Prostate Cancer: Imaging in Diagnosis and Treatment

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Introduction

• The prostate gland is a walnut-sized exocrine gland that surrounds the urethra between the bladder neck and the genitourinary membrane
• Its secretions primarily function in semen gelation, coagulation and liquefaction
  – Prostatic proteins are also involved in coating/uncoating the spermatozoa and in interactions with cervical mucus
• Disease processes range from benign (benign prostatic hyperplasia, BPH) to inflammatory (prostatitis) to malignant (prostate cancer)
Anatomic Relationships

Axial
- Symphysis pubis
- Obturator internus
- Urethra
- Transition zone
- Central zone
- Seminal vesicle
- Pubococcygeus
- Ischiococcygeal fossa

Sagittal
- Detrusor muscle of the bladder
- Symphysis pubis
- Anterior fibromuscular stroma
- Deep dorsal vein of the penis, draining to Santorini's plexus
- Corpus cavernosum
- Corpus spongiosus & bulbospongiosus
- Prostate
- Rectum
- Urethra
- Urogenital diaphragm
- Perineal body (central perineal tendon)

Coronal
- Vas deferens
- Seminal vesicle
- Prostate
- Opening of the ejaculatory duct at the verumontanum
- Obturator internus
- Levator ani
- Urogenital diaphragm
- Crus of corpus cavernosa & ischiocavernosa muscle

Prostate Anatomy

Lobar Anatomy

Prostate Cancer: Presentation

Prostate Cancer
- Detected Early
  - Elevated PSA
    - Prostate Cancer
    - False Positive
      - Acute
        - Biopsy
        - TURP
        - Acute Urinary Retention
        - Acute Prostatitis
        - Ejaculation
      - Chronic
        - BPH
        - Chronic Prostatitis
  - Abnormal DRE
    - Prostate Cancer
    - BPH
      - Extra-Prostatic Growth
    - Chronic Prostatitis
- Detected Late
  - Outflow Obstruction
    - Prostate Cancer
    - BPH
    - Bladder Disease
    - Urethral/Penile Disease
    - Malignant Extension
  - Metastatic Disease
    - Intrinsic Organ Pathology
    - Other Metastatic Disease
Prostate Cancer: Basics

• Prostate cancer is the most commonly diagnosed cancer in men (~200,000 cases/year)
  – Lifetime risk of developing prostate cancer: 16%
  – Risk of dying from prostate cancer: 3.4%
• It is the 2nd leading cause of cancer-related mortality among men (~40,000 deaths/year)
• In general, the malignancy is slow-growing, although the prognosis varies drastically according to stage
• PSA screening has undoubtedly detected more cancers, with a debatable survival benefit
• Risk factors include older age, black race (RR 1.5), family history (1st degree relative doubles risk)
• Radiology plays a vital role in diagnosis and treatment
Diagnosis

- Diagnosis is made by transrectal ultrasound (TRUS) guided prostate needle biopsy
- Classically the biopsies are performed using a sextant approach

http://www.marinurology.com/articles/cap/learning/trusp.htm
TNM Staging

- **T0**  No evidence of primary tumor
- **T1**  Clinically unapparent, not palpable or visible by imaging
  - T1a  Incidental histological finding in ≤ 5% of resected tissue
  - T1b  Incidental histological finding in > 5% of resected tissue
  - T1c  Identified by needle biopsy but not palpable or visible by imaging
- **T2**  Confined to prostate
  - T2a  Involves half a lobe or less
  - T2b  Involves more than half a lobe but not both lobes
  - T2c  Involves both lobes
- **T3**  Extends through the prostatic capsule
  - T3a  Extends unilaterally
  - T3b  Extends bilaterally
  - T3c  Invades seminal vesicles
- **T4**  Fixed or invades adjacent structures other than seminal vesicles
  - T4a  Invades bladder neck, external sphincter, or rectum
  - T4b  Invades levator muscles or is fixed to pelvic wall

Prognosis

- Patients can be risk-stratified into 3 groups based upon 1992 AJCC stage, PSA, and Gleason score

- **Low risk:** >85% 5-year PSA failure-free survival
  - Stage $T_{1c,2a}$ AND PSA $\leq 10$ ng/ml AND Gleason score $\leq 6$

- **Intermediate:** 50% 5-year PSA failure-free survival
  - Stage $T_{2b}$ OR $10 < \text{PSA} \leq 20$ ng/ml OR Gleason score 7

- **High risk:** ~33% 5-year PSA failure-free survival
  - Stage $T_{2c}$ OR PSA $> 20$ ng/ml OR Gleason score $\geq 8$

