Radiation therapy of prostate cancer
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Introduction

• Initial treatment plan focus:
  
  – Patients life-expectancy (age, comorbidities, and overall health status)
  
  – Biologic characteristics of the tumor (aggressiveness and behavior)
Introduction

• Treatments options for clinically localized prostate cancer include the following:

  – Active surveillance
  – Watchful waiting
  – Radical prostatectomy
  – Radiation therapy
  – Hormone therapy
Radiotherapy

• Radiotherapy uses:
  
  – High-energy rays (photons)
  – Particles (protons)

• To kill cancer cells by inducing DNA damage to all exposed cells thus interfering with cell division
Radiotherapy

• Patients with life-expectancy >10 y who decide against surgical intervention and accept treatment related complications

• Contra-indications to surgery
## Risk stratification

<table>
<thead>
<tr>
<th></th>
<th>Low risk</th>
<th>Intermediate risk</th>
<th>High risk</th>
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</thead>
<tbody>
<tr>
<td>PSA</td>
<td>&lt;10 ng/mL</td>
<td>&gt;10 to 20 ng/mL</td>
<td>&gt;20 ng/mL</td>
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<tr>
<td>Gleason score</td>
<td>6 or less</td>
<td>7</td>
<td>8 to 10</td>
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<tr>
<td>Clinical stage</td>
<td>T1c or T2a</td>
<td>T2b</td>
<td>T2c</td>
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Indication

• Treatment modality with curative intent for clinically localized prostate cancer:

  – Low-risk patients
  – Intermediate-risk in combination with short-term ADT (4-6 months)*
  – High-risk in combination with long-term ADT( 3 y)

* EUA 2014, AUA
Indication

• Optional in selected patients with:
  
  – Locally advanced disease (cT3b-T4 N0)
  – Long-term ADT (3 y)
Indication

• Adjuvant treatment:
  – Seminal vesicle invasion
  – Positive surgical margins
  – Extraprostatic extension

• Benefits:
  – Reduces risk of biochemical PSA recurrence
  – Reduces local recurrence
  – Reduces clinical progression of cancer
Indication

• Salvage treatment to patients with:
  
  – PSA (detectable or raising value after surgery that is > or equal to 0,2 ng/ml with a second confirmatory level) or local recurrence after radical prostatectomy
  
  – No evidence of distant metastatic disease
  
  – Effectiveness is greatest when administered at lower levels of PSA
Indication

• Metastatic prostate cancer as a palliative option in combination with ADT for treatment of local cancer-derived symptoms (ex: relief of bone pain)
Contra-indications

• History of IBD (Crohn's disease, ulcerative colitis)

• Diverticular disease

• Previous TURP or severe IPSS
Radiotherapy

• External-beam radiation therapy (EBRT)

• Brachytherapy (insertion of radioactive seeds into the prostate gland)
EBRT

• Use of beams of gamma radiation, usually photons, directed at the prostate and surrounding tissues
EBRT

- Conventional (two dimensional) EBRT
- 3-Dimensional Conformal Radiotherapy (3D-CRT)
- Intensity-Modulated Radiation Therapy (IMRT)
- Image-Guided Radiotherapy
- Proton Beam Therapy
EBRT

• Localization of the target and the adjacent normal tissue is critical in the planning of therapy
EBRT

• Simulation:

  – Conventional EBRT: fluoroscopy, plain radiography, retrograde urethrography

  – 3D-CRT and IMRT: CT scan
EBRT
EBRT

• Conventional EBRT is generally considered acceptable because the treatment borders (margins) are more inclusive than those used in 3D-CRT and IMRT
Complications

- Skin (reddenning, epilation)
- GI tract (diarrhea, **Radiation proctitis 1/3 of patients usually after the dose exceeds 50 Gy:** fecal urgency, mucous discharge, and rectal bleeding)
- GU tract ( Radiation cystitis: urinary frequency, urgency, dysuria, hematuria, urinary incontinence, urethral stricture )
- Erectile and ejaculatory dysfunction (50%)
- Fatigue
Advance in EBRT

• Newer EBRT techniques focus the radiation more precisely on the tumor

• Higher dose of radiation (escalation) can be given while reducing the radiation exposure to nearby healthy tissues
3-Dimensional CRT

- Computer alters the radiation beams to focus the radiation dose to the region of the prostate gland
3-Dimensional Conformal Radiotherapy

• Working knowledge of the following terms:

  • Gross tumor volume (GTV)
  • Clinical target volume (CTV)
  • Planning target volume (PTV)
3-Dimensional Conformal Radiotherapy

