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

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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
- Prior negative biopsy
- Active Surveillance
- Surgical planning: nerve sparing
- Surgical planning: resectability
- Local recurrence

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 (JNR), 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)

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- Biopsy naïve
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- Surgical planning: nerve sparing
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Potential Prostate MRI Applications

- Biopsy naïve
- Prior negative biopsy
- Active Surveillance

Rationale for Prostate MRI Before Biopsy

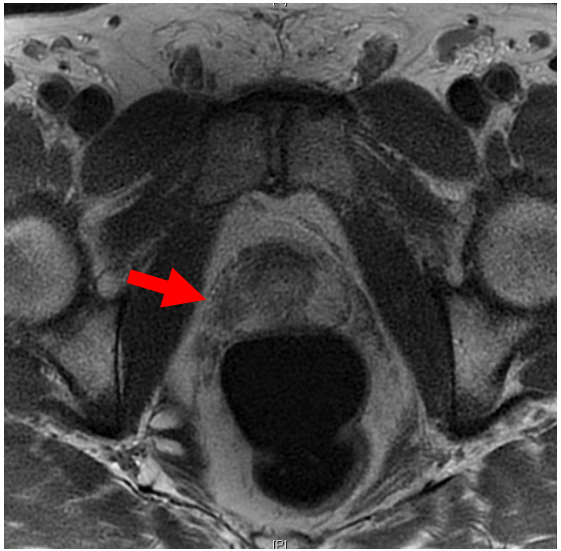
- Majority of initial prostate biopsies are negative
- Many clinically significant cancers are missed
- Extended templates and saturation biopsies are attempts to account for missed tumors

Biopsy Naïve: Clinical Scenario

- 50 year old African American
- PSA 8.6
- Positive Family History

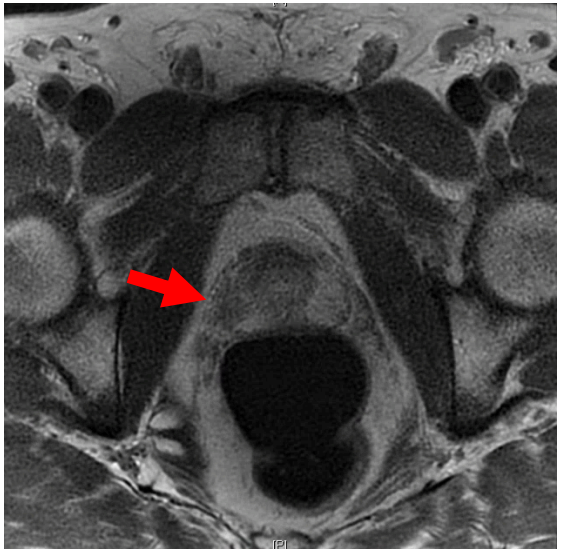
Biopsy Naïve

- 50 year old African American
- PSA 8.6
- Positive Family History
- Prostate MRI:
  - PI-RADS 4 lesion RML



Biopsy Naïve

- 50 year-old African American
- PSA 8.6
- Positive Family History
- Prostate MRI:
  - PI-RADS 4 lesion RML
- MRI/US Fusion Biopsy:
  - 12 core systematic: Negative
  - Target: Gleason 7 (4+3), GG 3



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

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.

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Evaluation of Biopsy Naïve Patients Utilizing mpMRI

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).

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Evaluation of Biopsy Naïve Patients Utilizing mpMRI

- Further refinements in imaging and MRI-targeting strategies required before routine use of 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.

