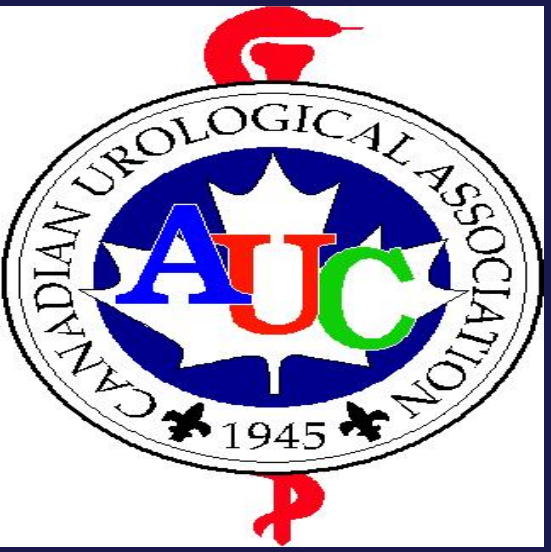
Canadian Undergraduate Urology Curriculum (CanUUC): Prostate Diseases

Last reviewed May 2017



Prostate 2: Prostate Cancer

- risk factors need to be updated
- disease screening recommendations and notes need to be updated to be in line with CUA recs
- patient decision aids on screening would likely be a good resource to get the point across at a student level on the current controversies
- again graphics need to be updated for presentation
- podcast length is a bit too in depth for med student level... again 10 minutes might be a good max with bookmarks.

Prostate Cancer Objectives

1. Discuss the pros/cons of early detection of prostate cancer.
2. Outline prostate cancer diagnosis
3. Define what PSA is and what causes it to be elevated.
4. Describe basic treatment options for prostate cancer both early and advanced.
5. Recognize that spinal cord compression due to metastatic prostate cancer can occur

Prostate Cancer Statistics

- Most common non-cutaneous malignancy in men in North America
- 2nd most common cause of cancer-related deaths in men
- 1 in 7 men will be diagnosed
- Lifetime risk of being diagnosed with prostate cancer is 18% but risk of dying of prostate cancer is only 3%

Prostate Cancer Risk Factors

- Established
  - Advancing age
  - Presence of androgens
  - Family history (1st degree relative)
  - African ancestry
- Potential
  - High dietary fat
  - Obesity
  - Inherited mutations (*BRCA1* or *BRCA2* genes)
  - Vitamin D or E deficiency
  - Selenium

Prostate Cancer: Presentation

- Early stages usually asymptomatic
  - Most cases detected by serum PSA **screening**
  - Palpable nodule or firmness on DRE
- Advanced stages
  - Urinary retention/renal failure
  - Bone pain
  - Anemia
  - Weight loss, fatigue
  - Spinal cord compression

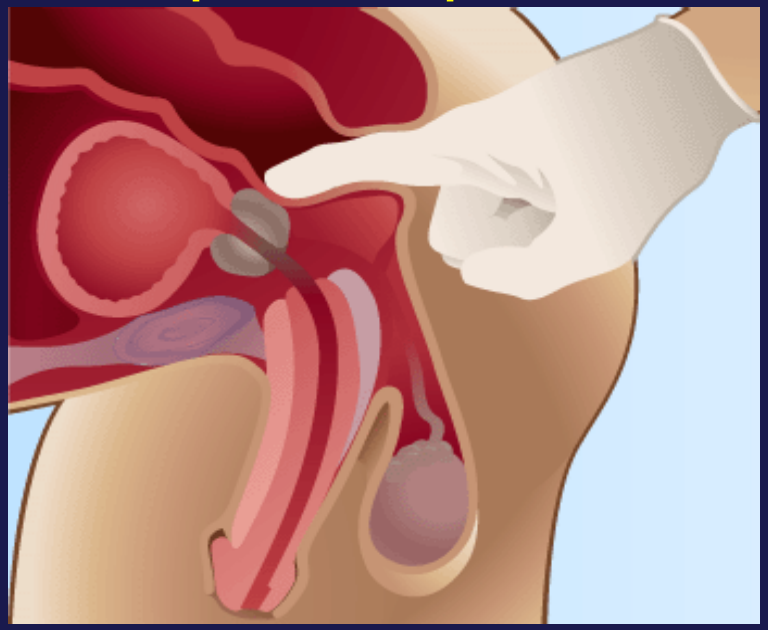
Disease Screening

- Goal
  - To identify the presence of disease at a stage when treatment can be given that will cure it

