MRI in the Enhanced Detection of Prostate Cancer: What Urologists Need to Know

Michael S. Cookson, MD, FACS
Professor and Chair
Department of Urology
Director of Prostate and Urologic Oncology
University of Oklahoma
Oklahoma City, Oklahoma
Disclosure

Michael S. Cookson, MD

I do not have any relevant financial relationship(s) with any commercial interest that pertains to the content of my presentation.
Potential Prostate MRI Applications

- Biopsy naïve: upfront assessment/targeting lesions
- Prior negative biopsy: targeting lesions
- Active surveillance: monitoring/targeting
- Surgical planning/Staging: nerve sparing, bladder neck, etc.
- Biochemical recurrence: local recurrence/pelvic nodes
American Urological Association (AUA)  
Society of Abdominal Radiology (SAR)  
Joint Consensus Statement

PROSTATE MRI AND MRI-TARGETED BIOPSY IN PATIENTS WITH PRIOR NEGATIVE BIOPSY

Collaborative Initiative of the American Urological Association and the Society of Abdominal Radiology’s Prostate Cancer Disease-Focused Panel

AUA Policy Statement on the Use of Multiparametric Magnetic Resonance Imaging in the Diagnosis, Staging and Management of Prostate Cancer

Pat F. Fulgham,* Daniel B. Rukstalis, Ismail Baris Turkbey, Jonathan N. Rubenstein, Samir Taneja, Peter R. Carroll, Peter A. Pinto, Marc A. Bjurlin and Scott Eggener

From the Texas Health Presbyterian Hospital of Dallas, Dallas, Texas (PFF), Wake Forest Baptist Medical Center, Winston-Salem, North Carolina (DBR), National Cancer Institute, National Institutes of Health, Bethesda, Maryland (IBT, PAP), Chesapeake Urology Associates, Baltimore, Maryland (LNR), NYU Langone Medical Center, New York, New York (ST, MAB), University of California San Francisco, San Francisco, California (PRC), and The University of Chicago Medical Center, Chicago, Illinois (SE)
Potential Prostate MRI Applications

• Biopsy naïve
• Prior negative biopsy
• Active Surveillance
  • Surgical planning: nerve sparing
  • Surgical planning: resectability
  • Local recurrence
Potential Prostate MRI Applications

• Biopsy naïve

• Prior negative biopsy

• Active Surveillance
Rationale for Prostate MRI Before Biopsy

• Majority of initial prostate biopsies are negative

• Many clinically significant cancers are missed by TRUS Bx

• Extended templates and saturation biopsies are attempts to account for false negatives/missed tumors
Evaluation of Biopsy Naïve Patients Utilizing mpMRI

1. Detects more clinically significant cancer when combined with systematic biopsy, and less clinically insignificant cancer, than systematic biopsy alone.
2. Targeted biopsy risks missing a small number of clinically significant cancers identified by systematic biopsy alone. Therefore, use of systematic biopsy in conjunction with MRI-targeted sampling is advisable.
3. The clinical impact of mpMRI-targeted biopsy in men with no previous history of prostate biopsy remains controversial, due to an unclear magnitude of clinical impact relative to cost. In considering its use, quality of mpMRI, experience of radiologist, cost of mpMRI, and availability of alternate biomarkers should be considered.
4. May be added value in selected patients where technical challenges prevent good prostate visualization by ultrasound. (e.g. Absent or restricted anal access. Large prostate or extensive calcification of prostate preventing evaluation of the anterior gland. Patient at risk for bleeding or infection where a negative MRI might obviate biopsy. Patient with a nodule when pre-treatment staging/planning is anticipated.)

5. There is insufficient data to recommend routine MRI in every biopsy naïve patient under consideration for prostate biopsy. Its use may be considered in men for whom clinical indications for biopsy are uncertain (minimal PSA increase, abnormal DRE with normal PSA, or very young or old patients).
Evaluation of Biopsy Naïve Patients Utilizing mpMRI

- Further refinements in imaging and MRI-targeting strategies required before routine MRI-targeted sampling in all men presenting for prostate biopsy should be considered.