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PROMIS Trial

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

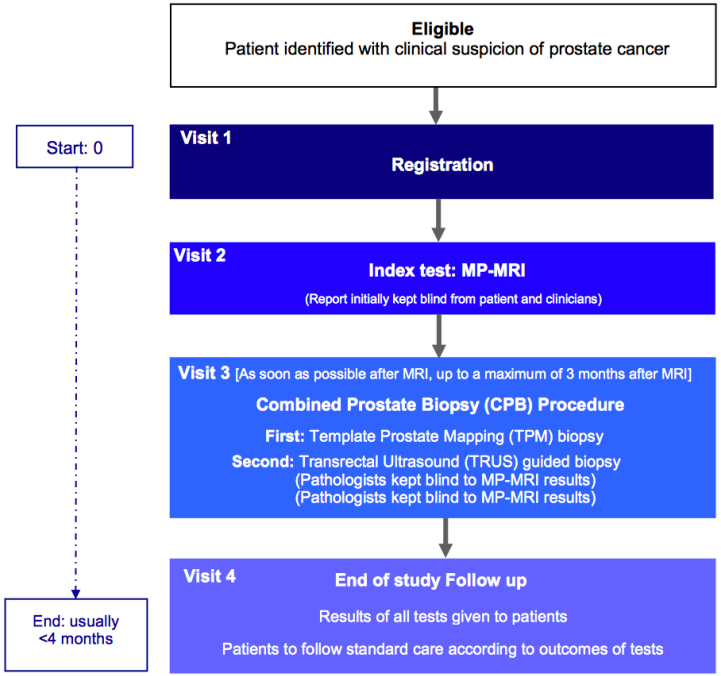
Diagnostic accuracy of multi-parametric MRI and TRUS biopsy in prostate cancer (PROMIS): a paired validating confirmatory study

Hashim U Ahmed, Ahmed El-Shater Bosaily*, Louise C Brown*, Rhian Gabe, Richard Kaplan, Mahesh K Parmar, Yolanda Collaco-Moraes, Katie Ward, Richard G Hindley, Alex Freeman, Alex P Kirkham, Robert Oldroyd, Chris Parker, Mark Emberton, and the PROMIS study group†*

www.thelancet.com **Vol 389 February 25, 2017**

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 Bx to Mapping Bx



PROMIS Trial: Results

- Cancer detection on Template (Reference) Biopsy:
  - All Cancers: 408 (71%)
  - Clinically Significant: 230 (40%)
- Clinically Significant Prostate Cancer:
  - mpMRI: Sensitivity: 93%, NPV: 89%
  - TRUS Bx: Significantly worse sensitivity: 48%, NPV: 74%
- Compared to TRUS biopsy for all
  - mpMRI as a triage test:
    - Avoid a biopsy in 158 (27%)
    - Cost: missed clinically significant cancer in 17 (3%)
  - Assuming mpMRI targeted biopsy has similar detection to template biopsy
    - Detect 102 (18%) additional clinically significant cancers

PROMIS Trial: Results

Gleason scores of men with clinically significant cancer on mapping biopsy

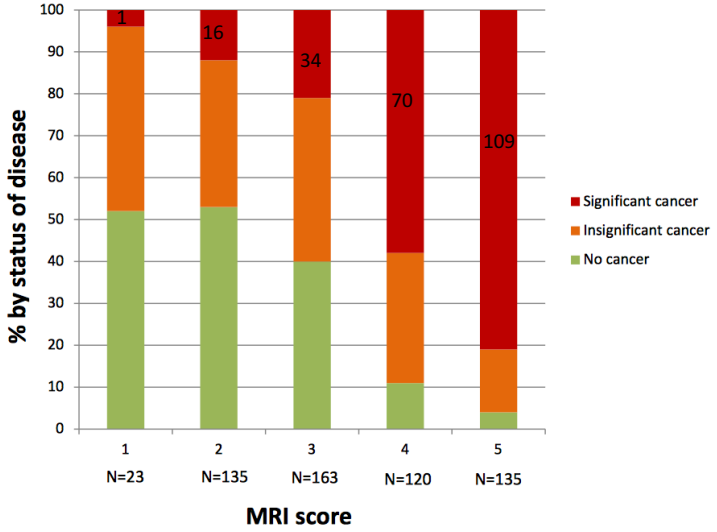
Gleason grades	Clinically significant cancer* N=230
Mean (SD) cancer core length, mm	9.1 (2.7)
3+3	10#
3+4	164#
3+5	1
4+3	44
4+4	0
4+5	7
5+3	0
5+4	4

**Defined as maximum cancer core length of 6mm or greater in any one location and/or the presence of dominant/primary Gleason pattern 4 or greater (i.e., Gleason >/=4+3).*
 # Men classified as clinically significant on the basis of core length despite having low Gleason grades

