

Radiation therapy of prostate cancer

Tuesday 17/12/2015

Mohamad Mokdad

PGY 3

Lebanese university

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

	Low risk	Intermediate risk	High risk
PSA	<10 ng/mL	>10 to 20 ng/mL	>20 ng/mL
Gleason score	6 or less	7	8 to 10
Clinical stage	T1c or T2a	T2b	T2c

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

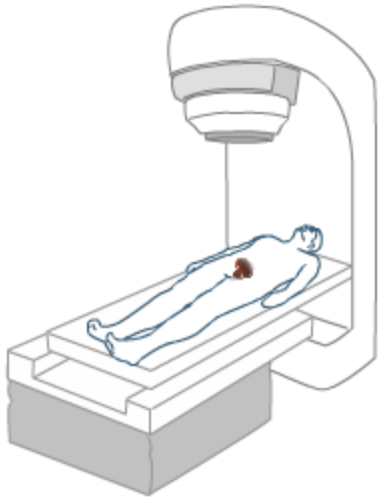
EBRT

- 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 (reddening, 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

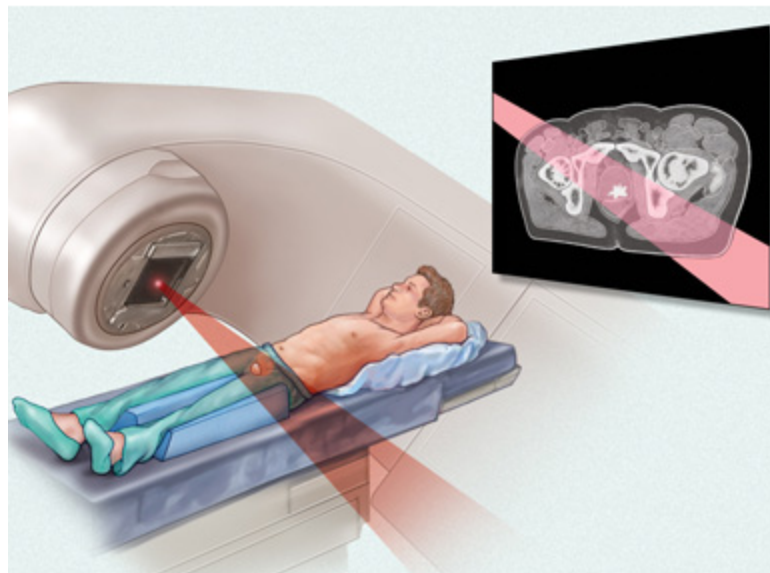


Image-Guided Radiotherapy

- 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 lower 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