Imaging Prostate Cancer: Diagnosis, Staging, and Radiotherapy

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July 2006
Overview

- **Prostate – Function and Anatomy**
- **Prostate Cancer – Role of Imaging**
  - Epidemiology and Presentation
  - Diagnosis: Transrectal U/S biopsy
  - Staging: Endorectal coil MRI +/- bone scan, CT
- **Radiotherapy – Reliance on Imaging**
  - Evolution: Conventional to 3D to 4D
  - External Beam RT
    - 3D Conformal RT Imaging using CT
    - MR Spectroscopy and Intensity-Modulated RT
    - 4D Image-guided RT with Electronic Portal Imaging
  - Brachytherapy
    - TRUS vs MR guidance
    - Post-implantation CT
Review

Prostate is a 4 x 3 x 2cm exocrine gland encircling the urethra between the bladder and urogenital diaphragm.

- Principal function = produce proteins that form the bulk of seminal fluid.

- At ejaculation, prostate and seminal vesicle secretions turn into a gel-like structure entrapping the spermatozoa. The ejaculated spermatozoa become progressively motile as the gel dissolves.

- Secretory function is mediated by cholinergic innervation (pelvic and hypogastric nerves); contractile function is mediated by alpha-adrenergic receptors of the fibromuscular stroma.

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http://www.malecare.com/services1.htm
http://www.mansgland.com
The prostate is surrounded by a 2-3mm capsule.
Zonal Anatomy

Prostate territories are now described in terms of zones instead of lobes

- Transition Zone = surrounds prostatic urethra
- Central Zone = posterior to urethra, located superiorly
- Peripheral Zone = mostly posterior to urethra, located inferiorly and laterally

“Central Gland”


Depending on the level, an axial slice may include bladder, prostate, and rectum, or just prostate and rectum.
Anatomy, cont’d.

The urogenital diaphragm marks the inferior border to the prostate

Anatomy, cont’d.

The ‘pelvic nodes’

These are the route of spread for nodal metastases.
Prostate Adenocarcinoma

- **Most common cancer in American men** except non-melanoma skin cancer
- American male **lifetime risk of prostate CA = 1 in 6** (lifetime risk of death from prostate CA = 3%)
- Second leading cause of cancer death in America
- 2006 estimate: ~ 235,000 men will be diagnosed, ~ 27,000 men will die
- Risk factors: age (>45), black race (RR = 1.5), brother/father with prostate CA (RR = 2)

- Most common presentation = **asymptomatic, with elevated serum PSA**
- Also presents early as asymmetry/induration on DRE
- Later presentation = urinary urgency, frequency, nocturia, hesitancy, ED, hematuria

Incidence of prostate CA has increased partly due to prevalent PSA screening, but incidence was increasing before introduction of PSA testing. Earlier CA detection has unclear mortality benefit.

Usual criteria for an **abnormal PSA**:
- an **absolute level of 4.0 ng/ml or greater**
- OR
- a **PSA velocity** (PSA increase) **of 0.75 ng/ml or greater over a 1 year period**

Prostate cancer is a tissue-based diagnosis.

**Imaging is used for:**
- guiding the tissue biopsy
- staging the cancer
- planning treatment

Transrectal Ultrasound (TRUS)

- TRUS imaging allows visualization of gland size, seminal vesicles, lesions, vasculature
- Prostate biopsy is the gold standard for cancer diagnosis and is done using TRUS

- TRUS-based measurement of **gland volume** = length $\times$ width $\times$ height $\times$ 0.52
- Knowing gland volume allows calculation of the following 2 related values, which help predict risk of malignancy in some studies:
  - **PSA density** = $\frac{\text{PSA}}{\text{TRUS gland volume}}$
  - **Predicted PSA** = TRUS gland volume $\times$ 0.12 ng/mL/mL

- Sensitivity of TRUS-guided biopsy depends on number of cores:
  - Traditional sextant biopsy (6 cores): **sensitivity ~80%**
  - Routine sextant biopsy plus lateral biopsies at base and mid-gland (10 cores): **sensitivity ~96%**

References:
TRUS Technique

**Technique:**
1. DRE
2. Gland volume (length x width x height x 0.52)
3. Axial scanning (base to apex)
4. Sagittal scanning (right to left)
5. Vascular imaging
6. Biopsy

**Biopsy:** Usually no sedation or analgesia is given; local anesthesia is injected or applied topically within the rectum.

