PROSTATE MPMRI AND TRUS/MRI FUSION BIOPSY: A REVIEW

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Goals and Objectives

- Discuss current and changing paradigms in the urologists’ diagnosis of prostate cancer
- The fundamentals of starting a multiparametric prostate program will be discussed, with an emphasis on the needs of referring urologists.
- Multiparametric MRI (mpMRI) of the prostate gland will be reviewed.
- The latest advancements in MRI/TRUS fusion biopsy will be discussed. Various software packages, and the benefits of each will be analyzed.
Fusion biopsy allows doctors to zero in on riskiest prostate cancers

For decades, doctors have diagnosed prostate cancer using what’s been called a “blind” biopsy, removing and testing a dozen tiny tissue samples to see if cancer is present. Now, new technology is taking the guesswork out of the procedure by allowing doctors to precisely target suspicious areas where deadly cells may be.

MR Fusion Guided Prostate Biopsy: A New Diagnostic Technique For Detecting Prostate Cancer

Technology to perform prostate biopsies has been relatively unchanged since the 1980’s. Traditional techniques of the prostate, yet nearly 30% of cancers are located outside this zone.

For men with ongoing concern for cancer—persistently elevated prostate specific antigen (PSA) (a blood marker) repeatedly negative or normal biopsies—a new technique, MR fusion guided prostate biopsy, may hold promise.

In a recent Phase 3 study, researchers from North Shore LIJ Medical Center demonstrated that using a specialized transrectal ultrasound (TRUS) in men with an elevated PSA resulted in a prostate cancer detection rate that...
Prostate Cancer Diagnosis

- Current standard of care in diagnosing prostate cancer
  - Screening patients with serum PSA and digital rectal examination (DRE).
    - Beginning at age 40 for high risk patients (African American men, men with first degree relative diagnosed with prostate cancer below age of 65)
    - Beginning at age 50 for general population (men at average risk with >10 year life expectancy)
  - Concern arises if PSA is elevated (above 4.0 ng/mL, or PSA velocity > 0.75 ng/mL/year) or the DRE is abnormal. Subsequently, a biopsy is usually performed.
  - PCA3 mRNA is utilized as adjunct by some urologists. This novel test improves sensitivity and specificity compared to PSA (67% and 71%).


Prostate Cancer Diagnosis: Biopsy

- **Standard systematic biopsy**
  - 12 core biopsies sampling posterior portion of prostate gland
  - As standard biopsy needle only extends 17 mm into the prostate, tumors in the anterior gland are often missed.

Example of prostate cancer in a 69 year old man with PSA of 10.6 and previous negative biopsy. Lesions in the anterior transition zone (arrows), are often missed by standard systematic biopsy. The dashed line demarcades anterior/posterior gland division, beyond which standard biopsy often fails to sample.


Systematic random 12-core biopsy

- Limited sensitivity of only 53%.

- Systematic biopsy has resulted in overdiagnosis of low grade, indolent disease (up to 50% of randomly biopsied cancer may be clinically insignificant).

- These limitations have led to an increasing utilization of multiparametric MRI (mpMRI).

Small lesions are susceptible to false negative biopsies, due to random sampling error. This 55 year old patient presented with a PSA of 4.3, and previous systematic biopsy showing low volume Gleason 3+3 in the right peripheral zone. Following targeted mpMRI/TRUS fusion biopsy, this lesion (arrows) was found to represent Gleason 4+4 prostate cancer, which was not detected during systematic biopsy.


Prostate mpMRI: Indications

- Prostate cancer diagnosed on biopsy, patient at low risk for advanced disease and/or metastases (PSA ≤10 and Gleason ≤6 and clinical stage T1 or T2a)
  - ACR Appropriateness criteria rating: 5

- Prostate cancer diagnosed on biopsy patient at intermediate risk for locally advanced disease and metastases (PSA 10-20 or Gleason 7 or clinical stage T2b)
  - ACR Appropriateness criteria rating: 7

- Prostate cancer diagnosed on biopsy patient at high risk for locally advanced disease and metastases (PSA ≥20 or Gleason 8-10 or clinical stage T2c or higher)
  - ACR Appropriateness criteria rating: 8

- Multiple negative prostate biopsies, but there is concern for prostate cancer based upon rising or persistently elevated serum markers suggestive of cancer.
  - ACR Appropriateness criteria rating: 7

  - ACR Appropriateness Criteria Rating Scale:
    - 1,2,3 Usually not appropriate
    - 4,5,6 May be appropriate
    - 7,8,9 Usually appropriate
Fundamentals of mpMRI Program: Components