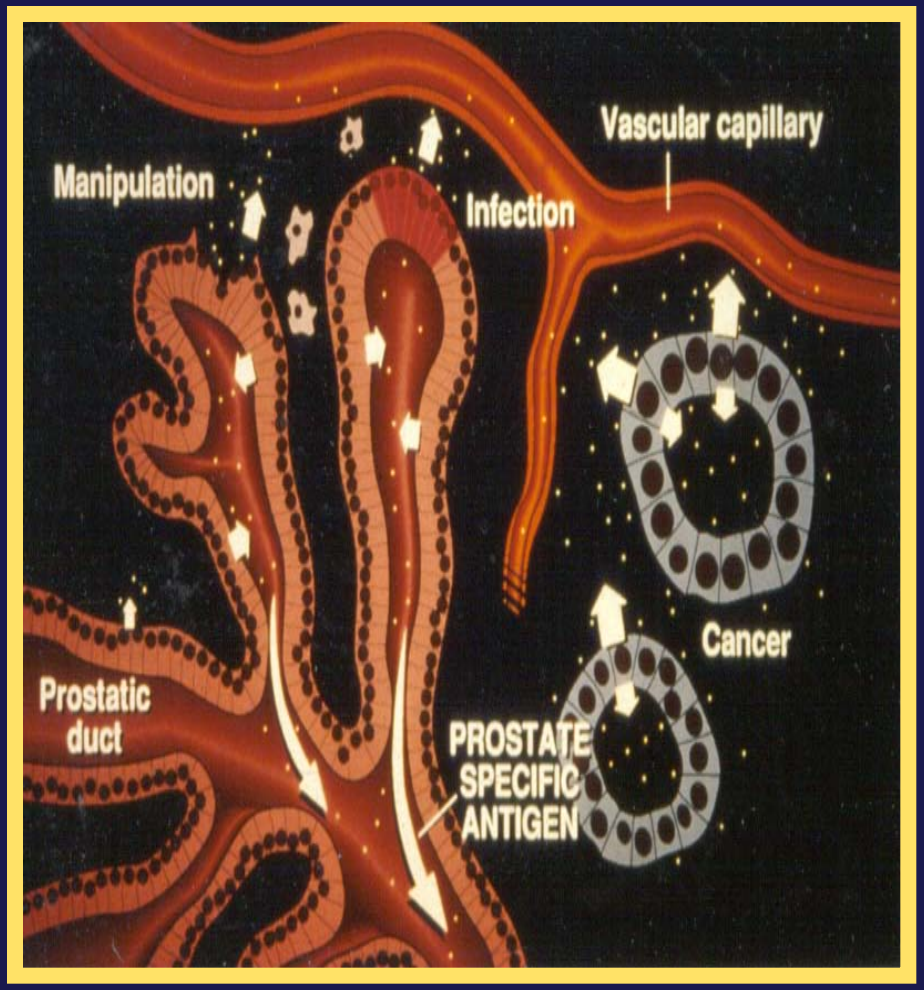
- Use a combination of DRE and PSA

Digital Rectal Examination

- DRE (digital rectal exam) has a 50% positive predictive value
- DRE alone is not a good screening tool
- BUT it is an important part of screening



What is PSA (Prostate Specific Antigen)?



- A Serine protease (enzyme) found in the prostate
- Secreted by prostate epithelial cells
- Found in ejaculate
- As diagnostic tool for:
  - Screening
  - Staging
  - Prognostic indicator
  - Surveillance

Prostate Cancer: Screening with PSA

- No clear cut-point between normal and abnormal PSA levels. Even PSA cut-off of 1.1 ng/ml misses up to 15% of prostate cancer **(The Cancer Prevention Trial – 2003)**
- Positive predictive value for PSA > 4ng/ml = 30% (i.e. About 1 in 3 men with elevated PSA have prostate cancer detected at time of biopsy
- PPV increases to 45-60% for PSA > 10ng/ml
- Nearly 75% of cancers detected in the grey zone (PSA 4-10) are organ confined; potentially curable.
- <50% of prostate cancers organ confined if PSA >10

Prostate Cancer Screening: Pros and Cons

Pros

- Early detection of disease leads to higher cure rates
- By the time symptoms of prostate cancer present usually not curable
- **Screening offers a modest effect on mortality**
- The “number needed to screen” is similar to studies on mammography for Breast Ca and fecal occult blood testing for Colon Cancer

Cons

- If tests abnormal, need for prostate biopsy
- If cancer found & treatment chosen, morbidity from therapy
- If insignificant cancer found, treatment was unnecessary
- Risk of overdiagnosis, overtreatment

Screening Recommendations

Discuss with the patient and if he decides to be screened

- Annual PSA and DRE
- Age 50-70 yrs (with at least 10 yr life expectancy)
- Begin screening at age 40 if risk factors
  - African ancestry
  - First degree relative(s) with prostate cancer

