All men should have an MRI prior to first prostate biopsy

PMH Dialogues – Sep 2019

Nathan Perlis, MD MSc FRCSC
Urologic Oncology, UHN, UofT
Disclosures

• None relating to this presentation
All men should have an MRI prior to first prostate biopsy

• What are the goals of a prostate biopsy?
  1. Identify clinically significant disease
  2. Avoid clinically insignificant disease
  3. Provide meaningful information to tailor treatment

“It may be more inconvenient, but the ‘reverse prostate exam’ is a lot less embarrassing for the both of us.”
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  3. Reproducible
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"It may be more inconvenient, but the ‘Reverse Prostate Exam’ is a lot less embarrassing for the both of us."

MRI identifies clinically significant cancer

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

On TRUS Bx:

- 452 no cancer or non-significant cancer
  - 119 significant cancer on TPM
  - 333 no cancer or non-significant cancer on TPM

On MRI:

- 158 no cancer or non-significant cancer
  - 17 significant cancer on TPM
    - 1 MRI 1
    - 16 MRI 2
  - 141 no cancer or non-significant cancer on TPM
    - 22 MRI 1
    - 119 MRI 2

www.thelancet.com  Published online January 19, 2017  http://dx.doi.org/10.1016/S0140-6736(15)32401-1
MRI identifies clinically significant cancer

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

<table>
<thead>
<tr>
<th></th>
<th>MP-MRI, % (95% CI)</th>
<th>TRUS-biopsy, % (95% CI)</th>
<th>Test ratio* (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any Gleason score 7 (≥3+4), prevalence of clinically significant cancer 308 (53%, 49-58%)</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Sensitivity test</td>
<td>88 (84-91)</td>
<td><strong>48 (43-54)</strong></td>
<td>0.55 (0.49-0.62)</td>
<td>p&lt;0.0001</td>
</tr>
<tr>
<td>Specificity test</td>
<td>45 (39-51)</td>
<td>99 (97-100)</td>
<td>2.22 (1.94-2.53)</td>
<td>p&lt;0.0001</td>
</tr>
<tr>
<td>PPV</td>
<td>65 (60-69)</td>
<td>99 (95-100)</td>
<td>40.8 (10.2-162.8)</td>
<td>p&lt;0.0001</td>
</tr>
<tr>
<td>NPV</td>
<td>76 (69-82)</td>
<td>63 (58-67)</td>
<td>0.53 (0.38-0.73)</td>
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MRI identifies clinically significant cancer

Table 2. Comparison of Cancer Detection between Groups.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>MRI-Targeted Biopsy Group (N = 252)</th>
<th>Standard-Biop Group (N = 248)</th>
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<tr>
<td>Biopsy outcome — no. (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No biopsy because of negative result on MRI</td>
<td>71 (28)</td>
<td>0</td>
</tr>
<tr>
<td>Benign tissue</td>
<td>52 (21)</td>
<td>98 (40)</td>
</tr>
<tr>
<td>Atypical small acinar proliferation</td>
<td>0</td>
<td>5 (2)</td>
</tr>
<tr>
<td>High-grade prostatic intraepithelial neoplasia</td>
<td>4 (2)</td>
<td>10 (4)</td>
</tr>
<tr>
<td>Gleason score</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3+3</td>
<td>23 (9)</td>
<td>55 (22)</td>
</tr>
<tr>
<td>3+4</td>
<td>52 (21)</td>
<td>35 (14)</td>
</tr>
<tr>
<td>3+5</td>
<td>2 (1)</td>
<td>1 (&lt;1)</td>
</tr>
<tr>
<td>4+3</td>
<td>18 (7)</td>
<td>19 (8)</td>
</tr>
<tr>
<td>4+4</td>
<td>13 (5)</td>
<td>6 (2)</td>
</tr>
<tr>
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<td>2 (1)</td>
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<tr>
<td>5+5</td>
<td>3 (1)</td>
<td>1 (&lt;1)</td>
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Level 1 evidence

Gl7 or worse 95 vs 64
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42 pts ≥Gl7 on TRUS Bx that were missed on MRI

74 pts Gl6 on TRUS Bx that would have been avoided on MRI Bx

91 ≥Gl7 that were Dx on MRI Bx and missed on TRUS Bx

Only 38 Gl6 Dx w MRI Bx that were avoided w TRUS Bx

---

Comparison of MR/Ultrasound Fusion-Guided Biopsy With Ultrasound-Guided Biopsy for the Diagnosis of Prostate Cancer

M. Minhaj Siddiqui, MD; Sorosh Rais-Bahrami, MD; Baris Turkbey, MD; Arvin K. George, MD; Jason Rothwax, BS; Nabeel Shalik, BS; Chinonyerem Okoro, BS; Dimo Raskolnikov, BS; Howard L. Barnes, MD; W. Marston Linehan, MD; Maria J. Merino, MD; Richard M. Simon, DSc; Peter L. Choyke, MD; Bradford J. Wood, MD; Peter A. Pinto, MD

Figure 3. Comparison of Pathology From Standard Extended-Sextant Biopsy and Targeted MR/Ultrasound Fusion Biopsy for Prostate Cancer
MRI avoids diagnosing clinically insignificant cancer

Use of prostate systematic and targeted biopsy on the basis of multiparametric MRI in biopsy-naïve patients (MRI-FIRST): a prospective, multicentre, paired diagnostic study

Olivier Rouvière, Philippe Puech, Raphaëlle Renard-Pennet, Michel Caudou, Catherine Roy, Florence Mège-Lechevallier, Myriam Decaussin-Petruci, Marine Dubreuil-Chambardel, Laurent Magnaud, Laurent Remontet, Alain Sufjani, Marc Colombel, Sébastien Crouzet, Anne-Marie Schott, Laurent Lemaitre, Muriel Rabilloud, Nicolas Grenier, for the MRI-FIRST Investigators*

250 men all had MRI, TRUS Bx and Fusion Bx.