10 (4%) Gleason 3+3, but classified significant based on core length

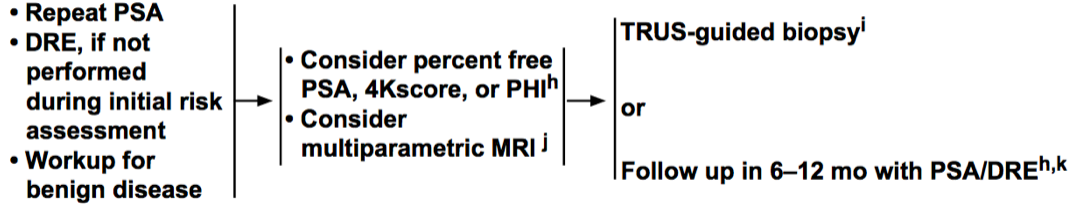
PROMIS Trial: Results

Cancer Detected on Mapping Biopsy Based on MRI Score



NCCN Guidelines: Post-PROMIS

Early Detection Evaluation: Indication for Biopsy



NCCN Guidelines: Post-PROMIS

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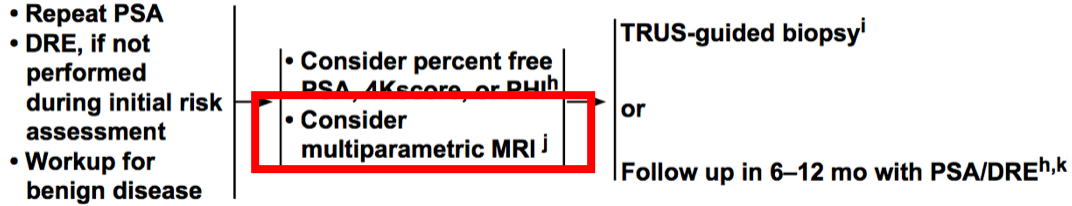

Potential Prostate MRI Applications

- 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.”

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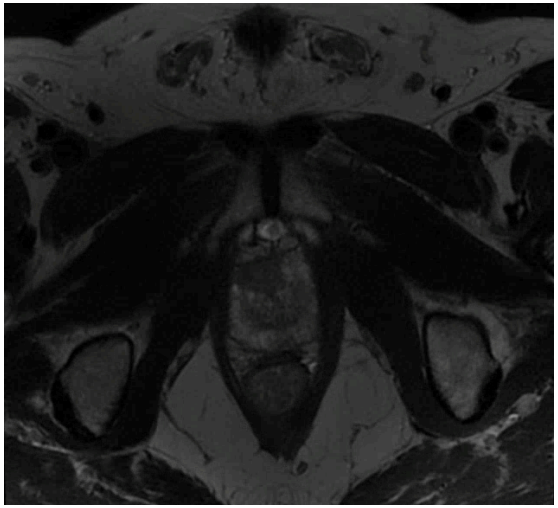
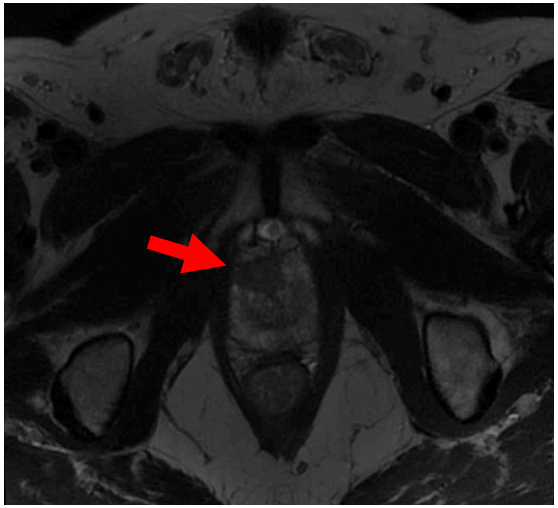
Prior Negative Biopsy: Clinical Scenario

