PROSTATE ULTRASOUND:
Detection of Tumor & Biopsy

Ewa Kuligowska, M.D.
PROSTATE CANCER

• Prostate cancer continues to be the most common lethal malignancy in American men
• is the second leading cause of cancer-related death in the male population over the age of 80 in the United States.
PROSTATE CANCER

It is estimated that:

- 232,090 new cases will be diagnosed in the U.S. for the year 2008
- 30,350 men will die from the disease
- The life time risk of developing prostate Cancer is 20% in the United States
PROSTATE CANCER

• One man in five will be diagnosed with prostate cancer during his lifetime

• One man in 33 will die of this disease
PROSTATE CANCER

- Incidence
- Mortality Rate
- Mean age at Diagnosis
- Similar to breast cancer statistics
BREAST CANCER

- 211,00 new cases to be diagnosed in the U.S. this year
- 44,000 deaths (including 260 men)
- Breast cancer is the most common cancer among women
Risk Factors

- Older age
- Family history
- Race and ethnicity
- Dietary fat?
• American men whose diets are rich in saturated fat from red meat have an approximately 80% greater risk of developing Cancer of Prostate

• These diets influence androgen levels leading to clinically significant and possible lethal malignancy

• In Japan, prostate cancer is rare. When Japanese men move to America, their incidence of carcinoma of the prostate increases
EPIDEMIOLOGY

• Positive family history in first- and second degree relatives

• The short arm of chromosome 8 is associated with prostate cancer

• Increased frequency of prostate cancer among relatives of women with breast cancer.

Other factors include:
geography,
prior vasectomy,
history of venereal disease.

• The role of geography is related to vitamin D, which has potent anti tumor properties. Interestingly, eunuchs do not get prostate cancer
From 1986 to 1991, there was an 82% rise in the incidence rate of prostate cancer.
THE BATTLE AGAINST PROSTATE CANCER

Men don’t like to talk about it, but 1 in 5 will get it. There’s a simple blood test everyone should know about. Here’s why
THE MAN'S CANCER

Prostate cancer is reaching epidemic levels in the U.S. This is no time for squeamishness

By Leon Jarriff, SAN FRANCISCO

Three years after his triumph in the Gulf War, General H. Norman Schwarzkopf was feeling invincible. But in March 1994, uncomfortable with nagging tenderness in one knee, he stopped by the MacDill Air Force Base Hospital in Tampa, Florida. While there, he decided to visit the urologist for an exam. "I feel something not quite right," the doctor said, after making a routine rectal exam. "But if it's cancer, I can tell 90% of the time, and I don't think so.

Schwarzkopf, then 59, had reason to feel confident. He had recently undergone a PSA (prostate-specific antigen) test and registered a count of only 2.8, well below the level considered indicative of cancer.

But to play it safe, the uskowitz performed an ultrasound exam. "It looks like a stone," he measured the (general), took a biopsy of the prostate gland and sent it off to a pathologist. Schwarzkopf left the hospital relaxed and optimistic. But a week later, the doctor called, parent and then said, "I don't know how to tell you this, but you have prostate cancer.

Shaken, like most men woefully uninformed about prostate cancer, Schwarzkopf began devouring books and medical journal articles. He overcame his squeamishness and started talking to friends and experts about this disease that seemed to strike at the very core of masculinity. "For me, it was like war," he says, "First thing you do is learn about the enemy."