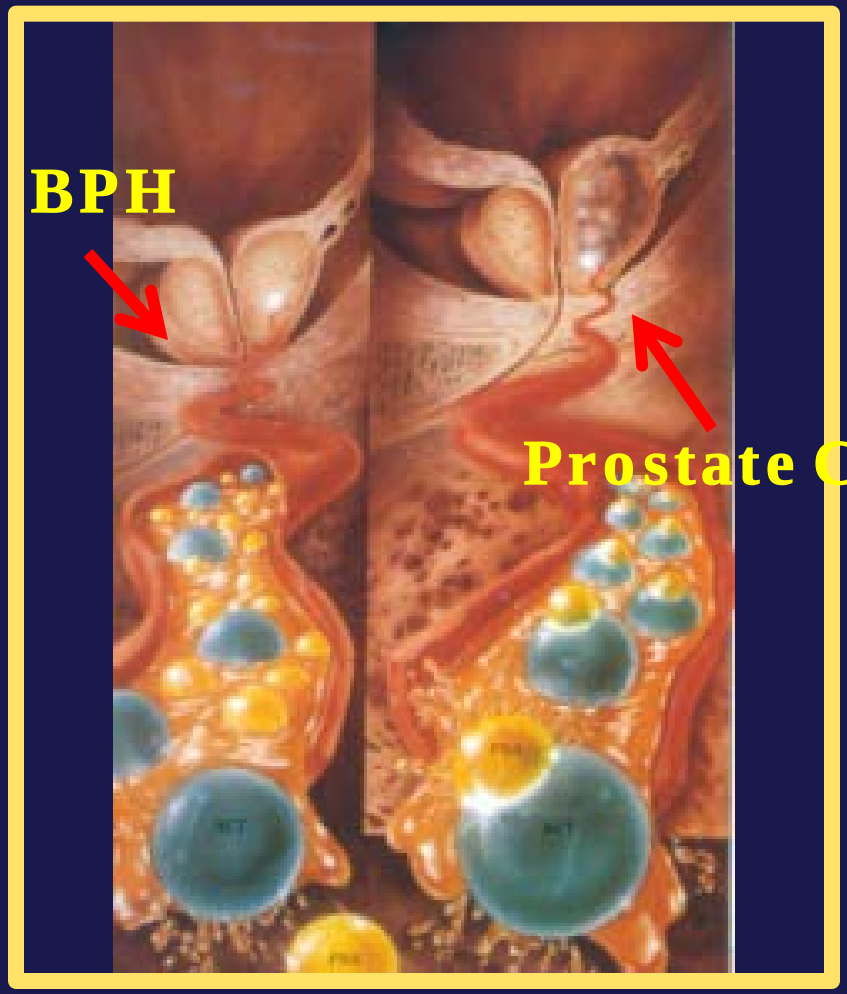
⇨ **A shared decision-making approach to PSA screening seems most appropriate**

Causes of an elevated PSA

1. Prostate cancer
2. Age
3. Prostate size (BPH)
4. Infection/inflammation
5. Recent instrumentation (biopsy, catheterization, etc)
6. Physiological variation
   - Recent ejaculation

Free/Total PSA Ratio:
A Way to Improve Specificity

- Prostate cancer maybe associated with more protein-bound PSA (less free PSA) than in BPH
  - F/T ratio is lower in patients with prostate cancer
  - Can improve test specificity
  - Useful when total PSA in 4-10 ng/ml range

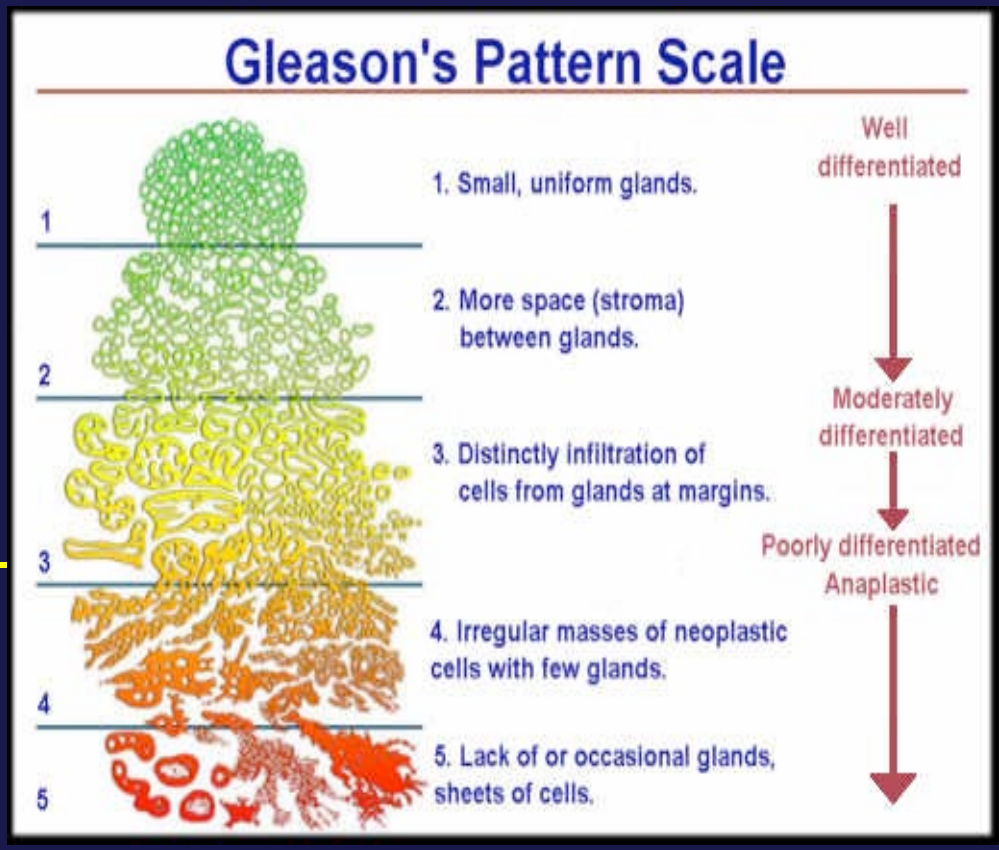


Prostate Cancer: Diagnosis

- Indications for transrectal ultrasound (TRUS) guided biopsy
  - Palpable nodule on DRE
  - Elevated serum PSA
- Biopsy involves 10-18 needle cores taken mostly from the peripheral zone of the prostate
- Transrectal ultrasound alone/CT scan/MRI not sensitive enough to make the Diagnosis