Workup for Prostate CA

• Following an abnormal PSA or DRE, the first step is transrectal ultrasound-guided biopsy
• Depending on risk-stratification, endorectal MRI is performed to evaluate extra-capsular spread
• A metastatic workup is required for patients at high-risk for metastasis: Gleason score > 7; PSA > 20; or clinical stage T3 or T4
• The result of these studies is critical to determining a treatment plan (i.e curative approach vs. palliative)
Transrectal Ultrasound (TRUS)

- Transrectal ultrasound is the imaging modality that has revolutionized prostate cancer diagnosis.
- TRUS utilizes a transrectal probe that operates at 5-7 MHz.
- TRUS allows the radiologist or urologist to:
  - Estimate the size of the prostate
  - Determine “estimated PSA” (.12 x volume)
  - Identify suspicious lesions
  - Image vascular flow
  - Biopsy the prostate
- Despite the rapidly improving technology, the sensitivity and positive predictive value of TRUS-directed biopsy remain low
  - A sextant biopsy technique has a sensitivity of 65%

TRUS: BPH, Patient 1

Hypertrophied central gland

Peripheral zone

Gland volume: 134 cc

Large central gland

Peripheral zone

Images courtesy Robert Kane, MD
TRUS: Prostate Cancer, Patient 2

TUR Defect

Hypoechoic nodule
Gland volume: 25 cc

Central gland

Hypoechoic nodule

Images courtesy Robert Kane, MD
TRUS: Prostate Cancer, Patient 3

Central gland

Peripheral zone

Hypoechoic nodule

Gland volume: 18 cc

Images courtesy Robert Kane, MD
85% of men with prostate cancers > 5mm have visibly increased flow on Doppler

In this healthy patient, the flow is symmetric and radial

The addition of a contrast agent (microbubbles) enhances the signal-to-noise ratio

This prostate cancer is clearly visible with contrast-enhanced color Doppler

Prostate MRI

- MRI of the prostate is the only imaging modality that can directly visualize the normal prostate substructure and cancers that arise therein.
- The optimal MRI technique uses a body excitation coil (at least 1.5 T), and a pelvic phased-array coil and endorectal coil for reception.
- The goal of imaging is tumor detection and staging:
  - Visualizing the capsule, neurovascular bundles, and seminal vesicles.
  - Staging accuracy is now 75-90%.
- The use of ERMR also allows for sophisticated applications:
  - MR spectroscopy.
  - MR-guided procedures (brachytherapy, biopsy).

Patient is a 61 yo man who p/w a PSA increase from 2.6 in 1993 to 9.5 in 2002. All biopsies were negative.

**MR Prostate: BPH, Patient 4**

- **Bladder**
- **Seminal vesicles**
- **Central gland**
- **Peripheral zone**
- **ER Coil in rectum**

BIDMC PACS
MR Prostate: BPH, Patient 4

- Seminal vesicles
- Peripheral zone
- Hypertrophied central gland (L>R)
- Corpus cavernosum
- Corpus spongiosum
- Corpus cavernosum
- Bladder
- Endorectal coil
- Peripheral zone
- Hypertrophied central gland (L>R)
Patient is a 61 yo man who p/w a PSA increase from 1.7 to 3.4. A palpable nodule was felt on DRE, and subsequent TRUS-guided biopsy revealed Gleason 4+3. He subsequently underwent a radical prostatectomy.

Central gland
Peripheral zone
Low-intensity signal in lateral left lobe, extending to capsule
Rectoprostatic angle preserved
Obdurator
Endorectal coil
Puborectalis
Axial

BIDMC PACS
The patient is a 69 yo man with long-standing Crohn’s whose PSA rose from 3.5 to 4.2 in 2002. A TRUS was performed. An MR was performed without ER coil.

Central gland
Calcifications
Hypoechoic nodule

Central gland
Peripheral zone
Hypointense region in right PZ
The patient is a 75 yo man with recurrent prostate cancer. He is currently on hormonal therapy. He recently presented to the BID with acute renal failure.
MR Spectroscopy

- Prostatic secretions contain 24-1300x more citrate than blood
  - Cancer cells are unable to produce this physiologic metabolite
  - In addition, both the density and metabolism of cancer cells lead to elevated concentrations of choline.
- Proton MR spectroscopy can evaluate these changing concentrations

- This image overlays the spatial signal intensity for citrate (normal tissue) with that choline (neoplasm)
- As this technology matures, it will provide a means of: localizing cancer, assessing ECE, measuring aggressiveness, and gauging treatment success

Prostate Metastasis

• Either advanced clinical stage or suspicion of recurrent disease (rising PSA or new symptoms) prompt a search for metastasis

• Work-up includes
  – **Plain films** of chest and bone
    • Cheap, can be used to detect bone or lung metastases
  – **Abdominal/pelvic CT (or MR)** to evaluate visceral metastases
  – **Bone scintigraphy** has a proven role in detecting bone metastases
    • In the initial work-up, it is most commonly used in intermediate to high-risk patients
    • It is always used in rising PSA following treatment
  – **Radioimmunoscntigraphy**
    • Currently in use (not at BID), but its merits are still under investigation
Metastatic Workup: Plain Films

