Multiparametric Prostate MRI and Fusion Biopsy- When and How

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Disclosures

• None
Prostate Cancer Detection

• Very imperfect
  • Triggered by PSA and DRE
  • TRUS-guided biopsies
    • Limitations:
      • 2D imaging
      • Few anatomical reference points to guide needle
      • Pathology rarely visible (systematic, “random” biopsies)
    • False negative ~10-30%
Prostate Cancer Detection

- Downward stage migration in PSA era
  - Fewer palpable tumors
  - Smaller lesions
  - Classic hypoechoic PZ lesion less common
    - Only 11-35% of malignancies seen on US
    - PPV of biopsy of lesion: 25-30%
- Accurate? mapping with systematic biopsy
Prostate Cancer Detection

- **Number**
  - Increased 6 to 12 (or more)

- **Location**
  - Target peripheral zone (~80%)
    - Laterally-directed cores
    - Apical biopsies have a higher detection rate for PCa (comprised entirely of PZ)
  - Routine transition zone or anterior biopsy unnecessary
    - Maybe at repeat biopsy
      - **BUT ~25% of TRUS biopsies are repeat**
Biopsy Sampling Error

- Random “sampling”
  - Single 18G biopsy core volume: 0.015mL
  - X 12 cores = 0.18mL
  - Of a 40mL prostate · 0.45% sampling

- Limited tissue from anterior zones
Biopsy Sampling Error

- Undersampling, undergrading and nondetection
  - Biggest limitation to active surveillance (or focal therapies)
    - (eg, missed anterior tumors)
- Overdetection of insignificant disease
- Image-guided (targeted) biopsy is becoming standard of care
Prostate Cancer Detection

- Biopsy technique continued evolution
  - Confirmatory - Finger-guided biopsy
  - Guided
    - Transrectal ultrasound (since 1981) guided
      - Extended template, saturation and transperineal
  - Targeted
    - MRI
      - “Cognitive registration”
      - MRI-US fusion

Multiparametric MR

- Tumor detection
  - Improved specificity for CS PCa
- Tumor localization
- Tumor characterization
  - Stage (good specificity for EPE)
  - Grade
- Guidance/Targeting biopsies
  - Risk stratification
  - Guiding therapy
Multiparametric MR Imaging

- Anatomic imaging (T2w, T1w)
- Functional imaging
  - MR Diffusion-weighted imaging (DWI)
    - Detects Brownian motion of extracellular water molecules
  - MR Dynamic contrast-enhanced (DCE)
    - Detects increases in vascularity
  - MR Spectroscopy
    - Provides metabolic information
Anatomic MRI

- **T1W images**
  - Outline of the gland
  - Presence of hemorrhage within prostate and SVs
  - Detection of nodal or skeletal mets (esp with gadolinium)

- **T2W images**
  - Prostatic zonal anatomy
  - Abnormalities within the gland
  - Staging
    - Seminal vesicle invasion
    - EPE
    - Nodal involvement
T2 weighted MRI

- Cancer → hypointense
  - But nonspecific in both PZ and TZ

Kumar et al 2012
T2 weighted MRI

- TZ typically has heterogeneous signal intensity
  - Glandular (T2-hyperintense); stromal (T2-hypointense)
  - Predominant benign stromal elements may mimic or obscure clinically significant cancer

- Cancer in TZ often non-circumscribed homogeneous, moderately hypointense lesions ("smudgy fingerprint")
MRI DWI

- Restricted H2O diffusion
  - Malignant tissues: more restricted diffusion from high cell densities
- DWI → hyperintense
- ADC → hypointense
  (calculated using at least 2 different diffusion gradients)

Bjurlin et al 2016
Prostatitis- enhancement is usually diffuse
BPH- often well-encapsulated and spherical
BUT non-specific nature of these patterns limits the utility of DCE findings in isolation
  • DCE largely an adjunct to primary on findings on T2WI and DWI