Prostate Cancer: Pathology

- Adenocarcinoma
- Gleason “grade” is from 1-5 based on glandular architecture
- Gleason score is the total primary grade (1-5) + secondary grade (1-5) = 2-10
  - 4-6/10=well-differentiated
  - 7/10=moderately differentiated
  - >8/10=poorly differentiated

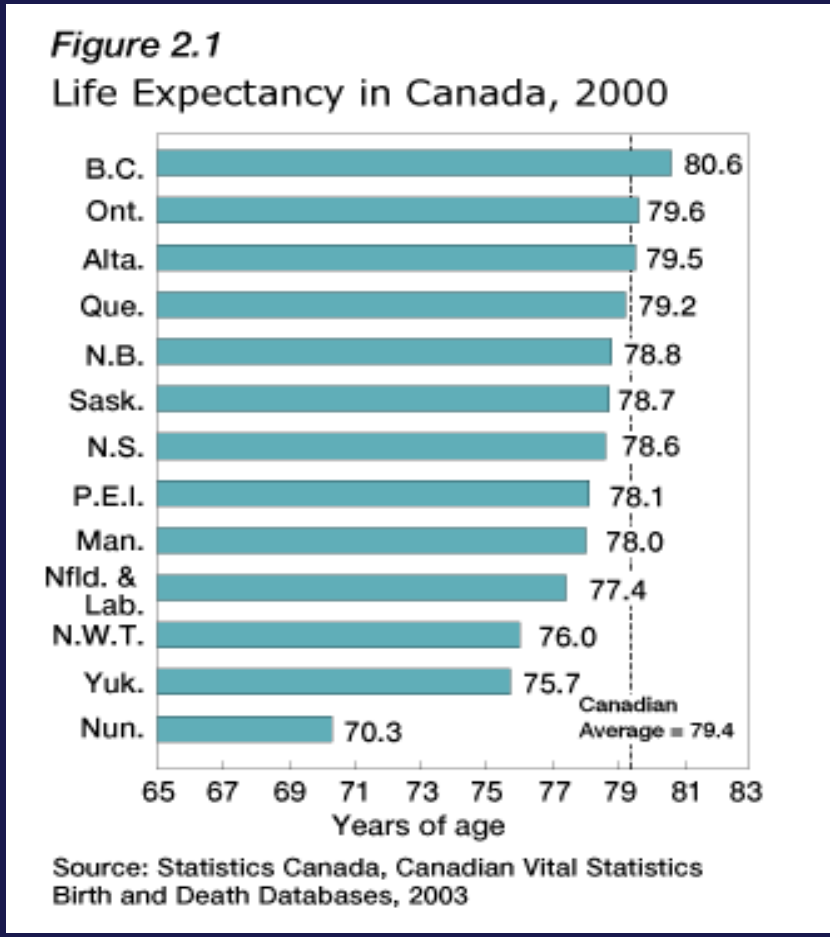


Prostate Cancer: Staging

- Can spread to adjacent organs (seminal vesicles, bladder), lymph nodes, bone
- Most bone mets are **osteoblastic**
- Prior to initiating treatment consider
  - Bone scan (PSA>10, Gleason Score >7)
  - CT scan pelvis/abdomen (PSA >10, Gleason Score >7))
  - These tests are typically not required in asymptomatic men with low risk prostate cancer

Prostate Cancer Treatment

- Considerations
  - Patient's age
  - Co-morbid health conditions
  - Tumor stage
  - Tumor grade (Gleason score)
  - Often a patient choice
  - Surgery and