- Ongoing randomized trials, such as the Prostate MR Imaging Study (PROMIS) and Prostate Evaluation for Clinically Important Disease: Sampling Using Image Guidance Or Not (PRECISION) trial, will offer further insight into utilization and adoption.
PROMIS Trial

• Patients:
  • Biopsy Naïve
  • Suspicion of cancer:
    • Elevated PSA (Up to 15)
    • Abnormal DRE
    • FH or ethnic risk group
  • Able to undergo MRI
PROMIS Trial: Design

- Multicenter UK study (11 Sites)
- From 5/2012 to 12/2015
- 576 men included
- All underwent:
  - 1.5T mpMRI
  - TRUS Biopsy
  - Template Prostate Mapping biopsy
    - Reference Test
- Primary endpoint:
  - mpMRI discrimination of clinically significant cancer (GS ≥4+3) or > 6mm core length
  - Compare TRUS Biopsy to Mapping Biopsy
### PROMIS Trial: Results

<table>
<thead>
<tr>
<th></th>
<th>Standard 12-core TRUS Bx</th>
<th>MRI-targeted Only</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. Pts.</td>
<td>576</td>
<td>576</td>
</tr>
<tr>
<td>No. pts. having a Bx.</td>
<td>576</td>
<td>418 (73%)</td>
</tr>
<tr>
<td>“Over” Dx. CaP</td>
<td>90 (16%)</td>
<td>62 (11%)</td>
</tr>
<tr>
<td>Significant CaP</td>
<td>111 (19%)</td>
<td>213 (37%)</td>
</tr>
</tbody>
</table>
PROMIS Trial: Results

Cancer Detected on Mapping Biopsy Based on MRI Score

1 to 5 Likert scoring system used to indicate probability of cancer.
1: highly likely to be benign
2: likely to be benign
3: equivocal
4: likely to be malignant
5: highly likely to be malignant
PROMIS Trial: Limitations

• MRI 1.5 Tesla
• Transperineal biopsy technique
• Did not use PIRADS Score
• Not targeted / fusion biopsies
MRI-Targeted or Standard Biopsy for Prostate-Cancer Diagnosis

PRECISION Trial

• Multicenter, randomized, noninferiority trial

• Biopsy naive with clinical suspicion of prostate ca to undergo MRI, with or without targeted biopsy, or standard TRUS biopsy

• MRI-targeted biopsy group underwent a targeted biopsy (without standard biopsy cores) if the MRI was suggestive of prostate ca; men whose MRI results were not suggestive of prostate ca were not offered biopsy

• TRUS-guided biopsy: standard biopsy was a 10-to-12–cores

• Primary outcome: clinically significant cancer Gleason score 3+4 (GS 7) or >

PRECISION Trial

- 500 men underwent randomization
- MRI-group: 28% (71/252) had negative MRI and did NOT undergo biopsy
- MRI-group: Sig. Prostate Ca 38% vs. 26% in standard-biopsy group (P=0.005)
- MRI, with or without targeted biopsy, was noninferior to standard biopsy, and 95% CI indicated the superiority of this strategy over standard biopsy
- Fewer men in the MRI-targeted biopsy group than in the standard-biopsy group received a diagnosis of clinically insignificant cancer (P<0.001)