- **Hardware**
  - MRI Scanner
    - 1.5 Tesla versus 3.0 Tesla
    - ± Endorectal Coil (ERC)
  - Guided Biopsy
    - MRI guided cognitive biopsy
      - Operator directs TRUS biopsy to area of abnormality on mpMRI by visual estimation
    - MRI/TRUS fusion biopsy
      - mpMRI findings digitally overlaid on real-time TRUS images for targeted biopsy
    - In bore direct MRI biopsy

Example of MRI/TRUS fusion biopsy system in NIH Interventional Urology Suite. mpMRI data is transferred to workstation, which then fuses with real-time ultrasound equipment with the aid of an electromagnetic field generator (EM-FG) for tracking and image registration.


Fundamentals of mpMRI Program: Components

- Software
  - Diagnostic Component:
    - mpMRI image analysis software (Hitachi/Eigen Profuse, Philips/Invivo DynaCAD)
  - Intervention Component:
    - Cognitive Biopsy
    - MRI/TRUS fusion biopsy
    - In bore MRI biopsy

Example of Hitachi/Eigen ProFuse mpMRI software. Entire prostate gland is semi-automatically segmented (green outline). Two lesions are outlined by green and yellow circles (region of interest/ROI 1 and 2), for targeting on subsequent fusion biopsy.

Magnetic Field Strength

1.5 Tesla

**Benefits**
- Less susceptible to metallic artifact
- Decreased cost
- Can be used in select patients who contain implanted devices deemed unsafe for 3T MRI

**Disadvantages**
- Endorectal coil usually required
- Lower signal to noise ratio, particularly problematic with high b-value diffusion weighted imaging (DWI)

3 Tesla

**Benefits**
- Higher signal to noise ratio
- Improved sensitivity in detection of prostate cancer
  - 3T is recommended by PIRADS steering committee
- Diagnostic images can be obtained without ERC

**Disadvantages**
- More susceptible to metallic artifacts
- Increased cost
- Increased RF energy deposition
Example of the same patient undergoing MRI at 1.5 Tesla with endorectal coil (ERC) on left and 3.0 Tesla without ERC on right. The patient had a PSA of 6.9, and a previous positive systematic biopsy. Images obtained at higher magnetic field show improved signal and contrast resolution, despite lack of endorectal coil. There is improved conspicuity of two lesions in the prostate (arrows). Note presence of motion artifact in image obtained with ERC, due to rectal peristalsis.
Endorectal Coil

Benefits:
- Increases signal to noise ratio in prostate gland
- Improves detection of prostate cancer, particularly small lesions (76% vs 45% sensitivity)
- Aids DWI and improves temporal resolution of DCE sequences

Disadvantages:
- Discomfort
- Susceptibility and motion related artifacts
- Increased Cost
- Increased Exam Time


Examples of different agents within ERC: MRI at 1.5 Tesla with barium insufflated endorectal coil (A). MRI at 3.0 Tesla with perfluorocarbon (PFC) compound (B).
Multiparametric prostate MRI combines anatomic **T2 Weighted** images with functional and physiologic assessment using **diffusion weighted imaging** (DWI) and **dynamic contrast enhanced** (DCE) MRI.

The combination of these sequences have led to substantial improvements in the detection of clinically significant cancer.
Example of T2 Weighted imaging in a patient with a normal prostate MRI. Peripheral Zone (asterisks), anterior fibromuscular stroma (S), prostate capsule (arrowheads), prostatic urethra (arrows), and neurovascular bundles (NV). Note hypointense signal from PFC gas within endorectal coil.
Example of mpMRI in a 61 year old man with serum PSA of 22.64 ng/mL. T2WI show a focal hypointense lesion in the right peripheral zone (arrow), with corresponding restricted diffusion on ADC map and B2000 DWI, as well as early hyper-enhancement on DCE-MRI. Interpreting all sequences simultaneously increases the confidence in identifying this PIRADS 5 lesion.
Example: 61 year old man with serum PSA of 22.64 ng/mL

PiRADS 2.0 Score:
- T2W MRI=5
- DW MRI=5
- DCE MRI=+
- Overall PiRADS score=5. Targeted biopsy showed 4+4 disease
Fundamentals of mpMRI Program: Components

- Intervention Component:
  - mpMRI data uploaded to TRUS fusion software system with lesions demarcated by radiologist.
  - Ultrasound data is then linked to fusion system for biopsy with targets visualized on ultrasound screen.