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



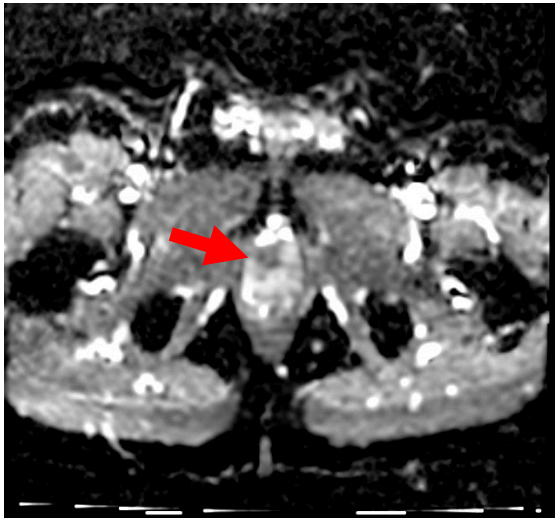
Prior Negative Biopsy

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



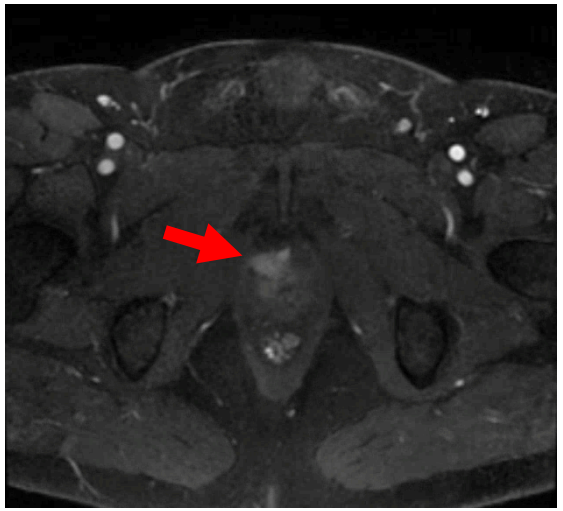
Prior Negative Biopsy

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



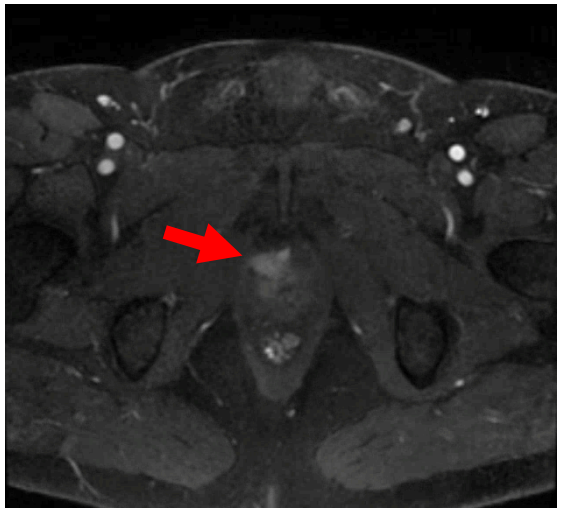
Prior Negative Biopsy

- 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)



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

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 any other biomarkers, the cost of the examination, as well as availability of high quality prostate MRI interpretation

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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 in skilled hands.
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.

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Evaluation of Men with Previous Negative Biopsy by mpMRI

7. In patients with a negative or low-suspicion MRI (PI-RADSTM 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.

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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

Magnetic Resonance Imaging–Ultrasound Fusion Biopsy During Prostate Cancer Active Surveillance

Geraldine N. Tran [a,], Michael S. Leapman [b,d], Hao G. Nguyen [b,d], Janet E. Cowan [b], Katsuto Shinohara [b,d], Antonio C. Westphalen [c,d], Peter R. Carroll [b,d]*

- 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

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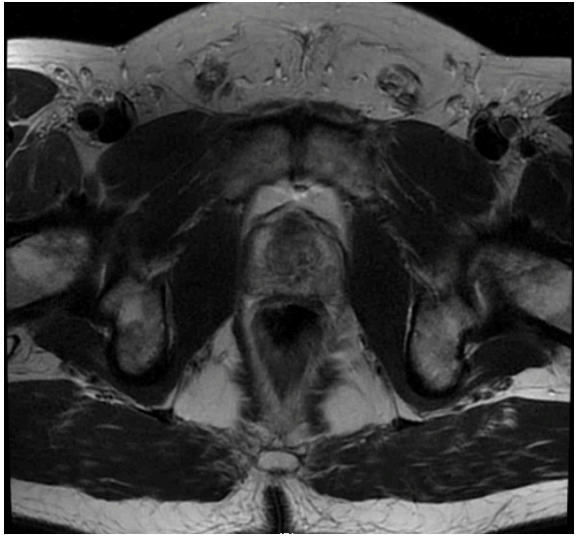
Active Surveillance: Clinical Scenario