<table>
<thead>
<tr>
<th>Outcome</th>
<th>MRI-Targeted Biopsy Group (N=252)</th>
<th>Standard-Biopsy Group (N=248)</th>
<th>Difference †</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biopsy outcome — no. (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No biopsy because of negative result on MRI</td>
<td>71 (28)</td>
<td>0</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td>Importantly, †</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High-grade prostatic intraepithelial neoplasia</td>
<td>4 (2)</td>
<td>10 (4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gleason score</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3+3</td>
<td>23 (9)</td>
<td>55 (22)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3+4</td>
<td>52 (21)</td>
<td>35 (14)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3+5</td>
<td>2 (1)</td>
<td>1 (&lt;1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4+3</td>
<td>18 (7)</td>
<td>19 (8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4+4</td>
<td>13 (5)</td>
<td>6 (2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4+5</td>
<td>7 (3)</td>
<td>2 (1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5+5</td>
<td>3 (1)</td>
<td>1 (&lt;1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No biopsy‡‡</td>
<td>4 (2)</td>
<td>3 (1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Withdrawal from trial</td>
<td>3 (1)</td>
<td>13 (5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clinically significant cancer ‡‡</td>
<td>95 (38)</td>
<td>64 (26)</td>
<td>12 (4 to 20)</td>
<td>0.005</td>
</tr>
<tr>
<td>Intention-to-treat analysis — no. (%)</td>
<td>95/245 (39)</td>
<td>64/235 (27)</td>
<td>12 (3 to 20)</td>
<td>0.007</td>
</tr>
<tr>
<td>Modified intention-to-treat analysis — no./total no. (%)</td>
<td>95/245 (39)</td>
<td>64/235 (27)</td>
<td>12 (3 to 20)</td>
<td>0.007</td>
</tr>
<tr>
<td>Per-protocol analysis — no./total no. (%)</td>
<td>92/235 (39)</td>
<td>61/232 (27)</td>
<td>12 (3 to 20)</td>
<td>0.007</td>
</tr>
<tr>
<td>Clinically insignificant cancer — no. (%)</td>
<td>23 (9)</td>
<td>55 (22)</td>
<td>-13 (-19 to -7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Maximum cancer core length — mm</td>
<td>7.8±4.1</td>
<td>6.3±4.5</td>
<td>1.5 (0.0 to 2.1)</td>
<td>0.053</td>
</tr>
<tr>
<td>Core positive for cancer — no./total no. of cores (%)</td>
<td>422/967 (44)</td>
<td>515/2788 (18)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Men who did not undergo biopsy — no. (%)</td>
<td>78 (31)</td>
<td>16 (6)</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>
Figure 3. Percentages of Men with Clinically Significant, Clinically Insignificant, and No Cancer, Identified According to PI-RADS v2 Score.
PRECISION Trial

Conclusion:
The use of risk assessment with MRI before biopsy and MRI-targeted biopsy was superior to standard transrectal ultrasonography–guided biopsy in men at clinical risk for prostate cancer who had not undergone biopsy previously

Early Detection Evaluation: Indication for Biopsy

- Repeat PSA
- DRE, if not performed during initial risk assessment
- Workup for benign disease

- Consider percent free PSA, 4Kscore, or PHI<sup>h</sup>
- Consider multiparametric MRI<sup>i</sup>

Either:
- TRUS-guided biopsy<sup>j</sup>
- Follow up in 6–12 mo with PSA/DRE<sup>h,k</sup>
At this time, the panel believes that the use of multiparametric MRI can be considered prior to TRUS-guided biopsy to inform biopsy decisions and to help identify regions of the prostate that may harbor cancer. However, the panel cautions that false negatives can occur and proceeding to TRUS-guided biopsy should still be an option.\textsuperscript{182}

The panel does not uniformly recommend that MRI-guided targeted biopsies be used in place of or in addition to standard 12-core TRUS biopsies in the initial biopsy setting (see \textit{Targeted Biopsy Techniques for Initial Biopsy}, below), because some significant cancers may sit outside targets identified on MRI. More information is needed in such a setting. However, the panel believes that multiparametric MRI may help identify regions of cancer missed on prior biopsies and should be considered in selected cases of men with at least 1 negative biopsy
### Recommendations in biopsy naïve patients

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>LE</th>
<th>Strength rating</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perform mpMRI before prostate biopsy.</td>
<td>1a</td>
<td>Strong</td>
</tr>
<tr>
<td>When mpMRI is positive (i.e., PI-RADS ≥3), perform the combination of targeted biopsy and systemic biopsy</td>
<td>2a</td>
<td>Weak</td>
</tr>
<tr>
<td>When mpMRI is negative (i.e., PI-RADS ≤2) AND the patient has low-risk of clinically-significant disease based on risk calculator or biomarker results, consider not to perform systematic biopsies</td>
<td>2a</td>
<td>Weak</td>
</tr>
</tbody>
</table>

### Recommendations in patients with prior negative biopsy

<table>
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<tr>
<th>Recommendation</th>
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</tr>
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<tr>
<td>Perform mpMRI before prostate biopsy.</td>
<td>1a</td>
<td>Strong</td>
</tr>
<tr>
<td>When mpMRI is positive (i.e., PI-RADS ≥3), perform only targeted biopsy</td>
<td>2a</td>
<td>Weak</td>
</tr>
<tr>
<td>When mpMRI is negative (i.e., PI-RADS ≤2), do not perform systematic biopsy, unless the patient has high-risk of clinically-significant disease based on risk calculator or biomarker results</td>
<td>2a</td>
<td>Weak</td>
</tr>
</tbody>
</table>
Potential Prostate MRI Applications

• Biopsy naïve

• Prior negative biopsy

• Active Surveillance
Prostate MRI After Prior Negative Biopsy

• “While blood, urine and tissue based biomarkers may improve patient selection for repeat biopsy, such tests do not help to improve the diagnostic yield of the biopsy itself.”

