Introduction

- Prostate cancer is most frequently diagnosed non-cutaneous cancer in males (25%)
- Second leading cause of cancer related deaths
- 1 in 6 males will develop prostate cancer during their lifetime
- Prevalence increases with age, up to 70% of men >80 have prostate cancer
The Good News . . .

- 5-year survival – 99%
- 10-year survival – 93%
- 15-year survival – 79%
- As the saying goes – most men with prostate cancer die with the disease not from the disease

Screening

- Currently, prostate cancer screening is primarily:
  - Assessment of prostate-specific antigen (PSA) elevation
  - Digital rectal examination (DRE)
- These are supplemented by:
  - Transrectal US
  - US-guided biopsy
  - Prostate MRI
- Both PSA and DRE have suboptimal accuracy for the diagnosis of prostate cancer
Digital Rectal Exam

- DRE – important because
  - Low cost
  - Ubiquitous availability
  - Identifies tumor in 14% of men who have cancer
  - Builds strong doctor/patient relationship

- DRE – disadvantages
  - High interexaminer variability
  - Limited to assessment of posterior peripheral zone tumors

Prostate-Specific Antigen

- Normal < 4 ng/mL
- In patients with PSA of 4-10 ng/mL, 70-80% have benign causes (BPH, prostatitis)
- 15-44% of biopsy-proven cancers occur in patients with normal PSA levels
- Many measures:
  - PSA doubling time/velocity (>0.75 ng/mL/y biopsy)
  - Free PSA/Total PSA ratio (>18% benign, <10% biopsy)
  - PSA Density (Total PSA/prostate volume) > 0.15 biopsy

Transrectal US

- Not recommended for initial screening
- Used to provide prostate volume and visual guidance for biopsy
- 15.2% PPV in detection of prostate cancer (vs. 28% for DRE)
- Only 30-40% of prostate cancers can be visualized with transrectal US in the absence of palpable findings
Transrectal US-guided Prostate Biopsy
- 1.3 million performed annually
- Many approaches – sextant, octant, 5-16 region, saturation (40-80 cores)
- Apical, lateral, and anterior cancers are not well evaluated. Transperineal approach improves access but is seldom used – this is attributed to men not liking needles stabbed in their perineum??
- Cancer is missed in up to 10-38% of men with prostate cancer
- Cancer detection rates: 34%, 25%, 24%, 21% for first, second, third, and fourth biopsies

Transrectal US-guided Prostate Biopsy
- Apical cancers not well evaluated. Higher sensitivity reported for MRI. Wefer AE, J Urol, 2009

Staging
- Most important predictors of prognosis:
  - Gleason score
  - Clinical stage at the time of diagnosis
Staging

- The clinical stage is the best estimate of the extent of disease, based on the results of the physical exam including DRE, lab tests, prostate biopsy, any imaging tests

- With clinical staging, prostate cancer stage is underestimated in 30-60% of cases – may cause unnecessary surgery

- Most important aspect of local staging is organ-confined disease vs. extracapsular extension (T2 vs. T3)

Tumor Staging

- TX: cannot evaluate the primary tumor
- T0: no evidence of tumor
- T1: tumor present, but not detectable clinically or with imaging
  - T1a: tumor was incidentally found in less than 5% of prostate tissue resected (for other reasons)
  - T1b: tumor was incidentally found in greater than 5% of prostate tissue resected
  - T1c: tumor was found in a needle biopsy performed due to an elevated serum PSA
- T2: the tumor can be felt (palpated) on examination, but has not spread outside the prostate
  - T2a: tumor is in half or less than half of one of the prostate gland's two lobes
  - T2b: tumor is in more than half of one lobe, but not both
  - T2c: tumor is in both lobes
- T3: the tumor has spread through the prostate capsule; if it is only part way through, it is still T2
  - T3a: the tumor has spread to one or both seminal vesicles
  - T3b: the tumor has invaded other nearby structures
- T4: the tumor has invaded other nearby structures

It should be stressed that the designation "T2c" implies a tumor which is palpable in both lobes of the prostate. Tumors which are found to be bilateral on biopsy, but which are not palpable clinically should not be staged as T2c.
Gleason system of histologic prostate cancer staging

- Tumors assigned a primary grade based on predominant pattern of tissue differentiation and a secondary grade based on second most common pattern of tissue differentiation. These are added to get the Gleason score.
- The biologic behavior of a Gleason score 7 (4+3) would be more aggressive than a 7 (3+4).
- In the U.S. the lowest score considered cancer is 6, which is well differentiated.