Tumor angiogenesis using contrast uptake and washout

Cornud et al. 2012
piRADS v2

- **Prostate Imaging Reporting and Data System (ESUR and ACR)**
  - Timing - at least 6 (8-12) wks post biopsy (takes ~6 months for hemorrhage to resolve in PZ)
  - No consensus on patient preparation but BM before important
  - 3 T or 1.5 T (3T typically better but 1.5 T only option with some implants)
  - Endorectal coil not necessary (helpful in some 1.5 T for DWI and DCE)

piRADS v2

PIRADS 1 – Very low (clinically significant cancer is highly unlikely to be present)

PIRADS 2 – Low (clinically significant cancer is unlikely to be present)

PIRADS 3 – Intermediate (the presence of clinically significant cancer is equivocal)

PIRADS 4 – High (clinically significant cancer is likely to be present)

PIRADS 5 – Very high (clinically significant cancer is highly likely to be present)

Table 1. PIRADS 2.0 scoring for peripheral zone

<table>
<thead>
<tr>
<th>DW MRI</th>
<th>T2W MRI</th>
<th>DCE MRI</th>
<th>Overall PIRADS</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>Any*</td>
<td>Any</td>
<td>1</td>
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<td>2</td>
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<tr>
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DW MRI, diffusion-weighted magnetic resonance imaging; T2W MRI, T2-weighted magnetic resonance imaging; DCE MRI, dynamic contrast-enhanced magnetic resonance imaging. PIRADS, prostate imaging reporting and data system.

Table 2. PIRADS 2.0 scoring for transition zone lesions

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piRADS v2

- "Dominant sequence"
  - Depends on lesion location
    - In **peripheral** zone
      - Diffusion-weighted MRI
      - Look for restricted diffusion
    - In **transition** zone
      - T2-weighted MRI
    - Secondary role of DCE MRI

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piRADS on T2W
piRADS on DWI- PZ

1 3 5

DWI

ADC
piRADS on DWI- TZ

1

3

5

DWI

ADC
piRADS on DCE

Negative

Positive

PZ

TZ

DCE

T2W
PI- RADS2 Summary

- PI-RADS 1 & 2 - mostly benign*
- PI- RADS 3 - equivocal*
  * Consider variables (4K, PHI, free/total PSA, family history)
- PI-RADS 4 & 5 - likely significant PCa
When to get MP MRI

• **Prostate cancer**
  • **Low risk**
    – Active surveillance patients before confirmatory biopsy
    – To risk stratify need for another surveillance biopsy
  • **High risk (or high volume intermediate)**
    – Evaluate for EPE or SV involvement
• **No prior diagnosis**
  • Before repeat biopsy (initial**)
INDICATIONS FOR BIOPSY

- PSA >3.0 ng/mL
- DRE
- Workup for benign disease

**Initial biopsy**

- TRUS-guided biopsy
  - See Management of Biopsy Results (PROSD-4)
  - or
  - Follow up in 6–12 mo with PSA/DRE
  - or
  - Percent free PSA, 4Kscore, or PHI

**Repeat biopsy**

**MRI** is not recommended routinely prior to initial prostate biopsy, but emerging data suggest that, in men undergoing initial biopsy, targeting using MRI/ultrasound fusion may increase the detection of clinically significant, higher-risk (Gleason grade ≥ 4+3=7) disease while lowering the detection of lower-risk (Gleason sum 6 or lower-volume Gleason grade 3+4=7) disease. Siddiqui M, Rais-Bahrami S, Turkbey B, et al. Comparison of MRI/Ultrasound Fusion–Guided Biopsy With Ultrasound-Guided Biopsy for the Diagnosis of Prostate Cancer. JAMA 2015;313:380–7.