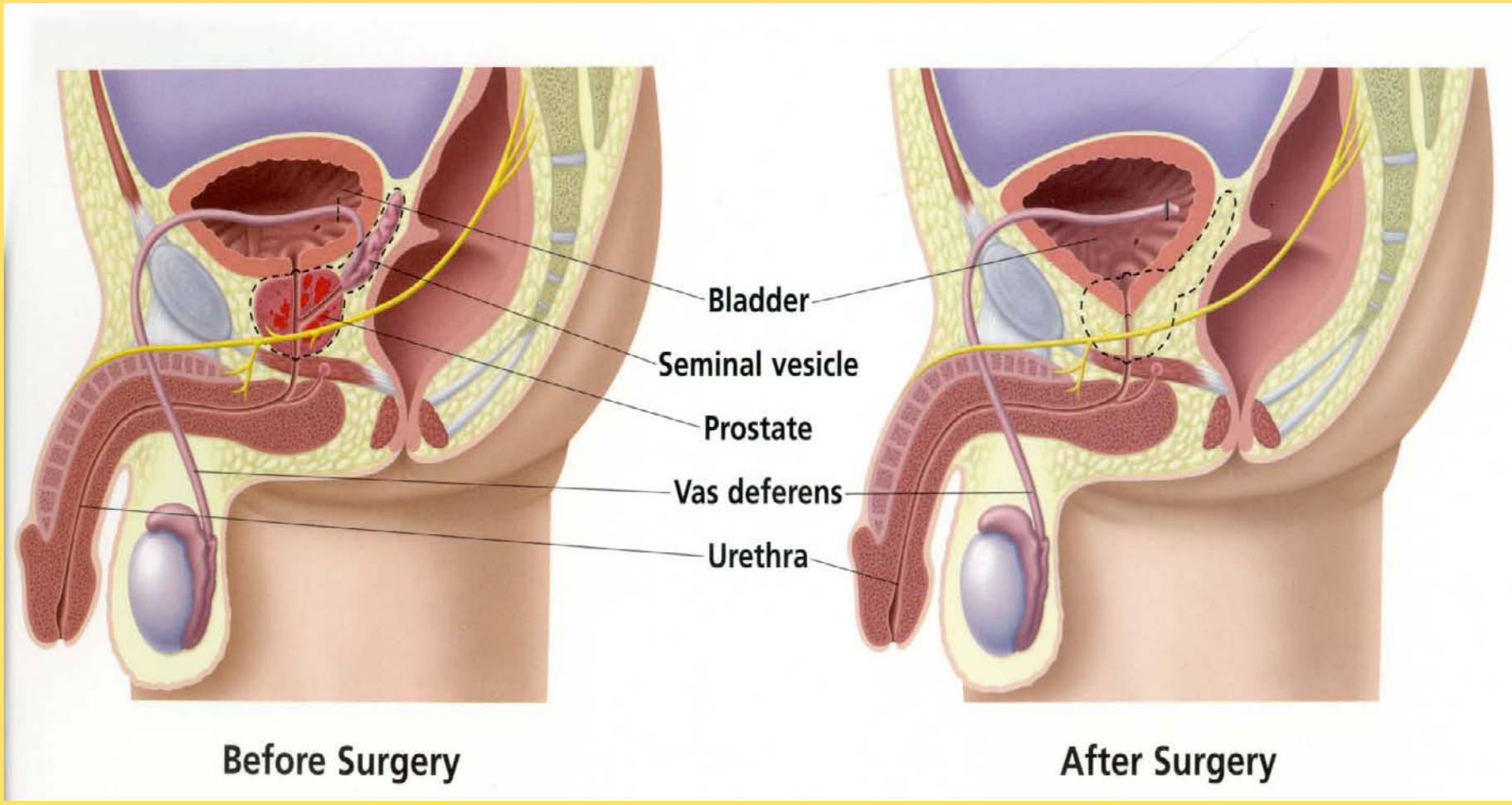
Early Stage Prostate Cancer Treatment

- Early stage Cancer
  1. Radical Prostatectomy
  2. External Beam Radiotherapy
  3. Radioactive Seeds (Brachytherapy)
  4. Active Surveillance
  5. Observation – Watchful Waiting

Prostate Cancer Treatment:
1. Radical Prostatectomy

- Radical Prostatectomy
  - Complete surgical removal of entire prostate, seminal vesicles
  - Considered a good treatment for men <70 years of age with clinically organ confined cancer who are healthy
  - Open or laparoscopic/robotic approaches