Similar detection of >=Gl7

But still 7.6% clinically significant PC would be missed without MRI, impressive since:

All hypoechoic lesions were targeted during TRUS
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MRI provides meaningful information to tailor treatment

Length of Capsular Contact for Diagnosing Extraprostatic Extension on Prostate MRI: Assessment at an Optimal Threshold

Andrew B. Rosenkrantz, MD,1* Alampady K. Shanbhogue, MD,1 Annie Wang, MD,1 Max Xiangtian Kong, MD,2 James S. Babb, PhD,1 and Samir S. Taneja, MD3


EPE is strongly predicted by lesion capsular contact

Any EPE – 6mm contact on T2 image

Non-focal EPE – 10mm contact T2 image

AUC 0.81

FIGURE 2: A 67-year-old man with Gleason score 3+4 tumor in left posteromedial peripheral zone on radical prostatectomy. (a) Axial T2WI and (b) axial ADC map show dominant lesion (arrow) matching prostatectomy findings. Lesion was not considered to exhibit EPE based on subjective interpretation by either reader. Length of capsular contact measures over 6 mm on both image sets. Focal EPE was present pathologically.

FIGURE 3: A 60-year-old man with Gleason score 4+3 tumor in the right posterolateral peripheral zone on radical prostatectomy. (a) Axial T2WI and (b) axial ADC map show dominant lesion (arrow) matching prostatectomy findings. Lesion was not considered to exhibit overt EPE based on subjective interpretation by either reader. Length of capsular contact measures over 10 mm on both image sets. Nonfocal EPE was present pathologically.
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MRI: **safe**, affordable, reproducible?

- Precision NEJM 2018
  - MRI w fusion Bx only vs TRUS Bx
    - Immediate HRQOL and pain similar
    - 2% in each arm serious adverse events
    - Fewer 30d complications in MRI Bx: hematuria, hematospermia, pain, ED, rectal bleeding

- Barnett et al, BJUI 2018
  - Decision tree analysis, multiple sensitivity analyses, Markov modelling
  - Best strategy: MRI if PSA ≥4, combined biopsy PIRADS ≥3, no Bx if MRI negative
  - Cost-effective strategy assuming a willingness-to-pay threshold of $100,000/QALY

- Rosenkrantz et al, RSNA 2016
  - Experienced radiologists achieved moderate reproducibility for PI-RADS v2
  - Agreement better in PZ than TZ
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TRUS Biopsy vs MRI and fusion biopsy
All men should have an MRI prior to first prostate biopsy

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Ideas for debate

PROMIS study
- MRI has greater sensitivity and specificity for clinically significant cancer than TRUS Biopsy

- PRECISION trial
  - RCT comparing two clinical approaches in men with AbN PSA and clinical history concerning for clinically significant prostate cancer:
    a) MRI approach: MRI for everyone \( \rightarrow \) then only perform fusion biopsy to visible lesions (and avoid biopsy for men with normal MRIs)
    b) No MRI approach: Systematic TRUS biopsy for everyone

<table>
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<th>No MRI approach</th>
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<tr>
<td>( \rightarrow ) More clinically significant cancer found</td>
<td>( \rightarrow ) Cheaper</td>
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<tr>
<td>( \rightarrow ) More men avoid biopsy altogether</td>
<td>( \rightarrow ) Easier</td>
</tr>
<tr>
<td>( \rightarrow ) MRI useful for future interventions</td>
<td>( \rightarrow ) Requires less expertise and re-training</td>
</tr>
<tr>
<td>• Surgical/Radiation/Ablation planning</td>
<td></td>
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<tr>
<td>• Tumour evolution on Surveillance</td>
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All men should have an MRI prior to first prostate biopsy rebuttal...

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Level 1 evidence for pre-biopsy MRI

Strategies vary

Each approach has a unique balance between morbidity of multiple tests and biopsies

Talk to your patients and learn about their own preferences and risk tolerance
EAU 2019 recommendations in biopsy naïve pt

- Perform mpMRI before prostate biopsy (1a, strong)
- When mpMRI is positive (PI-RADS >=3) perform combination of targeted and systematic (2a, weak)
- When mpMRI is negative and patient has low risk of clinically significant disease (risk calculator or biomarker) consider avoiding biopsy (2a, weak)
PRostate Evaluation for Clinically Important Disease: MRI vs Standard Evaluation Procedures (PRECISE)

The safety and scientific validity of this study is the responsibility of the study sponsor and investigators. Listing a study does not mean it has been evaluated by the U.S. Federal Government. Know the risks and potential benefits of clinical studies and talk to your health care provider before participating. Read our disclaimer for details.

Arms and Interventions

**Arm A**
MRI
Men in Arm A will undergo a MRI followed by either a targeted biopsy of suspicious areas or will be followed for two years if there is no suspicious areas identified by MRI. The unbiopsied men will have a repeat MRI at 2 years.

**Active Comparator: Standard of Care**
Men in Arm B will undergo a 12-core systematic TRUS guided biopsy. All men in the study will be followed for two years or until they have had radical treatment (whichever comes first).

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Principal Investigator: Laurence Klitz, MD

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Principal Investigator: Antonio Finelli, MD

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Principal Investigator: Franck Bladou, MD
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Lancet Oncol 2019; 20: 100–09

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