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TRUS, cont’d.

Cancer location by zone:
- Peripheral Zone (PZ) = 70%
- Transitional Zone (TZ) = 20%
- Central Zone (CZ) = 10%

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http://www.acuson.com/transducers/catalog/w_cat_r12_10-1-04/xdcr_son_acus%20_r12_10-1-04/son/adara_spec/endo-pit_adara.htm
TNM Clinical Staging

T1 = Microscopic tumor, cannot palpate or visualize on TRUS
T2 = Palpable, appears confined to gland
T3 = Protrudes beyond capsule OR into the seminal vesicle
T4 = Fixed tumor, and has extended well beyond prostate

2002 AJCC Staging System†

<table>
<thead>
<tr>
<th>Substage</th>
<th>Description</th>
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<tr>
<td>T1a</td>
<td>Tumor incident histologic finding in five percent or less of tissue resected</td>
</tr>
<tr>
<td>T1b</td>
<td>Tumor incident histologic finding in more than five percent of tissue resected</td>
</tr>
<tr>
<td>T1c</td>
<td>Tumor identified by needle biopsy (e.g., because of elevated PSA)</td>
</tr>
<tr>
<td>T2a</td>
<td>Tumor involves one-half of one lobe or less</td>
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<tr>
<td>T2b</td>
<td>Tumor involves more than one-half of one lobe but not both lobes</td>
</tr>
<tr>
<td>T2c</td>
<td>Tumor involving both lobes</td>
</tr>
<tr>
<td>T3a</td>
<td>Extracapsular extension (unilateral or bilateral)</td>
</tr>
<tr>
<td>T3b</td>
<td>Tumor invades the seminal vesicle(s)</td>
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Stage Grouping for Prostate Cancer, 2002 AJCC Criteria†

<table>
<thead>
<tr>
<th>Stage</th>
<th>T</th>
<th>N</th>
<th>M</th>
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<td>M0</td>
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<td>M0</td>
<td>Any 0</td>
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<td>Any 0</td>
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</table>

*Used with the permission of the American Joint Committee on Cancer (AJCC), Chicago, Illinois. The original source for the material is the AJCC Cancer Staging Manual, Sixth Edition (2002) published by Springer-Verlag New York, Inc.

※G: Tumor grade is assessed as follows:
G1: Well differentiated (slight anaplasia), Gleason 2-4
G2: Moderately differentiated (moderate anaplasia) Gleason 5-6
G3-4: Poorly differentiated (undifferentiated, marked anaplasia) Gleason 7-10
Gleason Grade

Based on degree of glandular differentiation and structural architecture
Provides some index of prognosis and may guide therapy
2 scores are reported: the 2 most prevalent patterns observed
Scores range 1-5. Most differentiated = 1, Least differentiated = 5.
Gleason grades thus range from 2 (low-grade) to 10 (high grade)
  e.g. “Gleason 3+5=8” means the most common histologic pattern observed had a score of 3, and the second most common pattern had a score of 5. Overall Gleason grade of 8.

Patient A

67M with slowly rising PSA over many years up to 7.9, asymptomatic. Imaged with TRUS, diagnosed with BPH, and underwent biopsy. No malignancy was identified.

Central gland has heterogeneous echogenicity in BPH

Gland volume = 102cc
Predicted PSA = 12

Peripheral zone

Enlarged central gland

Peripheral zone
Patient B

56M with abnormal DRE. PSA rose from 3.5 to 5.2 over 3.5 years.

TRUS biopsy was performed, and pathology showed 5 of 6 cores had adenocarcinoma, Gleason 3+3=6, with perineural invasion.
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Patient C

58M with PSA of 12.4, his first PSA test. Asymptomatic.

TRUS revealed significant central gland enlargement. Also seen is a vague hypoechoic region in the left peripheral zone. Doppler revealed this region to be relatively avascular, less concerning for malignancy.

