tissue BED [α/β=3]</th>
<th>% Grade 2 + 3</th>
<th>% Grade 2 + 3 Gl Tox</th>
<th>% Grade 2 + 3 Gi Tox</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radical Prostatectomy</td>
<td>Walsh</td>
<td>Johns Hopkins Hospital</td>
<td>1994</td>
<td>995</td>
<td>48</td>
<td>NA</td>
<td>NA</td>
<td>18</td>
<td>NA</td>
<td>18</td>
<td>8*</td>
<td>1*</td>
<td></td>
</tr>
<tr>
<td>Robotic Prostatectomy</td>
<td>Badani</td>
<td>Henry Ford Hospital</td>
<td>2007</td>
<td>2,766</td>
<td>22</td>
<td>NA</td>
<td>NA</td>
<td>16</td>
<td>NA</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td></td>
</tr>
<tr>
<td>High Dose Brachytherapy</td>
<td>Grills</td>
<td>William Beaumont Hospital</td>
<td>2004</td>
<td>65</td>
<td>34</td>
<td>38</td>
<td>4</td>
<td>279</td>
<td>2</td>
<td>158</td>
<td>28+4</td>
<td>0+0</td>
<td></td>
</tr>
<tr>
<td>Permanent Seed Implant</td>
<td>Eade</td>
<td>Fox Chase Cancer Center</td>
<td>2008</td>
<td>158</td>
<td>48</td>
<td>145</td>
<td>NA</td>
<td>NA</td>
<td>6</td>
<td>NA</td>
<td>19+6</td>
<td>8+0</td>
<td></td>
</tr>
<tr>
<td>3D Conformal Radiotherapy</td>
<td>Kaban</td>
<td>M.D. Anderson Cancer Center</td>
<td>2008</td>
<td>151</td>
<td>104</td>
<td>78</td>
<td>39</td>
<td>184</td>
<td>22</td>
<td>130</td>
<td>7+3</td>
<td>19+7</td>
<td></td>
</tr>
<tr>
<td>High Dose IMRT</td>
<td>Cahlon</td>
<td>Memorial Sloan-Kettering</td>
<td>2008</td>
<td>478</td>
<td>53</td>
<td>86.4</td>
<td>48</td>
<td>190</td>
<td>15</td>
<td>138</td>
<td>13+3</td>
<td>2+1</td>
<td></td>
</tr>
<tr>
<td>Hypofractionated RT</td>
<td>Kupelian</td>
<td>Cleveland Clinic</td>
<td>2007</td>
<td>770</td>
<td>45</td>
<td>70</td>
<td>28</td>
<td>187</td>
<td>18</td>
<td>128</td>
<td>4+1</td>
<td>3+1</td>
<td></td>
</tr>
<tr>
<td>SBRT</td>
<td>Madsen</td>
<td>Virginia Mason</td>
<td>2007</td>
<td>40</td>
<td>41</td>
<td>33.5</td>
<td>5</td>
<td>183</td>
<td>29</td>
<td>108</td>
<td>20+0</td>
<td>8+0</td>
<td></td>
</tr>
<tr>
<td>SBRT</td>
<td>Pham</td>
<td>Virginia Mason</td>
<td>2010</td>
<td>40</td>
<td>60</td>
<td>33.5</td>
<td>5</td>
<td>183</td>
<td>29</td>
<td>108</td>
<td>12.5+2.5</td>
<td>7.5+0</td>
<td></td>
</tr>
<tr>
<td>SBRT</td>
<td>King</td>
<td>Stanford University</td>
<td>2011</td>
<td>67</td>
<td>33</td>
<td>36.25</td>
<td>5</td>
<td>211</td>
<td>3</td>
<td>124</td>
<td>5+3.5</td>
<td>2+0</td>
<td></td>
</tr>
<tr>
<td>SBRT</td>
<td>Mantrz</td>
<td>21st Century</td>
<td>2010</td>
<td>54</td>
<td>26</td>
<td>40</td>
<td>5</td>
<td>253</td>
<td>0</td>
<td>147</td>
<td>14+0</td>
<td>0+0</td>
<td></td>
</tr>
</tbody>
</table>

**References**

1. American Cancer Society, Cancer Facts and Figures 2010
2. Catalona WJ et al. JAMA 1993; 270:948-954
18. Wyma M et al. NEJM 2008; 358:1250-1261