Stereotactic Ablative Radiotherapy for Prostate Cancer

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## Scope of the Problem

### Estimated New Cases

<table>
<thead>
<tr>
<th></th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prostate</td>
<td>164,690</td>
<td>266,120</td>
</tr>
<tr>
<td>Lung &amp; bronchus</td>
<td>121,680</td>
<td>112,350</td>
</tr>
<tr>
<td>Colon &amp; rectum</td>
<td>75,610</td>
<td>64,640</td>
</tr>
<tr>
<td>Urinary bladder</td>
<td>62,380</td>
<td>63,230</td>
</tr>
<tr>
<td>Melanoma of the skin</td>
<td>55,150</td>
<td>40,900</td>
</tr>
<tr>
<td>Kidney &amp; renal pelvis</td>
<td>42,680</td>
<td>36,120</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>41,730</td>
<td>32,950</td>
</tr>
<tr>
<td>Oral cavity &amp; pharynx</td>
<td>37,160</td>
<td>26,240</td>
</tr>
<tr>
<td>Leukemia</td>
<td>35,030</td>
<td>25,270</td>
</tr>
<tr>
<td>Liver &amp; intrahepatic bile duct</td>
<td>30,610</td>
<td>22,660</td>
</tr>
<tr>
<td>All sites</td>
<td>856,370</td>
<td>878,980</td>
</tr>
</tbody>
</table>

### Estimated Deaths

<table>
<thead>
<tr>
<th></th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung &amp; bronchus</td>
<td>83,550</td>
<td>70,500</td>
</tr>
<tr>
<td>Prostate</td>
<td>29,430</td>
<td>40,920</td>
</tr>
<tr>
<td>Colon &amp; rectum</td>
<td>27,390</td>
<td>23,240</td>
</tr>
<tr>
<td>Pancreas</td>
<td>23,020</td>
<td>21,310</td>
</tr>
<tr>
<td>Liver &amp; intrahepatic bile duct</td>
<td>20,540</td>
<td>14,070</td>
</tr>
<tr>
<td>Leukemia</td>
<td>14,270</td>
<td>11,350</td>
</tr>
<tr>
<td>Esophagus</td>
<td>12,850</td>
<td>10,100</td>
</tr>
<tr>
<td>Urinary bladder</td>
<td>12,520</td>
<td>9,660</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>11,510</td>
<td>8,400</td>
</tr>
<tr>
<td>Kidney &amp; renal pelvis</td>
<td>10,010</td>
<td>7,340</td>
</tr>
<tr>
<td>All sites</td>
<td>323,630</td>
<td>286,010</td>
</tr>
</tbody>
</table>
Incidence Trends

• An estimated 164,690 new cases of prostate cancer will be diagnosed in the US during 2018

• In the late 1980s and early 1990s, incidence rates for prostate cancer spiked dramatically, (widespread screening with the PSA blood test)
Incidence Trends

• Decline in rates since around 2000
• Likely due to recommendations against routine PSA screening beginning in 2008
• From 2010 to 2014, the rate decreased by about 10% per year
Mortality Trends

• An estimated 29,430 deaths from prostate cancer will occur in 2018

• Prostate cancer death rates have been decreasing since the early 1990s, although rates appear to have stabilized from 2013 to 2015
<table>
<thead>
<tr>
<th>Risk group</th>
<th>Clinical/pathologic features</th>
</tr>
</thead>
</table>
| Very low                | • T1c AND  
• Gleason score ≤6/grade group 1 AND  
• PSA <10 ng/mL AND  
• Fewer than 3 prostate biopsy fragments/cores positive, ≤50% cancer in each fragment/core AND  
• PSA density ≤0.15 ng/mL |
| Low                     | • T1-T2a AND  
• Gleason score ≤6/grade group 1 AND  
• PSA <10 ng/mL |
| Favorable Intermediate  | • T2b-T2c OR  
• Gleason score 3+4=7/grade group 2 OR  
• PSA 10–20 ng/mL AND  
• Percentage of positive biopsy cores <50% |
| Unfavorable Intermediate| • T2b-T2c OR  
• Gleason score 3+4=7/grade group 2 or Gleason score 4+3=7/grade group 3 OR  
• PSA 10–20 ng/mL |
| High                    | • T3a OR  
• Gleason score 8/grade group 4 or Gleason score 4+5=9/grade group 5 OR  
• PSA >20 ng/mL |
| Very high               | • T3b-T4 OR  
• Primary Gleason pattern 5 OR  
• >4 cores with Gleason score 8–10/grade group 4 or 5 |
Treatment of Localized Disease

