Prostate Cancer 101 GU Oncology Nursing Education

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Part 2

Treatment of Localized Prostate Cancer, Management of Side Effects

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Objectives

- Identify various treatments for localized disease.
- Define strategies for managing treatment side effects.

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Treatment

Active Surveillance

- Candidates: Very low, low, and favorable intermediate risk; life expectancy > 10 years
- Confirmatory testing: Within 6-12 months
  - Prostate MRI, +/- prostate biopsy
  - All patients should have confirmatory biopsy within 1-2 of diagnostic biopsy
- Follow up:
  - PSA every 6 months
  - DRE every 12 months
  - Biopsies
  - Prostate MRIs

Walker CH, et al. Active surveillance for prostate cancer: selection criteria, guidelines, and outcomes. World J Urol. 2022 Jan;40(1):35-42.

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Treatment

Active Surveillance

- Intervention:
  - Grade reclassification on repeat biopsy
  - Increase in tumor volume
  - Change on PSA density
  - Patient preference
- Other
  - Not appropriate for all men who meet criteria
  - Different than Watchful Waiting/observation

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Active Surveillance

Benefits

- Over 50% of eligible patients may safely avoid treatment for at least 10 years
- Avoid possible side effects
- QoL less affected
- Reduce risk of unnecessary treatment of indolent cancer
- Treatment delays do not seem to impact cure rates

Limitations

- 30-50% of patients will undergo treatment by 10 years
- Risk of regional or metastatic spread (while very low, <0.5%)
- Uncertainty
- Follow up with recommended surveillance protocols

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Treatment

Life Expectancy Calculators

- Can be helpful with informed-decision making in early detection and treatment
- Estimation of life expectancy is easier for groups, challenging for individuals
- Several options available
- Questions related to co morbidities, smoking, prostate cancer characteristics

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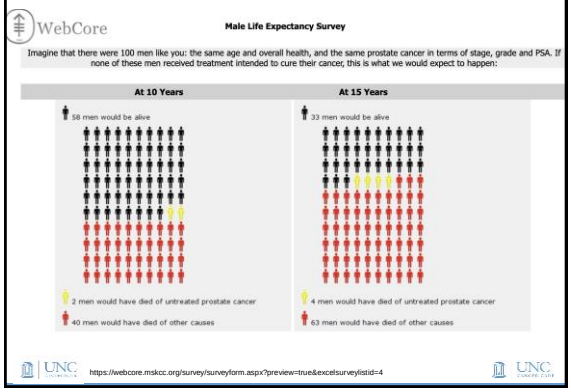

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Treatment

Radical Prostatectomy

- Surgical removal of the prostate gland and seminal vesicles
- Open, laparoscopic, robotic techniques
- Considerations: Age, comorbidities, prior abd surgeries
- Nerve-sparing: Preservation of neurovascular bundle
- Pelvic lymph node dissection (PLND)
- 1 night in hospital, d/c with catheter
- SE: ED, UI, infertility
- Follow up: q 3 months x 1 year; q 6 months until yr 5; annually until year 10

Kesch C, et al. Radical Prostatectomy: Sequelae in the Course of Time. Front Surg. 2021 May 28;8

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Treatment

Radiation Therapy

- Intensity Modulated Radiation Therapy: gives higher dose to prostate and less to surrounding tissue
- Fiducials: Gold markers used to help visualize prostate
- Usually 5 days/week, 4-6 weeks
- If ≥ intermediate risk disease will get ADT
- Side effects: urinary symptoms, diarrhea, proctitis, fatigue, erectile dysfunction, hemorrhagic cystitis
- PSA bounce

Weg ES, et al. Dose-Escalated Intensity Modulated Radiation Therapy for Prostate Cancer: 15-Year Outcomes Data. Adv Radiat Oncol. 2019 Apr 4;4(3):492-499

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Treatment

Stereotactic body radiation therapy

- Cyberknife
- 4-5 fractions (~ 1 week)
- 9.5 Gy/day x 4 = 38 Gy total
- Low risk or favorable intermediate

Patel, S.A., *et al.* Stereotactic body radiation therapy use for high risk prostate cancer in the United States. *Prostate Cancer Prostatic Dis* **24**, 578–581 (2021).

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Treatment

Brachytherapy

- Radioactive seeds implanted in the prostate via perineum
- Low dose vs. high dose
- Low risk disease, prostate <60g, no h/o BOO
- Side Effects: Retention, dysuria, ED
- Avoid close contact with children and pregnant women (permanent seeds); condom x 2 weeks

Ali S, Esper P. Brachytherapy: Increased use in patient with intermediate and high risk prostate cancers. CJON 2021, 25(3), 321-328.

