Radiation Therapy for Prostate Cancer: Treatment options and future directions

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Radiation Therapy for Prostate Cancer: Treatment options and future directions

- Review indications for radiation in the management of prostate cancer
- Review modalities of radiation therapy
- Discuss the side effect profile of radiation
- Future directions
Radiation Therapy for Prostate Cancer: Indications

- **Definitive**
  - An alternative to surgery for curative treatment

- **Post-operative**
  - Selective use after surgery for adverse pathologic findings

- **Salvage**
  - Treatment of prostatic and seminal vesicle fossae after biochemical failure following surgery

- **Palliation**
  - Most commonly for painful osseous metastases
Radiation Therapy for Prostate Cancer: Options for definitive treatment

External beam radiation

Brachytherapy
External beam radiation therapy

- Linear accelerator delivers high dose radiation, while rotating 360° around patient

- Multi-leaf collimators in the head of the machine shape the beam
IMRT vs. VMAT

- Originally, intensity modulation via “step and shoot” was used to create a dose distribution.

- Improvement in planning and delivery software now allows for rotational therapy.
External beam radiation therapy
Accounting for intrafraction target motion

- Management of rectal and bladder filling
- Gold fiducial placement:
  - TRUS guidance
  - Avoid midline (urethra) and areas of known cancer
  - Place in different planes (example: R Base, L Mid, R apex)
Brachytherapy

Prostate gland implants
- Permanent implants: Iodine 125
- Temporary catheters: Iridium 192
Radiation Therapy for Prostate Cancer: options for definitive treatment

**EBRT**
- ~8 weeks of daily treatments
- Appropriate for most patients
- Widely available
- More normal tissue receives low dose
- High-risk: add Androgen deprivation

**Brachytherapy**
- 1 day surgical procedure
- Appropriate only for selected patients, eg. AUA score < 15
- Not available in all centers
- Most favorable therapeutic index
- High-risk: not treated with brachy
Radiation Therapy for Prostate Cancer: side effect profile

<table>
<thead>
<tr>
<th></th>
<th>Acute</th>
<th>Long-Term</th>
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<tbody>
<tr>
<td>Urinary</td>
<td>Urinary symptom flare</td>
<td>stricture</td>
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<tr>
<td>Gastrointestinal</td>
<td>Diarrhea, tenesmus, hemorrhoid flare</td>
<td>Radiation proctitis</td>
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<tr>
<td>Sexual</td>
<td></td>
<td>Erectile dysfunction, decreased ejaculate volume</td>
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Urinary:
- Acute symptoms resolve, ~5% late Grade 3, stricture, but no incontinence

Sexual:
- ~50% with late developing ED; ~75% improve with Viagra

GI:
- Painless rectal bleeding 2-3 years following treatment
Radiation proctopathy

- Painless rectal bleeding 2-3 years following treatment

- Underscores the importance of baseline colonoscopy prior to RT – do not biopsy!

- Rectal bleeding at 5+ years following radiation more likely to have malignant etiology
Future Directions: hypofractionation

Most tumor types: insensitive to changes in daily dose

Most normal tissue: very sensitive to changes in daily dose
Prostate cancer: reversed survival curves

![Graph showing reversed survival curves for conventional and hypofractionation treatments. The graph plots surviving fraction against dose (Gy). The conventional treatment shows a higher surviving fraction at lower doses, while hypofractionation shows a lower surviving fraction at the same dose, indicating superior tumor kill compared to normal tissue kill.]
"Moderate" hypofractionation is now a reasonable option for low risk patients

- Multiple randomized trials demonstrate no difference in biochemical control, with comparable toxicity
  
  e.g. MD Anderson study, examining 6 vs. 8.5 weeks of treatment

- Await long term follow up, results of RTOG and European studies

- Difference in biochemical failure will be hard to detect in low-risk patients
“Extreme” hypofractionation is an emerging option

- Stereotactic body radiation therapy leverages increased certainty about target motion to allow for very high doses per fractions
- Platforms such as the CyberKnife allow for interfraction motion management and the use of non co-planar beams, and deliver very high doses per fraction
- 5 vs. 39 treatment sessions
RTOG 0938

- Phase III, Randomized
- Low Risk Localized Prostate Ca

- Health related QOL, rate of toxicity, PSA
Prostate Cancer:

Many clinical studies supporting the efficacy and safety of SBRT in the treatment of prostate cancer have been published. At least one study has shown excellent five year biochemical control rates with very low rates of serious toxicity. Additionally, numerous studies have demonstrated the safety of SBRT for prostate cancer after a follow-up interval long enough (two to three years) to provide an opportunity to observe the incidence of late GU or GI toxicity. While it is necessary to observe patients treated for prostate cancer for extended intervals to gauge the rate of long term (beyond 10 years) biochemical control and overall survival, the interim results reported appear at least as good as other forms of radiotherapy administered to patients with equivalent risk levels followed for the same duration post-treatment.

It is ASTRO’s opinion that data supporting the use of SBRT for prostate cancer have matured to a point where SBRT could be considered an appropriate alternative for select patients with low to intermediate risk disease.
Conclusions

- Radiation therapy is frequently indicated as a component of definitive, post-op, or salvage therapy for prostate cancer

- Radiation therapy can be delivered via external beam radiation or brachytherapy implants

- Radiation is generally well tolerated, with ~5-10% incidence of significant late toxicity; the majority of patients with ED respond well to PDE therapy

- Ongoing trials continue to investigate moderate and “extreme” hypofractionation with an eye towards shorter treatment time and cost effectiveness