- Surgery
- Radiotherapy (RT)
- Active surveillance (low risk only)
- No difference in risk of dying of prostate cancer 10 years after diagnosis between these options
  - Surgery and RT associated with lower risk of disease progression and metastasis

Patient Reported Outcomes

• 1643 men in the Prostate Testing for Cancer and Treatment (ProtecT) trial
• Questionnaires before diagnosis, at 6 and 12 months after treatment, and annually thereafter
  – urinary, bowel, and sexual function
  – quality of life
  – anxiety and depression
  – general health

Patient Reported Outcomes

• Prostatectomy had the greatest negative effect on sexual function and urinary continence
  – Although there was some recovery, these outcomes remained worse in the prostatectomy group than in the other groups throughout the trial

• The negative effect of radiotherapy on sexual function was greatest at 6 months
  – sexual function then recovered somewhat and was stable thereafter
  – radiotherapy had little effect on urinary continence

Patient Reported Outcomes

- Sexual and urinary function declined gradually in the active-monitoring group.
- Bowel function was worse in the radiotherapy group at 6 months than in the other groups but then recovered.
- Urinary symptoms were worse in the radiotherapy group at 6 months but then mostly recovered and were similar to the other groups after 12 months.
- No significant differences were observed among the groups in measures of anxiety, depression, or general health-related or cancer-related quality of life.

Radiotherapy 101

- Radiotherapy uses a focused beam of energy to damage cancerous cells while minimizing exposure to healthy tissue.
- Radiation damages the DNA in cancer cells, which interrupts their ability to reproduce, causing them to die.
- Normal cells can recover from radiation more easily.
- Treatment is delivered to the target site with a machine called a linear accelerator (linac).
How Radiotherapy Works
Linear Accelerator
Types of Linacs
Radiosurgery

• Radiosurgery is a non-invasive treatment technique used primarily to ablate tumors
• Most suitable for small, well-defined tumors
• Despite the use of the word "surgery" in its name, radiosurgery does not involve removing the tumor
• Instead, a focused high-intensity beam of radiation is used to target a tumor while minimizing dosage to healthy tissue
• Highly precise, intensified form of radiotherapy
Radiosurgery

• Traditional radiotherapy can include up to 40 treatments (5 days a week for several weeks)
• Radiosurgery is performed in five sessions or less over a period of two weeks.
• Although the total number of radiosurgery treatments is fewer, each session usually takes more time in order to make sure the patient is accurately positioned
• Stabilization devices are often used to ensure proper positioning
Treatment Techniques

• Stereotactic radiosurgery (SRS) refers to the treatment of tumors in the brain or spinal column.
• Stereotactic body radiation therapy (SBRT) is a very similar technique to SRS but is used for targets that are outside the brain (lung, prostate, liver, pancreas).
• The latest term for these treatments is stereotactic ablative radiotherapy (SABR).
Technology

- Intensity modulated radiation therapy (IMRT) uses 3-D scans of your body to guide the beams of radiation to the tumor from many different angles.
- At each of these angles, the intensity of the radiation is varied (modulated) and the shape of the beam is changed to match the shape of the tumor.
- These adjustments enable the prescribed amount of radiation to be delivered to each part of the tumor, while minimizing exposure to the surrounding healthy tissue.
Technology

• Image-guided radiation therapy (IGRT) is a technique that uses 2D and 3D scans of the patient to guide the beams of radiation to the tumor from many different angles.