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National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2023
Prostate Cancer

NCCN Guidelines Index
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Discussion

PRINCIPLES OF RADIATION THERAPY

Table 1: Below are examples of regimens that have shown acceptable efficacy and toxicity. The optimal regimen for an individual patient warrants evaluation of comorbid conditions, voiding symptoms and toxicity of therapy. Additional fractionation schemes may be used as long as sound oncologic principles and appropriate estimate of BED are considered.
See PROS-3, PROS-4, PROS-5, PROS-6, PROS-7, PROS-8, PROS-12, and PROS-I for other recommendations, including recommendations for neoadjuvant/concomitant/adjuvant ADT.

Regimen	Preferred Dose/Fractionation	NCCN Risk Group (✓ indicates an appropriate regimen option if RT is given)					
		Very Low and Low	Favorable Intermediate	Unfavorable Intermediate	High and Very High	Regional N1	Low Volume M1[a]
EBRT							
Moderate Hypofractionation (Preferred)	3 Gy x 20 fx 2.7 Gy x 28 fx 2.5 Gy x 28 fx	✓	✓	✓	✓	✓	
	2.75 Gy x 20 fx						✓
Conventional Fractionation	1.8–2 Gy x 37–45 fx	✓	✓	✓	✓	✓	
	2.2 Gy x 35 fx + micro-boost to MRI-dominant lesion to up to 95 Gy (fractions up to 2.7 Gy)		✓	✓	✓		
SBRT Ultra-hypofractionation	9.5 Gy x 4 fx 7.25–8 Gy x 5 fx 6.1 Gy x 7 fx	✓	✓	✓	✓		
	6 Gy x 6 fx						✓
Brachytherapy Monotherapy							
LDR Iodine 125 Palladium 103 Cesium 131	145 Gy 125 Gy 115 Gy	✓	✓				
HDR Iridium-192	13.5 Gy x 2 implants 9.5 Gy BID x 2 implants	✓	✓				
EBRT and Brachytherapy (combined with 45–50.4 Gy x 25–28 fx or 37.5 Gy x 15 fx)							
LDR Iodine 125 Palladium 103 Cesium 131	110–115 Gy 90–100 Gy 85 Gy			✓	✓		
HDR Iridium-192	15 Gy x 1 fx 10.75 Gy x 2 fx			✓	✓		

[a] High-volume disease is differentiated from low-volume disease by visceral metastases and/or 4 or more bone metastases, with at least one metastasis beyond the pelvis vertebral column. Patients with low-volume disease have less certain benefit from early treatment with docetaxel combined with ADT.

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Treatment

Cryotherapy

- Surgical freezing of the prostate with cryoprobe
- Cell necrosis caused by apoptosis, cell rupture, ischemia
- Rapid freezing more effective
- -100º to -200º for 10 minutes
- Candidates: Unfit for RP, XRT, obesity
- Side Effects: ED (near 100%), rectal pain, retention, UI
- Targeted/partial cryo

High-intensity focused ultrasound (HIFU)

- Ablates prostate tissue using heat and cavitation
- Low risk prostate cancer
- SE: Retention, BOO, UTI, ED
- Trials comparing HIFU to RP

Kotamarti S, Polascik T.J. Focal cryotherapy for prostate cancer: a contemporary literature review. Ann Transl Med. 2023 Jan 1;S1(1):25

Francesco Ziglioli et al., Oncologic outcome, side effects and comorbidity of high-intensity focused ultrasound (HIFU) for localized prostate cancer. A review, Annals of Medicine and Surgery. 58; 2020: 110-115

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Treatment

Special populations

- Very high risk: EBRT + ADT + abiraterone
  - Other options, but this one is unique given addition of oral antiandrogen
  - In STAMPEDE trial, patients had two of the following: cT3-4, Grade Group 4 or 5 and PSA > 40
- Regional risk group (Any T, N1, M0)
  - EBRT + ADT + abiraterone (for 2 years)
  - EBRT + ADT
  - ADT with or without abiraterone
  - RP + PLND

Attard G et al. Abiraterone acetate and prednisolone with or without enzalutamide for high-risk non-metastatic prostate cancer: a meta-analysis of primary results from two randomized controlled phase 3 trials of the STAMPEDE platform protocol. Lancet 2022; 399: 447-60

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Localized Prostate Cancer

- Nursing considerations
  - Pre and post treatment education
    - Treatment details, outcomes, side effects, follow up schedules, etc.
  - Catheter care
  - Side effect management
  - Psychological support
  - Survivorship issues

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Localized Prostate Cancer

Side effect management

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Side Effect: Erectile Dysfunction

- Review pre-treatment SHIM score
  - Questions to determine severity of ED
- Orgasm is still possible
- Recovery: Age, Preop sexual function, surgical technique
- Average time to recovery (spontaneous with minimal aid) is 24 months