- Atypia, suspicious for cancer
  - Multifocal (>2 sites)
  - Extended pattern rebiopsy (within 6 mo) with increased sampling of the affected site and adjacent areas. If no cancer is found, close follow-up with PSA and DRE is recommended at 1 year interval initially

- High-grade prostatic intraepithelial neoplasia (PIN)
  - Focal
  - Follow-up:
    - PSA and DRE at 6-24 month interval and
    - Consider percent free PSA, 4Kscore, PHI, PCA3, or ConfirmMDx and/or Multiparametric MRI and/or refined prostate biopsy techniques
  - Repeat prostate biopsy, based on risk

- Benign
  - Repositioning, especially if prior biopsy showed benign disease
If MP MRI negative- NPV

- EAU Meta-analysis of 48 studies
- NPV of mpMRI varies greatly depending on cancer prevalence
- PCa prevalence for a cut-off score of 3/5
  - 30% - NPV 88% (95% CI, 77–99%)
  - 60% - NPV 67% (95% CI, 56–79%)

“whilst it is a promising tool, it is not accurate enough to replace prostate biopsy in such patients, mainly because its accuracy is variable and influenced by the prostate cancer risk.”
MP MRI in multivariate model

- Multivariable model for prediction of significant Pca
  - 393 men for development
    - AUC
      - PSA: 0.598
      - MV: 0.797
      - MV+MRI: 0.883
  - 198 men for external validation
    - AUC for MV+MRI: 0.864

**Figure 1.** AUCs PSA based model, multivariable model (PSA + DRE + prostate volume + age), and advanced model (PSA + DRE + prostate volume + age + mpMRI).

**A Multiparametric Magnetic Resonance Imaging Based Risk Model to Determine the Risk of Significant Prostate Cancer prior to biopsy.**

MP MRI → biopsy

- "Cognitive" Fusion (visual registration)
  - MRI image available for physician review during biopsy to then aim at abnormal areas
  - See it on MRI, hit it on US
- MRI/US Fusion
  - UroNav (Phillips-Invivo)
  - Koelis Urostation (Koelis)
  - Artemis (Eligen)
  - Others [Virtual Navigator (Esaote); Real-Time Virtual Sonography (Hitachi); BiopSee (Pi Medical), and BioJet (BK Ultrasound)]
MRI Fusion... briefly

- MP MRI (>1wk pre biopsy)
  - Acquisition
  - MRI segmentation (→ 3D MRI model of prostate)
  - Regions of interest (ROI) identified and scored by radiologist using PIRADSV2

- Biopsy day
  - US acquisition
  - US segmentation (→ 3D US model of prostate)
  - Fusion/registration of MRI and US
  - Needle tracking (Electromagnetic, robotic arm or imaging alone)
  - Mapping and navigation
Elastic registration allows prostate deformations to be “incorporated” into the fusion

- US and MRI prostate shape differences
- Limited visualization nearest to the probe

- Ukimara et al 2012
MRI/US Fusion

Cornud et al. 2012
MRI Fusion

- +/- Patient movement compensation
- Displacements and deformations
- No published comparison between MR/US fusion platforms

Table 2. Summary of MRI-US fusion platforms

<table>
<thead>
<tr>
<th>System trade name (manufacturer)</th>
<th>US image acquisition</th>
<th>Image registration</th>
<th>Biopsy route</th>
<th>Tracking mechanism</th>
</tr>
</thead>
<tbody>
<tr>
<td>UroNav (Philips, In Vivo)</td>
<td>Manual sweep from base to apex</td>
<td>Rigid</td>
<td>Transrectal</td>
<td>Electromagnetic tracking</td>
</tr>
<tr>
<td>Artemis (Eigen)</td>
<td>Manual rotation along fixed axis</td>
<td>Rigid and elastic</td>
<td>Transrectal</td>
<td>Mechanical arm with encoders</td>
</tr>
<tr>
<td>Urostation (Koelis)</td>
<td>Automatic probe rotation</td>
<td>Elastic</td>
<td>Transrectal</td>
<td>Image-based (TRUS-TRUS) registration</td>
</tr>
<tr>
<td>HI-RVS (Hitachi)</td>
<td>Real-time biplanar TRUS</td>
<td>Rigid</td>
<td>Transrectal or transperineal</td>
<td>External magnetic field generator</td>
</tr>
<tr>
<td>Biojet (DK Technologies)</td>
<td>Manual sweep</td>
<td>Rigid</td>
<td>Transrectal or transperineal</td>
<td>Mechanical arm with encoders, stepper</td>
</tr>
<tr>
<td>BiopSee (MedCom)</td>
<td>Manual sweep with biplanar probe</td>
<td>Manual, marker based, or automatic</td>
<td>Transperineal</td>
<td>Stepper with encoders</td>
</tr>
</tbody>
</table>