THE SURVIVORS: These men are fighting or have already defeated prostate malignancies.
SOME WHO HAVE LOST THE BATTLE
Cancer Detection

• Early detection reduces mortality
• Detection of early localized disease is the only chance for cure but...
• Most men with prostate cancer are diagnosed with advanced disease with poor long-term survival
PROSTATE CANCER

• Unfortunately, it is difficult to distinguish at an early stage those cancers that will likely progress and produce clinical disease from those that can be safely observed.
PROSTATE CANCER

Pathologic Parameters:

- Tumor Grade
- Extent
- Volume
- Reflect the behavior of Cancer
Detecting Prostate Cancer

- What is the best method for detecting cancer?
- No clear consensus
- Variable practice among institutions
- Variable practice can exist even in the same institution
Cancer Detection Methods

• Digital rectal exam (DRE)
• Serum prostate specific antigen (PSA)
• Transrectal ultrasound (TRUS)
• DRE-guided biopsy
Cancer Detection Methods

- Digital rectal exam-DRE
- Physical palpation of the gland from inside the rectum
- Only evaluates posterior gland
- Poor sensitivity
- Difficulty to reach the entire gland
DRE

• Even the largest finger cannot evaluate the whole gland
Cancer Detection Methods

- Digital rectal exam (DRE)
- Serum prostate specific antigen (PSA)
- Transrectal ultrasound (TRUS)
- DRE-guided biopsy
Prostate Cancer

Screening

American Cancer Society and American Urological Society recommend:

• Annual DRE and PSA beginning at age 50
• Annual DRE and PSA beginning at age 40 for high risk men
Prostate Specific Antigen (PSA)

- Serine protease discovered in 1979 by Wang
- Secreted by prostatic acinar cells and ductal epithelium
Prostate Specific Antigen

Potential Uses

• Screening- diagnosis
• Staging
• Predicting or reflecting tumor behavior
• Predicting prognosis
• Help determine therapy
Prostatic Specific Antigen (PSA)

Risk of prostate cancer

- PSA < 1 ng/ml < 1% risk
- PSA > 2.5 ng/ml = 20% risk
- PSA > 10 ng/ml > 50% risk
- 75% with PSA > 4 ng/ml do not have cancer
- 20% with biopsy proven cancer have PSA < 4 ng/ml
Prostate Cancer

Screening

• Increased PSA - tumor larger and more aggressive
• Increased PSA - detect tumor at an early stage
• Increased PSA - biopsy positive in 30%
Prostate Cancer

PSA an indicator for staging

- PSA < 10 – no metastatic lesions
- PSA ≥ 40 – metastatic lesions
- PSA ≥ 50 – invasion of SV
# Prostate Cancer

## Age specific PSA

<table>
<thead>
<tr>
<th>Age</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>40-49</td>
<td>0.0-2.5 ng/ml</td>
</tr>
<tr>
<td>50-59</td>
<td>0.0-3.5 ng/ml</td>
</tr>
<tr>
<td>60-69</td>
<td>0.0-4.5 ng/ml</td>
</tr>
<tr>
<td>70-79</td>
<td>0.0-6.5 ng/ml</td>
</tr>
</tbody>
</table>
Prostatic Specific Antigen

- Serum marker
- Elevation is non-specific
  - Prostate cancer
  - Benign Hyperplasia
  - Prostatic Inflammation
  - Prostatic manipulation (DRE)
Prostate Specific Antigen

Causes of Elevated PSA

• Prostate cancer
• BPH
• Prostatitis
• Prostatic infarct
• Acute urinary retention
• Cystoscopy
• Biopsy
• Transurethral resection of prostate
Elevated PSA

Is the elevation of PSA the result of a malignancy or a benign process?

Trans-rectal Ultrasound of the Prostate
PSA elevation: Benign vs. Malignant

- **PSA + TRUS (Combination Techniques)**
  - Methodology to remove contribution of prostatic hypertrophy
  - Use TRUS to measure volume of gland
- **Predicted PSA (ng/ml) = 0.12 x volume**
- **Excess PSA = Predicted PSA - Serum PSA**
Prostate Cancer

Prostate Specific Antigen Velocity (PSAV)

• Increased PSA < 0.75 mg/ml/year or > 20%
• Increased suspicion for carcinoma by 90%
Prostate Cancer

Positive Predictive Value (PPV) for DRE and PSA

- DRE+ 15-30%
- PSA+ 17-28%
- PSA+ (4-9 mg/ml) 22%
- PSA+ (>10 mg/ml) 67%
Cancer Detection Methods