• Before each treatment, a CT scan is taken in order to accurately capture the position of the tumor that day.

• Final adjustments are then made to position the patient for accuracies of less then half of a millimeter.
VMAT

• Volumetric Arc Therapy (VMAT) is an advanced form of radiotherapy

• Unlike older IMRT treatments, during which the machine must make repeated stops and starts to treat the tumor from a number of different angles, VMAT can deliver the dose to the entire tumor in a 360-degree rotation, typically in less than two minutes

• Up to eight times faster than what was previously possible
SABR for Early Prostate Cancer

• 5 treatments (delivered every other weekday)
• Theoretical advantage to delivering a higher daily dose over a shorter amount of time
• 8 studies published to date (over 2000 patients)
• Primarily used in low-risk patients
• Serious side effects seen in less than 5%

Anticancer Res. 2018 Mar;38(3):1231-1240
SABR for Early Prostate Cancer
SABR for Early Prostate Cancer

- PSA control approaches 100% for low-risk patients and is over 90% for intermediate-risk patients.
- This compares very favorably with longer treatment regimens.
- As of 2018, SABR now recommended as an option by the NCCN for patients with low-risk disease.

NCCN Guidelines

<table>
<thead>
<tr>
<th>Regimen for Definitive Therapy</th>
<th>Very-Low¹</th>
<th>Low¹</th>
<th>Favorable or good prognostic² intermediate</th>
<th>Unfavorable, or poor prognostic², intermediate</th>
<th>High and Very-High³</th>
<th>Node Positive</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Beam Therapies</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>72 Gy to 80 Gy at 2 Gy per fraction</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓ with 4-6 mo ADT</td>
<td>✓ with 2-3 y ADT</td>
<td>✓ with 2-3 y ADT</td>
</tr>
<tr>
<td>75.6 Gy to 81.0 Gy at 1.8 Gy per fraction</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓ with 4-6 mo ADT</td>
<td>✓ with 2-3 y ADT</td>
<td>✓ with 2-3 y ADT</td>
</tr>
<tr>
<td>70.2 Gy at 2.7 Gy per fraction</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓ with 4-6 mo ADT</td>
<td>✓ with 2-3 y ADT</td>
<td>✓ with 2-3 y ADT</td>
</tr>
<tr>
<td>70 Gy at 2.5 Gy per fraction</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓ with 4-6 mo ADT</td>
<td>✓ with 2-3 y ADT</td>
<td>✓ with 2-3 y ADT</td>
</tr>
<tr>
<td>60 Gy at 3 Gy per fraction</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓ with 4-6 mo ADT</td>
<td>✓ with 2-3 y ADT</td>
<td>✓ with 2-3 y ADT</td>
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<tr>
<td>51.6 Gy at 4.3 Gy per fraction</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓ with 4-6 mo ADT</td>
<td>✓ with 2-3 y ADT</td>
<td>✓ with 2-3 y ADT</td>
</tr>
<tr>
<td>37 Gy at 7.4 Gy per fraction</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>40 Gy at 8 Gy per fraction</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>36.25 Gy at 7.25 Gy per fraction</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
SABR for Metastatic Disease

- Traditional RT for metastases (bone, lymph nodes) is palliative (intended to relieve symptoms)
- SABR can be used for oligometastatic disease
- Oligometastatic disease refers to 4 or fewer small areas of involvement
- Goal of SABR ablative rather than merely palliative
- Typically 3 treatments
Spine Radiosurgery
Spine Radiosurgery
SABR Delays Progression

- Recent clinical trial randomized patients with oligometastatic disease to observation vs. metastasis directed treatment (surgery or SABR)
- MDT *nearly doubled* time to progression (defined as PSA rise requiring androgen deprivation therapy)

Conclusions

- SABR/SBRT now part of NCCN guidelines for primary treatment of low-risk prostate cancer
- Although a “newer” technique, 5 year results appear comparable to longer treatment regimens
- Side effects usually mild
- SABR can significantly prolong time to progression in patients with limited metastatic disease
THANK YOU!