Prostate Cancer Treatment:
1. Radical Prostatectomy



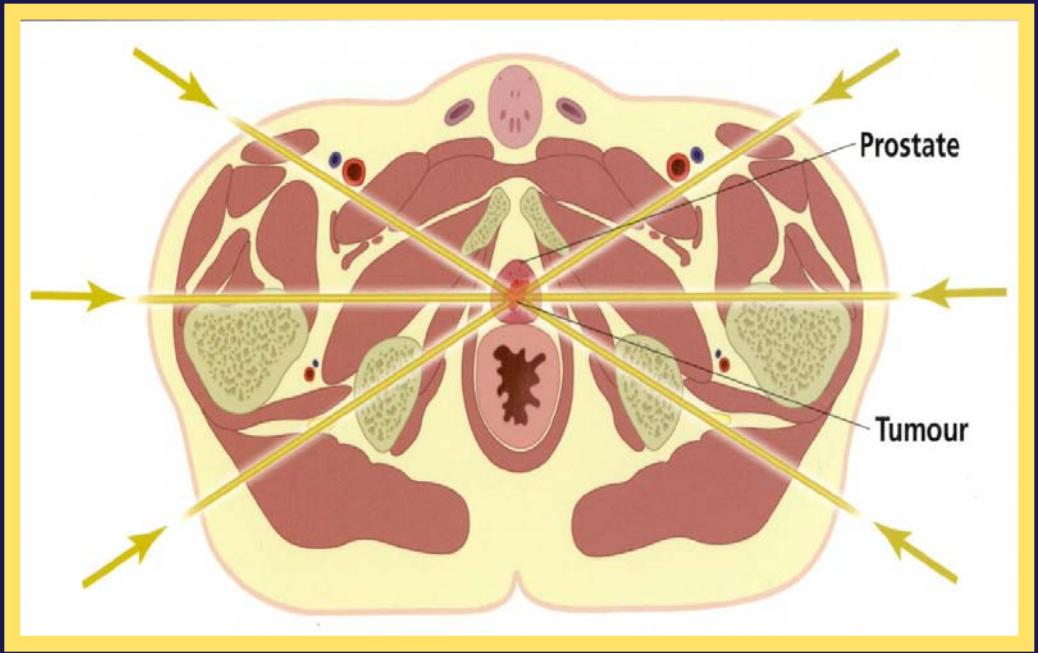
Complications of Radical Prostatectomy

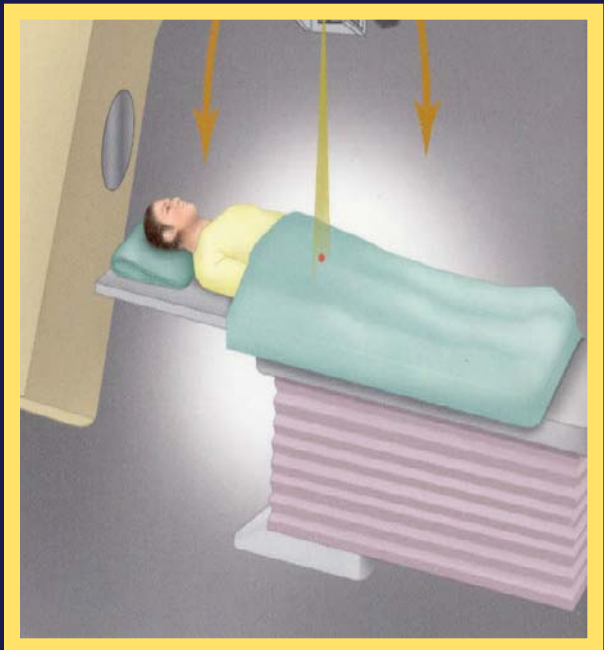
- <10% risk of blood transfusion
- Wound infection
- Rectal injury (<1%)
- Urinary incontinence (~10%)
- Erectile dysfunction (variable but common)
- Anesthetic related

Prostate Cancer Treatment: Radiotherapy

- Radiotherapy Options
  - External Beam
  - Brachytherapy (seed implant)
  - Concept of maximizing dose to the tumor and minimizing collateral damage
- Curative options for patients at high risk for morbidity from radical prostatectomy
  - Age, medical co-morbidities
  - Patient preference

Prostate Cancer Treatment:
2. External Beam Radiotherapy

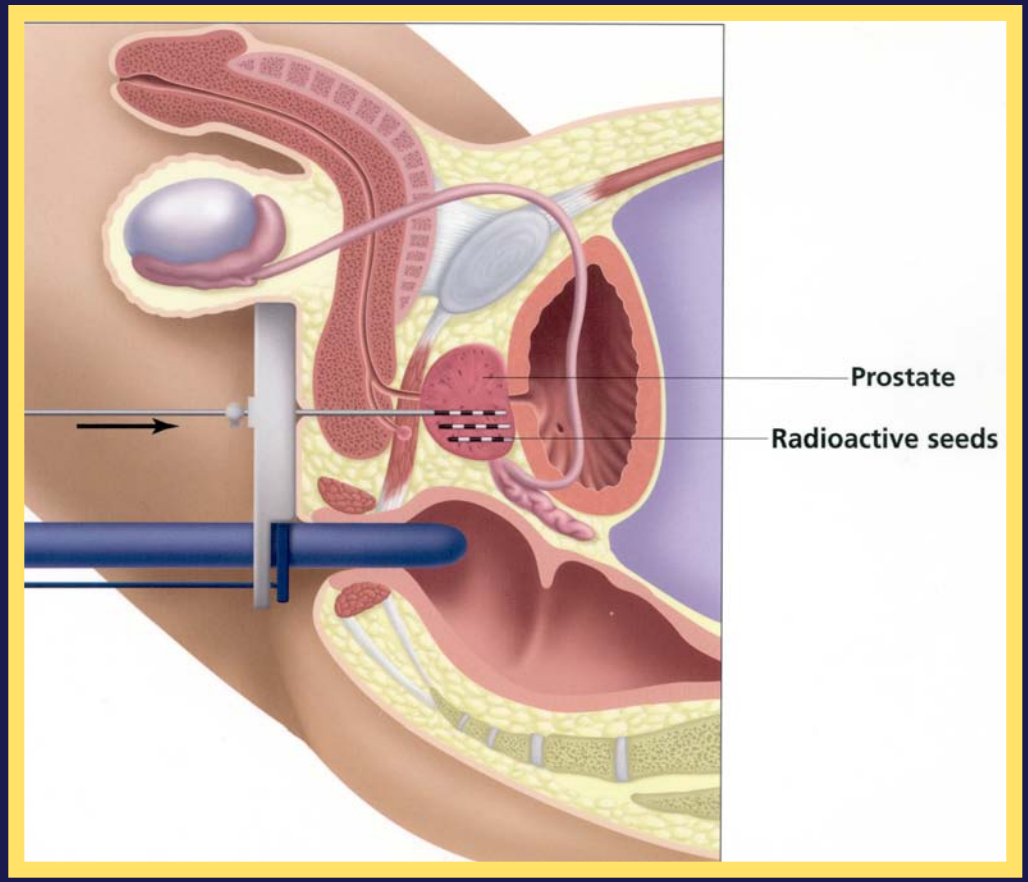




Complications of Radiation for Prostate Cancer

- External Beam Radiation Therapy
  - Hematuria
  - Radiation proctitis
    - Loose, bloody stools
  - Urinary retention
  - Strictures (urethra and ureter)
  - Erectile dysfunction
  - Secondary malignancies
    - Bladder, rectal, hematological