- Vendors:
  - Most Common:
    - Uronav
    - Artemis
  - Less frequently utilized in US:
    - Koelis/Urostation (France)
    - Hitachi/Hi-RVS (Japan)
    - Geoscan/BioJet

Example of Philipis/Invivo Uronav software. Top images show real-time TRUS image acquisition. Bottom left images show axial T2 weighted image of mpMRI dataset, which can be used for real-time coordination during fusion biopsy.

MRI/TRUS Fusion: Spatial Registration

- Registration of TRUS and mpMRI with a navigation device.
  - Spatial coordinates linked by communication between a receiver on/near TRUS probe and tracking device placed close to patient
  - Planning phase: at least three anatomic landmarks paired between MRI and TRUS
  - Guiding phase: MR guided navigation of real-time TRUS scanning

Example of landmark based registration between mpMRI and TRUS (red circles)


Organ Based Registration

- Registration of TRUS and mpMRI which accounts for prostate deformation (from ERC, pressure US transducer)
  - Software tracks the prostate gland itself, rather than the US probe
  - Planning phase: 3D acquisition of prostate volume, followed by:
    - Uses multiple point registration and elastic 3D organ based registration, in addition to standard three point landmark based registration
  - Organ based registration are optional packages offered some vendors

Example of spatial/rigid registration (A) as described by Cornud et al. Three point registration does show inaccurate registration in the presence of any prostate deformation. Algorithms can compensate for this using organ based/elastic registration (B)

Philips/Invivo UroNav:
- Planning phase: 2D TRUS acquisition to construct 3D volume. Registration is done manually by software (non-rigid registration)
- Electromagnetic navigation sensor attached to ultrasound transducer. A stationary navigation system is placed above the patient in order to track probe. Fusion software helps guide operator to pre-delineated lesions based on mpMRI.

Pros:
- Can integrate with existing ultrasound software (left)
- Technique familiar to urologist due to use of endocavitary US probe (right)
- Easy to adjust for patient motion

Cons
- More susceptible to prostate deformation
- Less accurate probe tracking compared to robotic system
- Requires manual calibration of ultrasound images

Sensor on TRUS probe, which is tracked by using a small electromagnetic field generator (white box placed above or below surgical field)

Example of UroNav fusion biopsy. Top, realtime TRUS biopsy, with red circle segmented prostate. Bottom, mpMRI T2 weighted image with previously delineated lesion/ROI.
MRI/TRUS Fusion Biopsy – Artemis

- Hitachi/Eigen- Artemis:
  - 3D Semi-robotic prostate navigation system. Needle and TRUS probe tracked by angle-sensing devices built into each joint of the arm.
  - Planning phase: 2D mode US scanning renders 3D image, which is segmented and registered to mpMRI data set with previously segmented prostate and lesions

- Pros: Automatic, Fast, Rigid and Elastic Image Fusion
  - Remote center of motion, minimizing prostate deformation that occurs during standard TRUS guided biopsy

- Cons:
  - Registration requires total patient immobility
  - Operator must learn a new technique to operate device

Example of MRI/TRUS fusion biopsy. Top left, bottom left real-time ultrasound, top right, segmented mpMRI with lesions delineated with ROIs. Bottom right, 3D model of prostate with previously delineated ROIs.
MRI-TRUS Fusion: The Cost?

- Health Systems/Urologists/Radiologists without the technology are increasingly losing patients to competitors.

- Acquisition of MRI/TRUS fusion systems come at significant expense to hospital, with reported costs ranging between $200,000 and $300,000.

- Difficult to recoup capital costs:
  - MRI/TRUS fusion does not have an independent CPT code, and is currently only reimbursed to same extent as a standard biopsy.
  - Fusion biopsies are usually acquired in conjunction with standard sextant biopsies. Thus, overall procedure time is generally increased with no change in reimbursement.

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Lee SM. Prostate diagnosis adds MRI to ultrasound for clearer view. www.SFGate.com 2014.

MRI-TRUS Fusion: The Cost?

- Potential to offset costs:
  - Patients who undergo mpMRI may not undergo biopsy if no lesion is found.
  - Although conventional biopsies are often still being acquired in addition to targeted lesions, the decrease in repeat biopsies leads to less specimens submitted for pathology review.
  - Decreased prostatectomy on low-risk patients

- A recent European study suggested the cost of mpMRI and TRUS/fusion to be comparable to the current standard of care

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- Lee SM. Prostate diagnosis adds MRI to ultrasound for clearer view. www.SFGate.com 2014.
mpMRI with MRI/TRUS fusion systems are increasingly utilized tools to aid in the detection, localization, and risk stratification of patients with prostate cancer.

These techniques represent significant advantages over the longstanding tools of serum PSA and systematic biopsy.
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