Gleason Grading System
Anatomy

- The prostate gland is situated directly under the bladder and envelops the prostatic urethra.
- The prostate is divided into apex and base. The latter is directed upward and is applied to the inferior surface of the bladder. The apex is directed downward and is in contact with the superior fascia of the urogenital diaphragm.
- Anteriorly, the prostate is directed to the pubic bone and is covered by a thick layer of fibromuscular stroma.

Anatomy

- Anterior fibromuscular stroma (no glandular tissue)
- Transition zone (5% of glandular tissue, blue)
- Central zone (20% of glandular tissue, yellow)
- Peripheral zone (75% of glandular tissue, pink)

Anatomy

- Volume of peripheral zone increases from base to apex
- Transition zone increases in size with age
- 95% of prostate cancers arise from glandular tissue (adenocarcinomas)
- 70% of prostate cancers originate in the peripheral zone
- On imaging the central zone and transition zone cannot be distinguished and are often referred to as the central gland
- No true prostate capsule – outer layer of fibromuscular tissue (conveniently called the “CAPSULE”)
Anatomy

- Neurovascular bundles (NVB) course posteriorly at 5 and 7 o’clock. At base and apex – penetrating branches extend through the capsule.
- Contain inferior hypogastric plexus or pelvic plexus which control erection, ejaculation, urinary continence.
- The NVB is in close, cage-like contact with seminal vesicles and prostate.

Prostate MRI

- Primary sequence is T2. Peripheral zone is heterogeneously hyperintense on T2 and central gland is variable.
- Discrete dark margin of the junction of the central gland and the peripheral zone.
- Well circumscribed hyperplastic nodules of BPH are commonly seen.
- T1 is of limited value in prostate cancer evaluation, used for postbiopsy hemorrhage, prostate contour evaluation, and precontrast baseline.

Prostate MRI

- Prostate Cancer
  - Most often T2 hypointense
  - Most often in peripheral zone
  - Limited sensitivity because
    - Some tumors are isointense
    - Other conditions are also low on T2 (hemorrhage, prostatitis, scarring, atrophy, radiation changes, cryosurgery, hormonal therapy)
    - Difficult to see tumors arising from transition zone.
Prostate Cancer

- Asymmetry of the neurovascular bundle
- Tumor encasement of neurovascular bundle
- Bulging prostatic contour
- Irregular or spiculated margin
- Obliteration of the rectoprostatic angle
- Capsular retraction
- Tumor-capsule interface of > 1 cm
- Direct tumor extension through capsule

Prostate MRI

- Criteria for extracapsular extension
  - Asymmetry of the neurovascular bundle
  - Tumor encasement of neurovascular bundle
  - Bulging prostatic contour
  - Irregular or spiculated margin
  - Obliteration of the rectoprostatic angle
  - Capsular retraction
  - Tumor-capsule interface of > 1 cm
  - Direct tumor extension through capsule

- Seminal Vesicle invasion
  - Low signal intensity within and along the seminal vesicle
  - Enlarged low signal intensity ejaculatory ducts
  - Obliteration of the angle between the prostate and the seminal vesicle
  - Demonstration of direct tumor extension from base of prostate
Prostate MRI
- Functional MRI
  - Diffusion-weighted imaging
  - Dynamic-contrast enhancement
  - Spectroscopy