Bjurlin et al 2016
• 1003 men who underwent standard and targeted biopsy
  • Similar number of cancer cases: 461 vs 469
  • 69% exact agreement
• Targeted biopsy
  • Diagnosed 30% more high grade cancers (173 vs 122)
  • Diagnosed 17% fewer low grade cancers (213 vs 258)
  • Missed 56 clinically significant tumors (high volume Gleason 3+4=7 or greater)- 18% were missed
MRI/US Fusion

Efficiency of Prostate Cancer Diagnosis by MR/Ultrasound Fusion-Guided Biopsy vs Standard Extended-Sextant Biopsy for MR-Visible Lesions

- 1003 men- Per patient mean
  - 12.3 standard cores
  - 5.3 targeted cores
- Efficiency
  - 13.5 % of standard cores positive
  - 27.9% of targeted cores positive (55.1% for piRADS 5 only)
- When MRI lesion is present, targeted biopsies are more efficient finding equal number of cases, more high grade cancers with 56% fewer cores

- Greatest benefit with higher PSA, higher MRI suspicion, smaller prostate volume, prior negative biopsy
Dramatic increase in the utilization of multiparametric magnetic resonance imaging for detection and management of prostate cancer

Daniel T. Oberlin,¹ David D. Casalino,² Frank H. Miller,² Joshua J. Meeks¹

¹Department of Urology, Feinberg School of Medicine, Northwestern University, Chicago, IL, USA
²Department of Radiology, Feinberg School of Medicine, Northwestern University, Chicago, IL, USA

Northwestern study of Greater Chicago area- 1521 mpMRI of the prostate were performed with an increase in the use of 486% over 26 months.
Challenges

- Image quality quite variable
- Image interpretation
  - Dedicated radiologists
  - Annotation of prostate ROI
- Do you eliminate systematic 12-core biopsy?
  - Depends but typically NO
- Do you avoid biopsy if MRI negative?
  - Depends
Challenges

• Systematic biopsy remains an essential component of a targeted biopsy
  • ~30% of concurrent systematic biopsies will reveal clinically significant disease (may be higher in “bad” prostates - piRADS 4 and 5)

• Major obstacles
  • Learning curve, dedicated radiologist, cost of machine, insurance coverage, time and reimbursement
Summary

- Prostate biopsy is evolving
  - Lesion-directed sampling → image-guided sampling → modeled systematic sampling with targeting
- Ideal PCa detection will involve combination
  - Targeting of image-visible suspicious lesions
  - Targeting to sites most likely to contain cancer
- MPMRI allows for identification/targeting of more “visible” lesions
- MP MRI should be done before repeat biopsy with TBx of suspicious lesions AND standard biopsy
References


• Oberlin DT, Casalino DD, Miller FH, Meeks JJ. Dramatic increase in the utilization of multiparametric magnetic resonance imaging for detection and management of prostate cancer. Abdom Radiol (NY). 2016 Nov 17.


References

References


Multicenter, paired-cohort, confirmatory study
740 men with no previous biopsy underwent 1·5 Tesla MP-MRI followed by both TRUS-biopsy and template transperineal prostate mapping biopsy (TPM-biopsy)
For clinically significant cancer, MP-MRI was
  • More sensitive (93%) than TRUS-biopsy (48%)
  • Less specific (41%) vs 96% for TRUS biopsy
MP-MRI might allow 27% to avoid a primary biopsy
  • Diagnosis of 5% fewer clinically insignificant cancers
  • 18% more cases of clinically significant cancer