Prostate Cancer Treatment:
3. Brachytherapy



Complications of Brachytherapy for Prostate Cancer

- Urethral strictures
- Seed migration
- Urinary retention
- Erectile dysfunction
- Irritative voiding symptoms

Prostate Cancer Treatment:
4. Active Surveillance

- Observing low grade tumors in men <70 yrs and >10 yr life expectancy
- Delay definitive treatment until it is necessary and cancer is still curable
- Goal is to delay potential treatment-related morbidity
- Monitor DRE, PSA, and periodic repeat biopsy
- Ideal candidate:
  - PSA < 10
  - Normal DRE
  - Gleason <7 (low grade)
  - Only 1-3 / 12 biopsy cores positive

Prostate Cancer Treatment:
5. Watchful Waiting

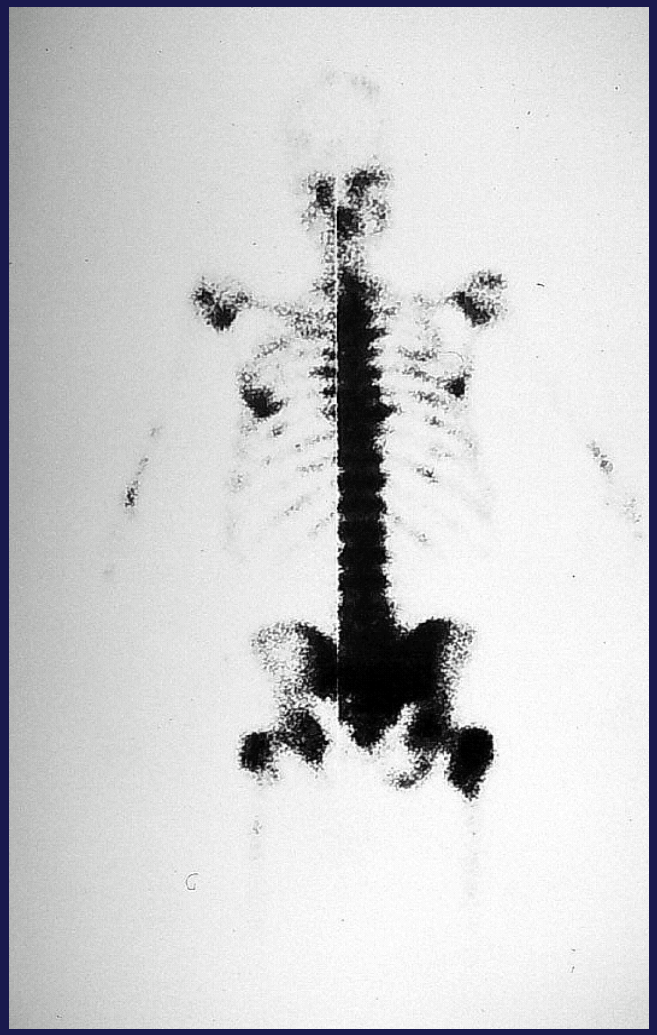
- Observing low grade tumors in men >70 yrs or <10 yrs life expectancy
- Institute hormonal therapy when patient becomes symptomatic
- No curative intent

Advanced or Metastatic Prostate Cancer

- Not curable disease
- Goals shift to disease control
- Development of cancer cells unresponsive to androgen deprivation
- Typically occurs slowly over time, although it can occur rapidly

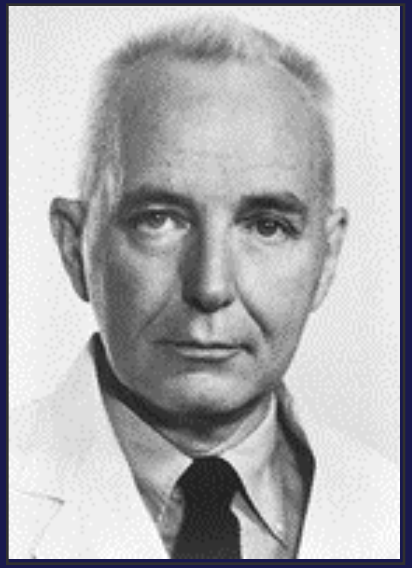
Advanced Prostate Cancer: Treatment

- Androgen Deprivation (Hormonal Rx)
  - Orchidectomy
  - LHRH analogues
  - Antiandrogens
- Supportive therapies
  - Analgesics
  - Steroids
  - Bisphosphonates/Vitamin D/Calcium for bone health
- Chemotherapy
  - Taxotere, Docetaxel
  - Last line of treatment