Limitations / Challenges
- Low sensitivity
- False positives can occur with inclusion of signal from seminal vesicle, BPH, prostatitis, and prostatic atrophy
- May require 3T for adequate spectral resolution
- Complex postprocessing
- Adequate saturation band placement is needed
- Optimal shimming must be performed (time consuming)
- Hemorrhage can degrade spectra

MR Spectroscopy
- Prostate cancer has reduced water diffusion resulting from increased cellularity and reduction of fluid in the extracellular space. This restricts the motion of a larger portion of water molecules to the intracellular space.
- Decreased apparent diffusion coefficient (ADC) is decreased diffusion. Malignant lesions have about 20-40% lower ADC values than benign prostatic tissue.
Diffusion-weighted Imaging

- Tumor foci:
  - Bright on DWI
  - Dark on ADC map
- Greater tumor conspicuity on ADC map than on DWI
- Discrete, round foci of low ADC in peripheral zone is reasonably specific for tumor

ADC Mapping of DWI

- Limitations
  - BPH exhibits lower ADC and low T2 signal, mimicking prostate cancer
  - Prone to susceptibility artifact (air in endorectal coil balloon)
- Advantages
  - Increases specificity (58-100%) and sensitivity (54-98%) of prostate cancer detection over T2 alone
  - Short acquisition time
  - High contrast resolution between tumors and normal tissues
Dynamic Contrast-Enhanced MRI

- In prostate cancer, increased tumor vascularity leads to early hyperenhancement and rapid washout of contrast material.
- Onset time and time to peak are lower and peak enhancement is higher.
- Parameters can be converted into pseudocolor parametric maps and overlaid on the anatomic T1 and T2 images.

Dynamic Contrast-Enhanced MRI

- Use of DCE MR allows for detection of prostate cancer in 46% of patients with prior negative transrectal US-guided biopsy compared to 24% for repeat biopsy.
- May increase sensitivity in post biopsy hemorrhage situations.

Dynamic Contrast-Enhanced MRI

- Challenges
  - Does not allow differentiation of prostatitis from cancer
  - Poor differentiation between BPH and cancer in transition zone
  - Low grade cancer has less neovascularity and therefore increased false negative results
  - Small tumors are affected by partial volume affects and are difficult to detect
Multiparametric approach

• Comparison of 3 protocols in 83 patients:

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<th>Protocol</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Accuracy</th>
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<tr>
<td>T2W</td>
<td>73%</td>
<td>54%</td>
<td>64%</td>
</tr>
<tr>
<td>T2W+DWI</td>
<td>84%</td>
<td>65%</td>
<td>84%</td>
</tr>
<tr>
<td>T2W+DWI+DCE</td>
<td>95%</td>
<td>74%</td>
<td>86%</td>
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</tbody>
</table>

• Tanimoto, A, JMRI, 2007

Multiparametric approach

Study of tumor detection using various combinations of T2, DWI, DCE, and spectroscopy:

Conclusion: The combination of two functional parameters is associated with significant improvement in prostate cancer detection over use of any parameter alone. Use of a third parameter does not significantly increase the rate of detection.

Tumor Visibility

- Well recognized that not all tumor foci will be visible on MRI.
- It is expected that some patients with low-grade/low-volume disease will have no visible tumor.
- Tumor more likely to be visible when:
  - Larger volume
  - Higher Gleason score
  - More dense histologic architecture
- In general, expect that a tumor with more aggressive features is more likely to be visible on MRI
  - Turkbey et al., Radiology, 2010
  - Langer et al., Radiology, 2008

Indications

- Staging
- Evaluate for recurrence
- Rising PSA with negative biopsy
- Pre-surgical planning
- Tumor description:
  - Location: anterior and apical
  - Size and extent
  - Extracapsular extension
  - Seminal vesicle involvement
  - NVB involvement
- Planning for IMRT
Recurrence

- Patient with elevated PSA 4 years after radical prostatectomy

Recurrence

- 65 yo with elevated PSA one year after prostatectomy

Staging
Elevated PSA, 2 negative biopsies

Elevated PSA, - Bx

Prostate MRI

Questions?
Prostate MRI

Thank you