- 85% of patients dying from prostate cancer have bone metastases
- 80% of bone metastases are osteoblastic
  - They have a tendency to diffusely infiltrate bone
- Plain radiographs are insensitive for picking up metastases, since the bone density must increase by 50% to be visualized

Metastatic Workup: Bone Scan

- Radionuclide bone scintigraphy is the most sensitive technique to detect bone metastases.
  - In one study that performed bone scans in asymptomatic patients with a PSA > 20 ng/ml, the sensitivity was 99%
  - This sensitivity comes at the cost of low specificity, as Paget’s disease, DJD and trauma can commonly produce false-positives

Metastatic Workup: CT

- The diagnostic use of CT is limited by its poor resolution of prostatic anatomy and capsule.
- It plays two key roles in prostate cancer:
  - Staging advanced cancer
  - Planning of external-beam radiotherapy

This is patient 5, whose MR was recently presented. This CT was part of his recurrent prostate CA workup.
Metastatic Workup: Radioimmunoscintigraphy

Radioimmunoscintigraphy consists of radiolabelled monoclonal antibodies to prostate antigen, using SPECT for acquisition

- The most studied antibody (trade name Prostascint) is to prostate specific membrane antigen (PSMA)

- Its use includes:
  
  • Evaluation of high-risk patients for nodal and visceral metastasis
    - Sensitivity 60%; Specificity 70%; PPV 60%; NPV 70%
  
  • Assessing recurrent disease in prostatic fossa
    - Sensitivity 49%; Specificity, 70%; PPV, 50%; NPV 70%
  
  • Assessing potential response to salvage radiotherapy
    - Preliminary reports suggest Prostascint stratifies responders

- Despite all of these data, its utility is hotly debated
  
  • Overall there are few studies of Prostascint
    - Of those studied, there are still strong detractors
  
  • Low signal-to-noise ratio (up to 40% are uninterpretable) makes interpretation difficult

Urology 2001. 57(3):399-401
Metastatic Workup: Prostascint

59 yo man with newly diagnosed prostate cancer

Mesenteric lymph nodes
(Positive biopsy)
Known prostate cancer

Supraclavicular lymph node
(Positive biopsy)
Suspicious punctate deposition
(Negative CT)

Treatment

- A treatment plan is dependent on the stage, overall health of the patient, and patient preference

- Localized disease
  - Watchful waiting
  - Radical prostatectomy
  - Radiation therapy
    - External beam radiation therapy (EBRT)
    - Brachytherapy

- Advanced disease
  - Hormonal therapy
  - Chemotherapy
External Beam Radiation Therapy

- External beam radiation therapy (EBRT) is an attractive option because it avoids surgery and has a lower rate of impotence and urinary incontinence.
- Long-term outcome in prostate cancer is similar to radical prostatectomy.
- Prior to the advent of CT, radiation fields were determined by contrast enhanced plain films.
- Classically, the superior border of the field was the L5-S1 interspace, and the inferior border was the inferior border of the ischial tuberosities.
3-D Conformal Beam Radiotherapy

- Conformal beam radiotherapy attempts to “conform” the radiation beam to the tumor in order to minimize exposure to healthy tissue.

This patient is a 61 yo man with a PSA 6. Cancer (Gleason 3+3) was detected by abnormal DRE.

**Step 1:** Create 3-D model from CT.
EBRT Continued

**Step 2:** Beams are created to treat planning target volume

*Images from BWH Radiation Oncology*
Brachytherapy

- Prostate brachytherapy is the placement of radioactive seeds into the prostate
- It is most effective in low-risk cancers, and the 5 year survival of this group is equal with RP and EBRT
- Typically, ~100 seeds containing I-125 or Pd-103 are permanently implanted into the prostate
- The seeds are usually implanted under real-time TRUS guidance
- Dosimetry is performed 1-30 days after the procedure, usually by CT
  - Newer systems allow real-time dosimetry

Algorithm courtesy Rob Cormack, Ph.D.
TRUS-Guided Brachytherapy

3-D Dosimetry

Planning Grid

http://www.emedicine.com/med/topic3147.htm
MR-Guided Brachytherapy

- BWH has pioneered the use of MR-guided brachytherapy, which takes advantage of its superior resolution
- Seed placement and dosimetry are essentially monitored in real time, optimizing dose distribution

The patient is a 65 yo man with T1c prostate cancer.

Images courtesy Rob Cormack, Ph.D.
MR Brachytherapy Continued

Planned isobars

3-D reconstruction

Images courtesy Rob Cormack, Ph.D.
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38
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