- Digital rectal exam (DRE)
- Serum prostatic specific antigen (PSA)
- Transrectal ultrasound (TRUS)
  - Imaging for detection
  - Guidance for biopsy
- DRE-guided biopsy
Clinical Indications for the Use of Prostatic Ultrasound

- Evaluation of a palpable mass
- Evaluation of an area of induration of the prostate on digital rectal examination
- Asymmetry of the prostate on digital rectal examination
Normal TRUS - Prostate

Central Gland

PZ

PZ
Peripheral Zone

Some 70% to 80% of prostate cancer originates in the PZ, usually within 3.0 to 4.0 mm of the prostate capsule.
Transition Zone

Initially the TZ makes up about 5% or less of the glandular prostate, in the aging prostate, it is the origin of benign prostatic hyperplasia.
Methods

- Curved linear array end-fire (5-9 MHz)
- CDI-PRF 800 Hz, WF 50 Hz
- Volume (cc) = H x L x W x 0.523
- Predicted PSA (ng/ml) = 0.12 x volume
- Excess PSA = PPSA – serum PSA
Conventional gray scale imaging has been shown to have low to moderate sensitivity for cancer. Tumors can appear hypoechoic, hyperechoic and even isoechoic.

Color Doppler may increase sensitivity. Tumors can appear hypervascular, hypovascular and with normal vascularity.
Hypoechoic / Hypervascular Tumor
Hypoechoic / Hypervascular Tumor
Izoechoic / Hypervascular Tumor
Izoechoic / Hypervascular Tumor
Results: CDI vs Gleason Score

• Tumors with a Gleason score of 7 or higher were significantly more likely to be CDI positive than negative (P<0.05)
Color Doppler of the Prostate

- 85% of cancers have abnormal flow
- Pitfalls - prostatitis
Cancer Detection Methods

- Digital Rectal Exam (DRE)
- Serum prostatic specific antigen (PSA)
- Transrectal ultrasound (TRUS)
  - Imaging for detection
  - Guidance for biopsy
- DRE-guided biopsy is no longer the method of choice for cancer detection
TRUS

• Patients are referred for TRUS for abnormal DRE or elevated PSA

• TRUS-guided biopsy is technique of choice for prostate cancer detection and pathologic sampling

• The decision to perform targeted versus routine sextant biopsy remains controversial
Ultrasound of the Prostate

• Transrectal Ultrasound (abbreviated TRUS) is the preferred method for visualizing the prostate and for guiding biopsy

• High frequency endocavitary transducer inserted into rectum

From:
http://www.phoenix5.org/glossary/biopsy.html
PSA Elevation: Benign vs. Malignant

• Biopsy is the best method to determine if elevation of PSA is due to a malignant process
• TRUS-guided biopsy is technique of choice for pathologic sampling of the prostate.
• But which patients should be biopsied?
Detecting Prostate Cancer

• What is the best method for detecting cancer?
  – Who to biopsy?
  – How many samples?
  – Where to take samples?

• No clear consensus
  – Variable practice among institutions
  – Variable practices exist in the same institution
TRUS Biopsy Methods

- **Targeted Biopsy Approach** - biopsy is only performed in the presence of either gray scale (GS) or color Doppler (CDI) abnormalities.

- **Sextant Biopsy Approach** - biopsy is performed in all patients regardless of TRUS findings and sampling of the entire prostate is undertaken.
Biopsy Technique: TRUS+
Biopsy Complications

- Extremely low morbidity
- No fatalities
- Added discomfort associated with multiple biopsies
- No significant bleeding complications in 544 patients
- 1 hospital admission for septicemia (0.002%)
ACCURACY OF GRAY SCALE/COLOR DOPPLER SONOGRAPHY AND SERUM MARKERS AS PREDICTORS FOR PROSTATE CARCINOMA