• Acquisition of imaging data

  – Consecutive CT scans or MRIs
  – 3 cm below the prostate, 3 cm above the superior tip of the seminal vesicles
IMRT

• Advanced form of 3D therapy
• Computer-driven machine that actually moves around the patient as it delivers radiation
Image-Guided Radiotherapy

• Some newer radiation machines have imaging scanners built into them
Proton beam therapy

• Beams of protons instead of X-ray

• More radiation to the prostate while doing less damage to nearby normal tissues
Advantage

• Dose escalation (from 66-70 Gy in conventional EBRT)

• Improve in results considerably
Advantage

• Dose escalation

– Low-risk patients are now frequently treated with 70 to 72 Gy
– Intermediate-risk patients with 75 to 76 Gy
– High-risk patients with 80 Gy
Disadvantage

• They can be too narrowly targeted

• Geographic miss of the tumor outlines especially in the important posterior peripheral region of the prostate
Brachytherapy (implantation or interstitial radiation therapy)

- Radioactive sources (seeds) are implanted:
  - Directly into the prostate gland
  - Sometimes into the surrounding tissues
Brachytherapy

• Relatively easy to perform
• Patients with clinically localized prostate cancer
• Can be performed under general or regional anesthesia
• Iodine-125 or palladium-103
Brachytherapy

- Men with early stage prostate cancer (low-risk)
- Its use is limited by several factors: previous TURP, those patients who already have urinary symptoms
- It might not be possible to place the seeds into all the correct locations in large volume prostate
Brachytherapy

• TRUS, CT, or MRI are used to help guide the placement of the radioactive pellets

• Special computer programs calculate the exact dose of radiation needed

• Poor implantation or migration of the seeds after implantation +++
Brachytherapy

• The radiation doses delivered to the prostate are approximately:
  
  – 145 Gy for iodine
  – 125 Gy for palladium
Permanent (low dose rate or LDR) brachytherapy

- Seeds are placed inside thin needles
- Pellets are left in place and give off low doses of radiation for weeks or months
- Radiation from the seeds travels a very short distance
- This lowers the amount of damage to healthy tissues
Permanent (low dose rate or LDR) brachytherapy

- Because they are so small, the seeds cause little discomfort

- EBRT combined with permanent-source brachytherapy has been reported to have an efficacy similar to high-dose EBRT alone for high risk cancers
Brachytherapy

• Patients with:
  
  – low-risk cancer
  – without a previous TURP
  – Good IPSS
  – Prostate volume < 50 mL

• LDR brachytherapy is a treatment option
Outcome

• Patients undergoing definitive radiotherapy are typically considered to have achieved biochemical control of disease if the PSA level is not rising and the serum PSA level is below 0.5 ng/ml
EBRT VS brachytherapy

• Direct comparisons of radiation doses between are not valid

• Because of the much higher doses of radiation delivered, brachytherapy causes more ablation of the prostate gland than EBRT does
EBRT VS brachytherapy

• Urinary symptoms are more common after brachytherapy, especially in patients with prostatic hyperplasia
• ED occurs more commonly with brachytherapy than with EBRT
• Proctitis and rectal injury are less common with brachytherapy
Comparison of Radiotherapy with Radical Prostatectomy

• It is impossible to compare the results of surgery with those of radiotherapy because of the difference in the end points used for treatment failure
• Valid comparisons of radiotherapy with current treatment methods are lacking
• However, the available evidence suggests that radical prostatectomy is more effective in achieving long-term progression-free survival in patients with clinically localized prostate cancer
Comparison of Radiotherapy with Radical Prostatectomy

• Adjuvant hormone therapy with radiation was associated with worse quality of life outcomes.
• Patients receiving brachytherapy reported having more long-lasting urinary irritation, bowel, and sexual symptoms and transient problems with vitality or hormonal function.
• The adverse effects of prostatectomy on sexual function were mitigated by nerve-sparing procedures.
• After prostatectomy, urinary incontinence was observed, but urinary irritation and obstruction improved, particularly in patients with a large prostate gland.
Comparison of Radiotherapy with Radical Prostatectomy

• Each treatment is associated with a distinct pattern of change in quality of life domains related to urinary, sexual, bowel, and hormonal function

• Concerns have been raised about highly aggressive second malignancies occurring after radiation therapy especially cancers of the bladder and rectum
References

• Campbell 2012
• EUA guidelines 2014
• AUA guidelines
Thank you