• “In comparison, imaging has the potential to both improve patient selection and the yield of repeat biopsy.”

www.auanet.org
Prior Negative Biopsy: Clinical Scenario

- 62 year-old with elevated PSA
- PSA: 18.59 ng/ml
- 5 prior negative biopsies
Prior Negative Biopsy

• 62 year-old with elevated PSA
• PSA: 18.59 ng/ml
• 5 prior negative biopsies
• Prostate MRI:
  • Right Anterior-Apical Lesion
Prior Negative Biopsy

- 62 year-old with elevated PSA
- PSA: 18.59 ng/ml
- 5 prior negative biopsies
- Prostate MRI:
  - Right Anterior-Apical Lesion
  - Restricted Diffusion
Prior Negative Biopsy

• 62 year-old with PSA: 18.59 ng/ml
• 5 prior negative biopsies
• Prostate MRI:
  • Right Anterior-Apical Lesion
  • Restricted Diffusion
  • Contrast Enhancement
  • PI-RADS 5
Prior Negative Biopsy

- 62 year-old with a PSA: 18.59
- 5 prior negative biopsies
- Prostate MRI:
  - Right Anterior-Apical Lesion
  - Restricted Diffusion
  - Contrast Enhancement
  - PI-RADS 5
- Transperineal Cognitive Biopsy:
  - Target: Gleason 9 (5+4)
Evaluation of Men with Previous Negative Biopsy by mpMRI

1. Current primary application of mpMRI is in men with a rising PSA for whom there is a suspicion for prostate cancer despite a previous negative prostate biopsy.

2. When high-quality prostate MRI is available, it should be strongly considered in any patient with a prior negative biopsy who has persistent suspicion for cancer and who is undergoing a repeat biopsy.

3. Decision whether to perform MRI in this setting must also take into account results of other biomarkers, the cost of the examination, as well as availability of high quality MRI interpretation.
Evaluation of Men with Previous Negative Biopsy by mpMRI

4. Patients receiving a PI-RADS™ v2 assessment category of 3-5 warrant repeat biopsy with image guided targeting.

5. While TRUS-MRI fusion or in-bore MRI-targeting may be valuable for more reliable targeting, in the absence of such targeting technologies, cognitive (visual) targeting remains a reasonable approach.

6. However, performing solely targeted biopsy should only should be considered once quality assurance efforts have validated the performance of prostate MRI interpretations with results consistent with the published literature.
7. In patients with a negative or low-suspicion MRI (PI-RADS™v2 category of 1 or 2), other ancillary tests (i.e., PSA, PSAD, PSAV, PCA3, PHI) may be of value to identify patients warranting repeat systematic biopsy, although further data is needed.

8. If a repeat biopsy is deferred on the basis of the MRI findings, then continued clinical and laboratory follow-up is advised and consideration should be given to incorporating repeat MRI in this diagnostic surveillance regimen.
Potential Prostate MRI Applications

• Biopsy naïve

• Prior negative biopsy

• Active Surveillance
Active Surveillance

- Imaging may detect tumors previously missed on biopsy.
- MRI could provide a non-invasive monitoring of prostate.
- Lesion location may influence monitoring and treatment.
Evaluated 207 active surveillance patients
All entered active surveillance based on systematic biopsy
mpMRI and fusion biopsy occurred on active surveillance
83 (40%) were upgraded
  • 49 (59%) based on systematic biopsy
  • 30 (36%) based on targeted cores
  • 4 (5%) on both systematic and targeted cores
Active Surveillance: Clinical Scenario

• 57 year-old male
• History of elevated PSA
• Initial TRUS Biopsy:
  • Low Risk, Gleason 6 (3+3) on the left
• Patient elected to undergo active surveillance
Active Surveillance