E. Kuligowska, M.A. Barish, H.M. Fenlon, M. Blake

Radiology 2001
Patients and Methods

• All 544 patients underwent prostate biopsy
• Targeted biopsy of GS/CD abnormalities
• Sextant biopsy of PZ and TZ
• TRUS findings recorded on standard data sheet
• Entered into computer database
• Correlated with pathology results
# Sensitivity of TRUS for Cancer

<table>
<thead>
<tr>
<th>TRUS Method</th>
<th>Cancers (190)</th>
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<tbody>
<tr>
<td>Gray Scale Alone</td>
<td>78 (41%)</td>
</tr>
<tr>
<td>Gray Scale + Color</td>
<td>108 (57%)</td>
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- Gray scale TRUS is relatively insensitive - 41%
- Color Doppler increases sensitivity but not enough – 57%
Results: Biopsy Method

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<tr>
<td>Targeted by GS</td>
<td>78 (41%)</td>
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<tr>
<td>Targeted by GS + CDI</td>
<td>108 (57%)</td>
</tr>
<tr>
<td>Total Sextant</td>
<td>190 (100%)</td>
</tr>
<tr>
<td>Sextant (US Occult)</td>
<td>82 (43%)</td>
</tr>
</tbody>
</table>

Targeted biopsy is insufficient, Sextant biopsy should be performed if PSA elevated.
Results: Biopsy Technique

- GS: 78
- CDI: 82
- GS/CDI: 108
- Targeted bx: 108
- Sextant bx: 190

# Cancers Detected
Conclusions

• Targeted biopsy of sonographically-visible lesions alone misses about half of all cancers

• Sextant biopsy dramatically increases sensitivity of sampling for prostate cancer

• A substantial number of sonographically-occult cancers have Gleason scores $\geq 6$
Conclusions

• Sextant biopsies are safe and mandatory in all patients with abnormal DRE or elevated PSA regardless of TRUS findings

• Primary value of TRUS is to guide systematic sampling of both sonographically normal and abnormal prostate parenchyma
MRI

- Endorectal coil & external multicoil array
- Multiplanar high-resolution T2-weighted images
  - Tumor detection
  - Tumor staging – extraprostatic spread
- Axial T1-weighted images
  - Detect hemorrhage
  - Detect nodes
MRI – Image Interpretation

• Anatomical Evaluation
  – Capsule
  – Neurovascular bundle
  – Seminal Vesicles
  – Nodes

• Signal Characterization
  – Tumor – low signal on T1 & T2
  – Hemorrhage – high T1 / Low T2
MRI – Appearance on T2-weighted Images

- Central Gland
  - BPH
  - Variable appearance

- Peripheral zone
  - Uniformly bright

- Tumor
  - Heterogeneous dark

Courtesy: C. Tempany
MRI – Appearance on T2-weighted Images

- Central Gland
  - BPH
  - Variable appearance

- Peripheral zone
  - Uniformly bright

- Tumor
  - Heterogeneous dark

From Radiology 2001; 218:365–374
T2 & T1-weighted Images

- T2W Hypointense nodules
  - Tumor
  - Hemorrhage

- T1W images
  - Tumor = hypointense
  - Hemorrhage = hyperintense

T2 Weighted

Courtesy: C. Tempany
MRI – Localized Disease

- 62 year old male
- PSA 6.0 ng/ml
- Large right sided tumor
  - Gleason (3 + 4)
  - No extra-capsular extent

From Radiology 2001; 218:365–374
T1-weighted Images & T2

- Hypointense nodule ? Tumor
- Hypointense nodule ? Tumor
- Hemorrhage
- Tumor

T2 Weighted  T1 Weighted

Courtesy: C. Tempany
Future Directions

- Spectroscopy
- Image Guided Therapy
Future Directions

• Spectroscopy
  – Proton Citrate/choline ratios
  – Normal
    • High Citrate
    • Low Choline
Future Directions

• Spectroscopy
  – Abnormal:
    Elevated Choline : Decreased Citrate
Thank you.