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Erectile Dysfunction

- Require nerves to work properly
  - Even with nerve-sparing, they do not always function well immediately after treatment
  - As nerves recover, meds may work better
  - Foundation of MOA is that they rely on the nerves to activate the chemicals within the penis that will lead to increased blood flow
- Timing
  - Penile rehab→ no consensus
  - Theory: drugs may improve blood flow & oxygenation to penis, leading to improved function

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Erectile Dysfunction

- Prostatectomy (10-100%)
  - Injury to neurovascular bundle (NVB) = cavernous blood vessels & nerves
  - Heat injury, ischemic injury, inflammatory rxn
  - Nerve-sparing = dissecting nerves away from prostate
  - 2-year recovery
- EBRT (20-80%)
  - Delayed SE
  - Affects NVB, arterial function, inflammation
- Brachytherapy (15-40%); Cryotherapy (100%)
  - Inflammation
  - Cryogenic injury of NVB

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ED: Vacuum Erection Device

- Drug-free
- No systemic SE
- Does not require stimulation
- Used for rehab and sexual activity
- Cumbersome
- Not covered by all insurance
- Cylinder, pump, elastic band (max 30 mins)
- Can be used alone or with other ED treatments

Burnett, Arthur et al, Allen D.; Shindel, Alan W. Erectile Dysfunction: AUA Guideline, Journal of Urology: September 2018 - Volume 200 - 3A1-A30, 467-668

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ED: PDE5-Inhibitors

- Block degradative action of PDE5 on cyclic GMP in the smooth muscle cells lining the blood vessels supplying corpus cavernosum.
- Do not initiate erection, make it stronger
- Contraindications: Nitrates, significant CAD
- Side Effects: Headache, flushing, nasal congestion, abnormal vision, back pain, priapism

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ED: PDE5-Inhibitors

- Sildenafil
  - 25, 50, 100 mg (or 20 mg)
  - 1 hour before sexual activity
  - Empty stomach
- Vardenafil
  - 10, 20 mg
  - 15-30 minutes before sexual activity
  - Rapid onset
- Tadalafil
  - 5mg daily
  - 2.5, 5, 10, 20 mg
  - 1 hour prior to sexual activity
  - Market 36-hour efficacy, longer half life (17 hours)
- Avanafil
  - 50, **100**, 200 mg
  - 30 minutes prior to sexual activity
  - Half life 5 hours
  - With or without food
  - Metabolized by liver

Dhaliwal A, Gupta M. PDE5 Inhibitors. [Updated 2023 Apr 10]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK549843/

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ED: Medicated Urethral System for Erection

- Binds to membrane receptor, activates adenylate cyclase, and increases intracellular cyclic AMP
- Size of a grain of rice
- Onset of erection within 5-20 minutes, lasts 30-60
- SE: Burning, bleeding, priapism, headache, dizziness
- Contraindications: Hx priapism, distal urethral stricture, penile fibrosis, urethritis, SSA, MM, DVT
- Condom use if intercourse with a pregnant partner
- No more than 2 pellets within 24 hours
- Impairs spontaneity due to short onset
- $$$$

Burnett, Arthur et, Allen D.; Shindel, Alan W. Erectile Dysfunction: AUA Guideline, Journal of Urology: September 2018 - Volume 200 ; 3A1-A30, 467-668

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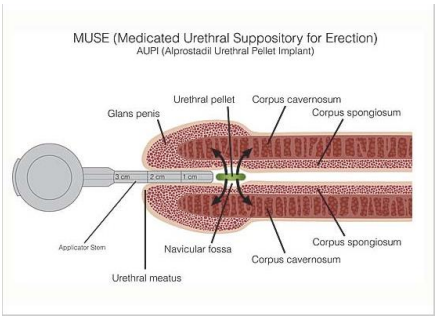

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ED: Intracavernosal Injections

- Alprostadil
- Papaverine: Nonspecific inhibitor of PDE
- Phentolamine: Inhibits α-adrenergic receptors
- Bi mix: Papaverine + Phentolamine
- Tri mix: All 3 drugs
- First dose with a health care provider
- Titrate dose depending on response
- Cost effective

Bobo W. Elena, et al (2023) Current status of intracavernosal injection therapy in erectile dysfunction, Expert Opinion on Pharmacotherapy, 24:8, 925-933

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ED: Intracavernosal Injections

- Priapism: Alprostadil 2%, Papaverine 10%
- Penile Fibrosis: Alprostadil 1%, Papaverine 12%
- Combo is better than papaverine and phentolamine alone, but similar to alprostadil alone
- 5-10 minutes before sexual activity
- Involve partner
- No more than 1 in 24 hours, 3 doses/week
- SE: Discomfort, bruising, priapism