- 57 y/o on Active Surveillance
- Initial Biopsy: Gleason 6
- MRI at 1 year
Active Surveillance

• 57 y/o on Active Surveillance
• Initial Biopsy: Gleason 6
• MRI at 1 year:
  • PI-RADS 3 lesion
Active Surveillance

• Initial Biopsy: Gleason 6
• MRI at 1 year:
  • PI-RADS 3 lesion
• Confirmatory Fusion Biopsy:
  • Target: Gleason 6
Active Surveillance

• Initial Biopsy: Gleason 6

• MRI at 1 year:
  • PI-RADS 3 lesion

• Confirmatory Fusion Biopsy:
  • Target: Gleason 6

• MRI at 2 years:
  • Stable lesion
Active Surveillance

• Initial Biopsy: Gleason 6
• MRI at 1 year:
  • PI-RADS 3 lesion
• Confirmatory Fusion Biopsy:
  • Target: Gleason 6
• MRI at 2 years:
  • Stable lesion
• MRI at 3 years:
  • Lesion Progression
Active Surveillance

- Initial Biopsy: Gleason 6
- MRI at 1 year:
  - PI-RADS 3 lesion
- Confirmatory Fusion Biopsy:
  - Target: Gleason 6
- MRI at 2 years:
  - Stable lesion
- MRI at 3 years:
  - Lesion Progression
  - Restricted Diffusion
Active Surveillance

• Initial Biopsy: Gleason 6
• MRI at 1 year:
  • PI-RADS 3 lesion
• Confirmatory Fusion Biopsy:
  • Target: Gleason 6
• MRI at 2 years:
  • Stable lesion
• MRI at 3 years:
  • Lesion Progression
  • Restricted Diffusion
  • Contrast enhancement
  • PI-RADS 4 lesion
Active Surveillance

• Initial Biopsy: Gleason 6
• MRI at 1 year:
  • PI-RADS 3 lesion
• Confirmatory Fusion Biopsy:
  • Target: Gleason 6
• MRI at 2 years:
  • Stable lesion
• MRI at 3 years:
  • PI-RADS 4 lesion
• Repeat Fusion Biopsy:
  • Gleason 7 (4+3), GG 3
Use of MRI for Surveillance of Prostate Cancer

1. Multi-parametric prostate MRI has been demonstrated to improve the diagnosis of intermediate risk and high-risk prostate cancer on targeted prostate biopsy which could be beneficial for identifying men as candidates for active surveillance protocols.

However, the current information about MRI is not sufficient to support a role for repeat MRI without a prostate biopsy in monitoring men on active surveillance.
Statement #6

• MRI-Ultrasound fusion and In-Bore MRI-targeting offer potentially improved targeting of small or difficult to biopsy lesions, however, cognitive (visual) fusion is a reasonable alternative
  • In-Bore and fusion devices are costly, limited availability
  • Cognitive fusion can be done without additional equipment
  • Relies on excellent MRI interpretation
Conclusions: mpMRI

- Significant addition to traditional imaging for management of and has the potential to improve the timely identification of clinically significant cancer.
- Enhanced targeting approaches have the potential to reduce the cost through reduction of unnecessary or inaccurate prostate biopsies.
- Current evidence supports the performance of mpMRI in men with a rising PSA following an initial negative standard prostate biopsy.
- Targeted biopsy, combining mpMRI and TRUS or transperineal biopsy, will likely become the preferred method of initial prostate biopsy in a biopsy naïve man based on data from PROMIS and PRECISION.
Conclusions: mpMRI

• In the future, mpMRI may be beneficial to men with a presumed clinically localized prostatic adenocarcinoma prior to selecting definitive therapy

• Offers useful information for surgical planning with both extirpative and ablative treatments.

• Current enthusiasm for the benefit of mpMRI suggests that more evidence will be forthcoming regarding the role in men managed with active surveillance and in population based screening programs.

• These applications should be considered investigational at this time.
Conclusions

• Increasingly urologists are using mpMRI to evaluate and guide treatment

• AUA Joint Consensus Statement and Policy statement recommend mpMRI for men with a prior negative biopsy and persistent concern for cancer

• NCCN and soon EAU Guidelines recommend mpMRI prior to initial biopsy

• Cost, quality of imaging and experienced interpretation remain important