On biopsy 4 months later, 1 of 13 cores showed adenocarcinoma in 10% of the core, Gleason 3+3=6.

Adding Doppler to TRUS can increase specificity and PPV for carcinoma, but generally does not improve sensitivity.

Shigeno K et al. The Role of Colour Doppler Ultrasonography in Detecting Prostate Cancer. BJU Int. 2000 Aug;86(3):229-33.
Risk Stratification and Imaging

- Risk of ‘biochemical failure’ (rising PSA) after treatment:
  - Low risk: T1c/T2a and PSA ≤ 10 and Gleason ≤ 6
  - Intermediate Risk: T2b or PSA >10, ≤ 20 or Gleason 7
  - High Risk: T2c or PSA >20 or Gleason ≥ 8

PSA
Clinical Stage
TRUS-guided biopsy
Gleason grade

Low risk  ----------------> ?

Intermediate risk  ---------> erMRI

High risk  -------------> erMRI
Radionuclide bone scan
CT Abd/Pelvis

Endorectal Coil MRI (erMRI)

- erMRI utilizes an endorectal coil in addition to a pelvic phased-array coil for highest image resolution
- Best imaging modality to visualize the anatomy of the prostate
- Used to stage prostate cancer, primarily by examining for extracapsular spread of the mass and seminal vesicle involvement
- Staging accuracy for high field strength (1.5T) MR imaging is ~ 85%

Normal Anatomy – T2-weighted erMRI

Metastatic Imaging for High Risk Patients

CT Abdomen/Pelvis

72M with prostate CA and left retroperitoneal adenopathy

Tc-99m diphosphonate bone scan

60 year old patient who presented with gross hematuria. Workup included MR urogram (no endorectal coil), which revealed an enlarged and grossly abnormal prostate gland.

Gland volume = 110cc
Dimensions = 5.8 x 5.8 x 6.3cm
Patient D, cont’d.

Concern for posterior bladder wall involvement

Bladder
Endorectal coil
Seminal vesicles

Central gland
Peripheral zone
Left peripheral zone enlarged, asymmetric
Concern for extracapsular extension (ECE) from left peripheral zone

Probable bladder wall involvement
Patient D, cont’d.

- Bladder
- Prostate mass along bladder wall
- Endorectal coil

Sagittal
Patient D, cont’d.

- Previous slide: ?? = tampon
- 60 y.o. male-to-female transsexual
  - Began Premarin (estrogen) at age 19
  - Gender re-assignment surgery at age 34
  - Stopped Premarin between ages 36 and 57 due to disclosure issues
  - Married at age 41
- Asian ethnic background, no family history of prostate CA
- No prior PSA screening

- Presented with intermittent gross hematuria and UTIs over past 2 yrs
- Workup: PSA = 252, prostate volume 110cc, Gleason 4+4=8 on b/l cores, bone scan and CT chest/abd/pelvis negative for mets
- Staging MRI revealed likely extracapsular extension in region of left peripheral zone, and apparent posterior bladder wall invasion

- Began Avodart (5-alpha reductase inhibitor) and Casodex (androgen receptor blocker) prior to External Beam Radiation Therapy

We will return later to Patient D...
Treatment Options for Localized Prostate Cancer

- Radical Prostatectomy
- Radiotherapy (RT)
  - External Beam RT
  - Brachytherapy
- + / – Androgen Deprivation Therapy
- Observation

Choice of therapy depends on patient’s medical condition/comorbidities, age, Gleason score, PSA, clinical stage, treatment-related side effects, and patient preference.
Goal: Maximize dose of ionizing radiation to the tumor and minimize dose received by surrounding normal tissue.

For prostate cancer, aim is to minimize dose received by the bladder, rectum, urinary sphincters, and neurovascular bundles.

Accurate dosing is highly dependent on imaging.

http://www.ucsf.edu/jpouliot/Course/Lesson12.htm
External Beam Radiation Therapy (EBRT)

Conventional EBRT relied on plain films with contrast enhancement to visualize the bladder and rectum, with limited ability to define anatomy.

Surrounding structures received relatively high amounts of radiation, since imaging technology did not exist to allow more precise targeting.