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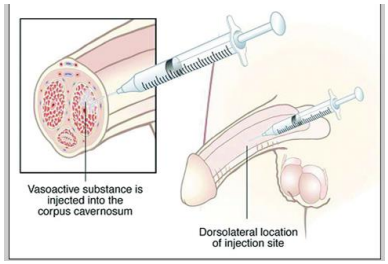

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ED: Inflatable Penile Prosthesis

- Surgical (risk vs. benefit)
- Noninflatable: 2 bendable rods inserted in corpora cavernosa, pt maneuvers
- Inflatable: 2 inflatable rods into corpora cavernosa connected to a pump reservoir. Pumps saline from reservoir into rods.
- SE: Infection, pain, device failure
- $$$$$

Wang VM, Levine LA. Safety and Efficacy of Inflatable Penile Prostheses for the Treatment of Erectile Dysfunction: Evidence to Date. Med Devices (Auckl). 2022 Feb 10;15:27-36

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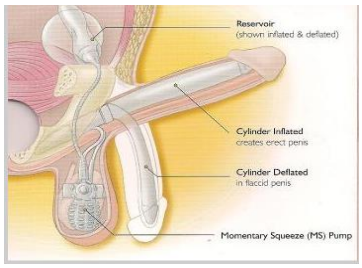

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Pros & Cons

Treatment	Pros	Cons
PO PDE-5I	• Easy to take • Discreet • Travel	• Poor efficacy after surgery • Side effects • Costly
VED	• Noninvasive • Highly efficacy rates • Fairly easy to use • Travel • Incorporate into foreplay • One-time cost	• Cumbersome • Messy • Penis may appear purple • Penis wobbly at base • Discomfort
MUSE	• Easy to use • Less invasive than injections	• Low efficacy • Side effects • Pain • Costly
ICI	• High efficacy • Reliable • No tension ring • Erection lasts longer than other tx	• Invasive • Side effects • Refrigeration • Anxiety
Implant	• High efficacy • High satisfaction	• Permanent • Side effects • Surgical procedure • Surgical costs

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Side effect: Urinary Incontinence

- **Stress urinary incontinence (SUI):** Most common following treatment due to muscle or nerve damage to urinary sphincter
- Also urge and mixed UI
- Continence pad, diaper, condom catheter, BioDerm, clamps
- Kegel exercises (teach pre op!)
- Pelvic Floor Physical Therapy
- Anticholinergic: inhibit detrusor contraction (best for urge UI)
- Recovery: Average 12 months
- If persistent and/or worsens, consider VUDS & cysto
  - Eval for BNC, urethral stricture, bladder dysfxn, sphincter dysfxn
- Surgical interventions
- Collagen

Castellan P, et al. Management of Urinary Incontinence Following Radical Prostatectomy: Challenges and Solutions. *Ther Clin Risk Manag.* 2023;19:43-56

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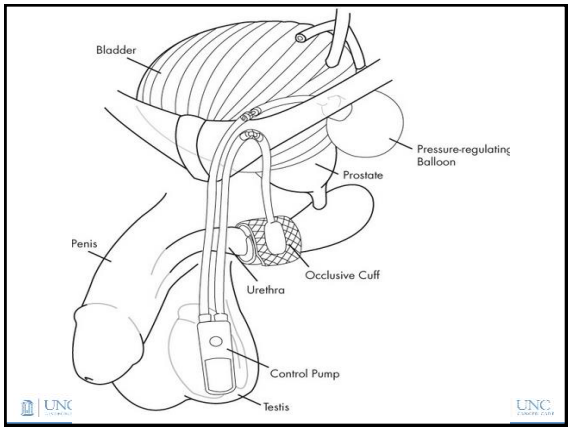

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Localized Prostate CA

Risks of Recurrence

- High grade tumors (≥ GG 7)
- High stage tumors (≥ T3)
- High pre-treatment PSA (≥ 10)
- Positive surgical margin
- Seminal vesicle invasion
- Capsular penetration
- Positive Lymph Nodes

After recurrence, a PSADT > 15 months is associated with a low risk of death from prostate cancer over 10 years.

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Survivorship

- Patients have unique needs post-treatment
- Follow up schedules
- Distress about fear of recurrence
- Post-treatment side effects
- Breaking stereotypes re: “manhood”
- Healthy lifestyle
- Caregiver support
- Emotional/mental well being

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Part 2 Takeaways

- Active surveillance is appropriate for a lot of men with early-stage prostate cancer
- Radical prostatectomy has been gold standard
- Radiation therapy comes in different forms, and is very dependent on grade/stage/patient characteristics
- Systemic treatment may be used for high/very high/N1 disease
- Side effects of treatment can be significant QoL issues
- Managing expectations about recovery time and side effects of treatment is crucial

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