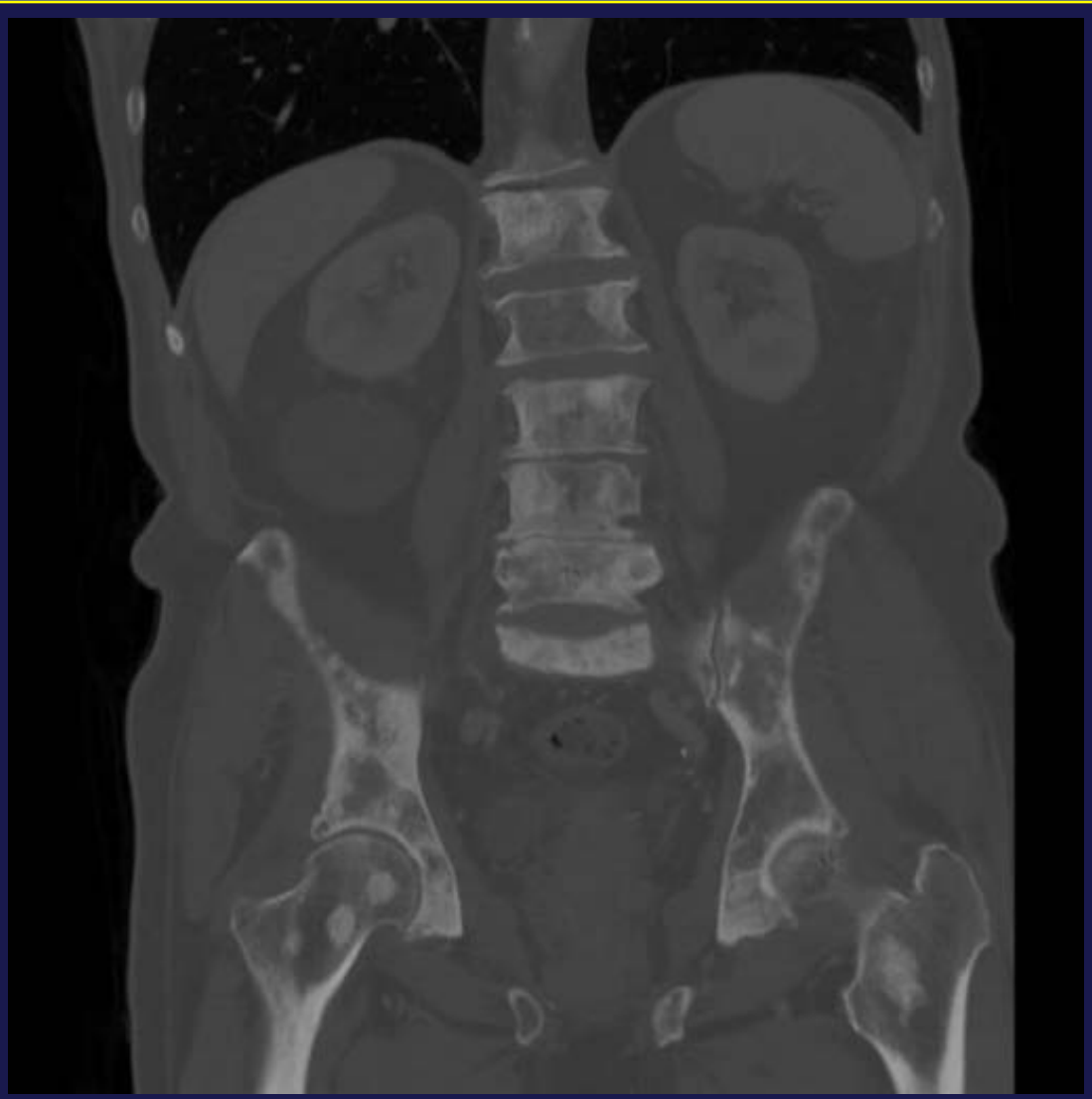


Charles Brenton Huggins (1901–1998)

- Only Canadian-born doctor ever to receive the Nobel Prize in Physiology or Medicine.
- Nobel Prize received in 1966.
- For his discoveries concerning hormonal treatment of prostatic cancer.
- Born in Halifax, Nova Scotia.
  B.A (Acadia)



Osteoblastic Bone Metastases



Spinal Cord Compression

- Metastatic prostate cancer is a common cause of spinal cord compression
  - Clinical recognition is critical
  - Signs and symptoms
    - Back pain
    - Neurological symptoms in saddle distribution
    - Lack of rectal tone, fecal and urinary incontinence
    - Paraplegia below the level of compression
    - MRI is diagnostic

Spinal Cord Compression

- Treatment
  - Emergency decompression laminectomy by spinal surgeons
  - Emergency radiation to affected level
  - Dexamethasone/steroids
  - Emergency bilateral orchidectomies if patient not already on androgen deprivation

Prostate Cancer Prognosis

- Depends upon grade, stage and treatment
- Early stage/well-differentiated Ca treated by radical prostatectomy:
  - 85% + 10 year survival
- Metastatic disease
  - <10% 5 year survival

Prostate Cancer Prevention

- Modifiable Factors
  - Diet
    - Saturated fats
    - Red Meat
    - BBQ meats
  - Lifestyle
    - Exercise
  - Drug therapy
    - 5 α reductase inhibitor
    - Vitamin D

Prostate Cancer Prevention

- Two major studies using 5 α reductase inhibitors vs placebo
- Similar reduction in prostate cancer diagnosis in the treatment arms (23-24%)
- Not currently approved by Health Canada for prostate cancer prevention
- PCPT (Thompson et al NEJM 2003)
  - Finasteride
- Reduce (Andriole et al NEJM 2010)
  - Dutasteride

Prostate Cancer Prevention

- Problems
  - Potential for the development of high risk prostate cancer
  - Expensive
  - Sexual/ejaculatory dysfunctions side effects may be occur and aren't always reversible
  - Long time to see the results of prevention
    - 10-20 years