Example:

<table>
<thead>
<tr>
<th>Field</th>
<th>Radiation</th>
<th>Example</th>
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<tbody>
<tr>
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<td>45 rads</td>
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</tr>
<tr>
<td>3 Field</td>
<td>30 rads</td>
<td><img src="image2.png" alt="Image 2" /></td>
</tr>
</tbody>
</table>

Prostate and surrounding structures all receive 90 rads.

Adding 1 more view/field:

- Prostate receives 90 rads, but surrounding structures receive closer to 60 rads.


http://lagrange.math.trinity.edu/tumath/research/reports/report86.pdf
3D Conformal RT

3D CRT utilizes CT reconstruction to depict accurate organ/tissue volumes.

Then beams from multiple angles plus lead ‘blocks’ or collimators allow radiation doses that conform to the edges of the prostate.

http://www.ecu.edu/ecuphysicians/radiation_ oncology/IMRT.htm

http://www.prostate-cancer-radiotherapy.org.uk/standard_ebrt.htm
Positioning for Imaging and Treatment

Body molds/casts
for reproducible body positioning
during imaging, simulation, and therapy

Example of a linear accelerator (linac)
3D CRT, cont’d.

Rectum-sparing with conformal RT

Dose-Volume Histogram (DVH)


http://www.prostate-cancer-radiotherapy.org.uk/standard_ebrt.htm
Intensity-Modulated Radiation Therapy (IMRT)

- Instead of beams of a single intensity, IMRT uses collimators that are dynamically adjusted during the exposure time, in effect creating beams of varying ‘intensities’
- Surrounding structures are thus spared even further from ionizing radiation, and regions of interest within the prostate can be more precisely targeted

[Diagram of prostate and rectum showing IMRT beams]

http://www.prostate-cancer-radiotherapy.org.uk/standard_ebrt.htm
Magnetic Resonance Spectroscopy Imaging (MRSI)

MRSI can identify characteristic peaks that correspond to various prostate metabolites.

Normal prostate secretions have high citrate concentrations, while malignant cells do not produce citrate.

Regions containing carcinoma will typically have reduced citrate and elevated choline.

MRSI with IMRT in theory can allow a region of malignancy within the prostate to be specifically targeted.

Electronic Portal Imaging Devices (EPID)

Portal imaging is done with the patient in position for therapy, to assess the exact position of the prostate within 2mm and display images of the treatment fields.

**Organ movement** from day to day can be considerable, and organ size/location may change in response to therapy, weight changes, etc. Displacement of the prostate’s center of as little as 3-8mm can result in dose reductions to the prostate of up to 10%, and dose increases to the rectum of up to 12%.

Thus EPID now allows for ‘4D’ radiation therapy, accounting for the variable of time (daily organ movement). Also referred to as image-guided radiation therapy (IGRT).

Real-time 3D imaging of 3 implanted markers

 Megavoltage cone-beam CT (MV CBCT) for imaging during therapy sessions

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Brachytherapy

- Used in capsule-confined prostate cancer, increasing in use
- Transperineal approach under general anesthesia
  - Low dose rate (LDR) = Permanent I-125 or Pd-103 seeds
  - High dose rate (HDR) = Temporary Ir-192 sources
- TRUS-guided needles are introduced, dosimetry is calculated, seeds are placed
- Post-implant CT imaging to re-calculate/refine dosimetry

http://www.prostatecancercentre.co.uk/treatments/brachy.html

No text content available.
Interventional MRI: Brachytherapy

- Brachytherapy seeds are now being placed using eMR-guidance rather than TRUS.
- Advantages include real-time imaging for more accurate seed position and dosimetry.

Patient D: Followup

Before treatment

- Gland volume = 110cc
- PSA = 252

s/p 8 weeks of External Beam RT + 8 months ADT

- Gland volume = 36cc
- PSA = <1

Obliterated zonal anatomy

Periprostatic fibrosis
Acknowledgments

- Jeff Velez, MD
- Mara Barth, MD
- Neil Rofsky, MD
- Gillian Lieberman, MD
- Daphne Haas-Kogan, MD
- Pamela Lepkowski
- Larry Barbaras

References

References, cont’d.

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