- 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

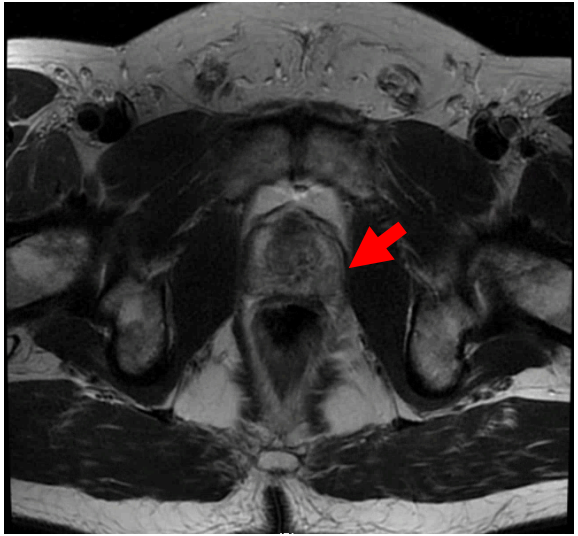
Active Surveillance

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



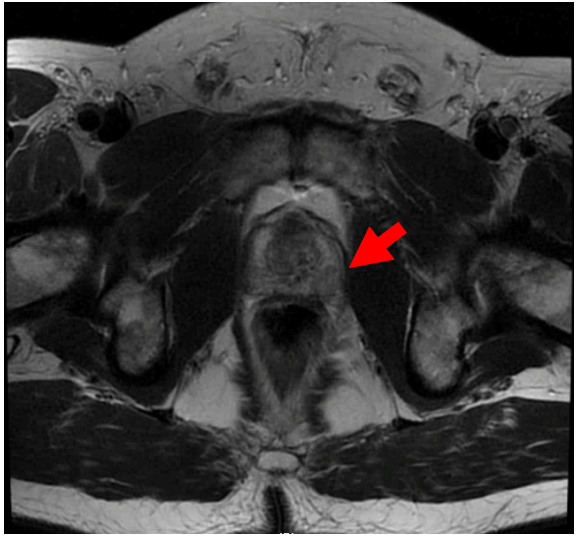
Active Surveillance

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



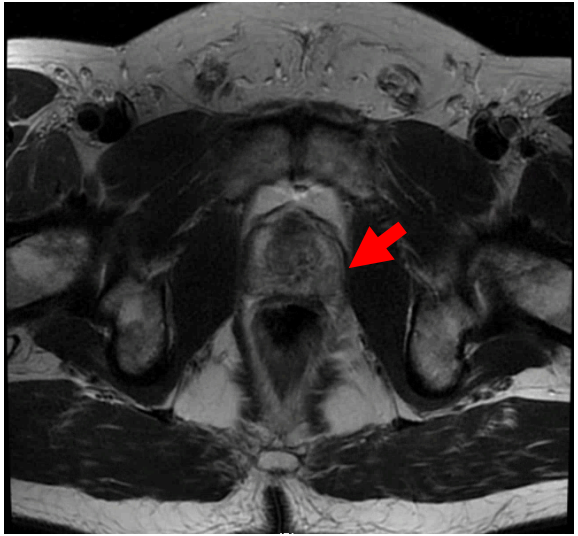
Active Surveillance

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



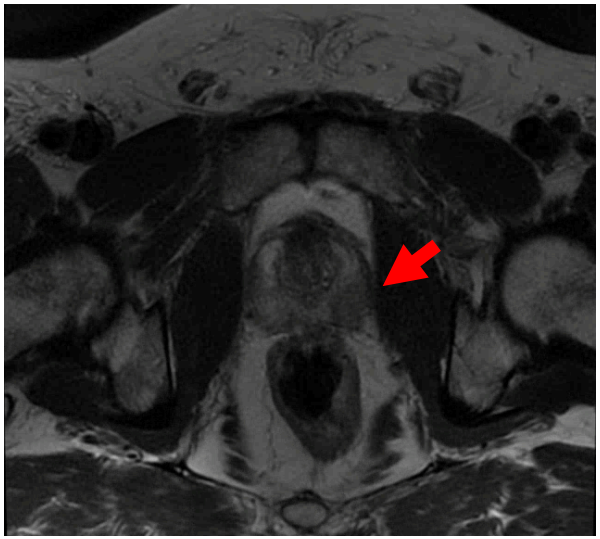
Active Surveillance

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



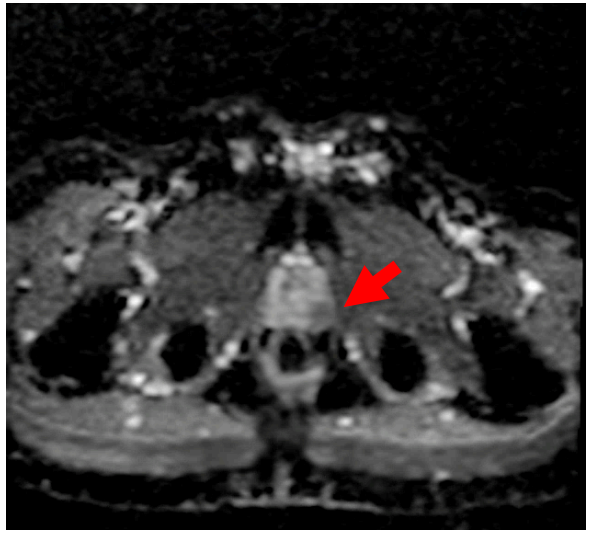
Active Surveillance

- 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



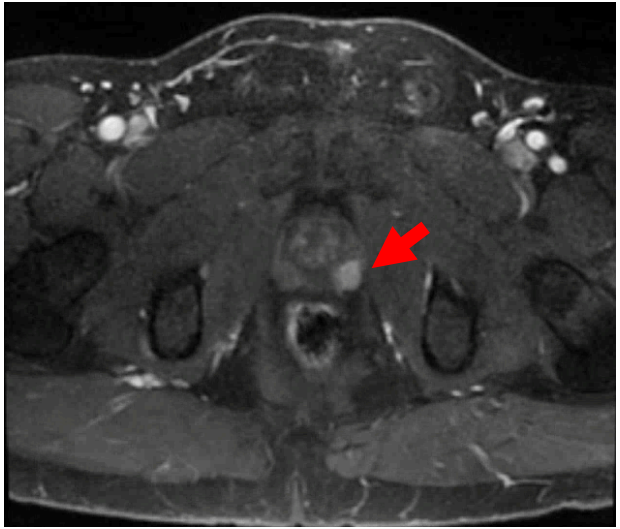
Active Surveillance

- 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



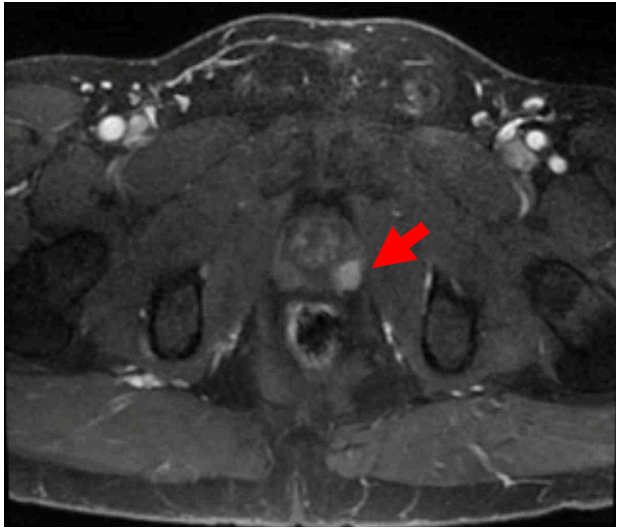
Active Surveillance

- 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



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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.

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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 prostate cancer 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 with an abnormal DRE or an elevated PSA value.

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 potential 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 urologist 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 Guidelines recommend consideration of mpMRI prior to initial biopsy
- Cost, Quality of imaging and experienced interpretation remain important

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