MRI Before Biopsy Should be the Standard of Care - Con

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Background

To be of value, MRI in biopsy-naïve men followed by TRUS-Fusion biopsy or MRI guided biopsy requires:

- MRI with excellent test performance
- A technology that is generalizable
- Fusion (regardless of approach) that is accurate in targeting the identified lesion
- A cancer biology associated with a dominant lesion that is high-grade and visualized by MRI
- Diminished morbidity
- Cost effective
mpMRI Performance

- Test performance varies with setting and the reference
  - Up to 20% of negative MRI have clinically significant prostate cancer (CSPC)
  - The prototypical Anterior Tumour that is always presented, over-represents the situation
How common is this?
What would MRI add?
What would MRI add?

And more importantly, which scenario is more common?
mpMRI Performance

• Biopsy naïve setting

  – MP-MRI fusion TB does not significantly improve detection of CSPC
    • Meng X (Taneja S) et al, Euro Urol 2015, Schoots et al, Eur Urol 2015, Finelli, Haider (CCO systematic review 2015)

  – False positive rate of 17%
    • Bains et al, J Urol 2014

• One can not separate the necessity of fusion biopsy if unable to perform MR guided biopsies
And even if you could, MRI Bx results are imperfect!
• 16 studies that used both MRI-TBx and TRUS-Bx

• A cumulative total of 1926 men with a positive MRI were included, with prostate cancer prevalence of 59%.

• Detection rates MRI-TBx and TRUS-Bx did not significantly differ in overall cancer detection (Sn 0.85, 95% CI 0.80–0.89, and 0.81, 95% CI 0.70–0.88, resp).
MRI-TBx had a:
- higher rate of detection of significant prostate cancer compared to TRUS-Bx (Sn 0.91 vs 0.76) and a
- lower rate of detection of insignificant prostate cancer (Sn 0.44 vs 0.83).

Subgroup analysis revealed an improvement in significant prostate cancer detection by MRI-TBx in men with previous negative biopsy, rather than in men with negative initial biopsy (relative Sn 1.54, 95% CI 1.05–2.57 vs 1.10, 95% CI 1.00–1.22).
mpMRI PiRADS 2 Test Performance

- 62 consecutive patients with 116 lesions who underwent mpMRI at 3T with PI-RADSv2 evaluation and subsequent targeted **MRI/TRUS fusion-guided biopsy** (FgBx) and concurrent 12-core systematic systematic prostate biopsy (SBx) between May-Sept 2015.

- Mean lesion size was 1.27cm overall.

- Lesion-based cancer detection rates (CDR) for all tumors and Gleason ≥3+4 tumors at each PI-RADSv2 score were calculated.
  - Mertan FV (Pinto PA) et al, J Urol 2016
mpMRI PiRADS 2 Test Performance

• Based on targeted biopsy on a per lesion basis

• CDRs for Gleason ≥3+4 tumors was:

  – PI-RADS score
    • 2 – 5.6%
    • 3 – 0
    • 4 – 21.3%
    • 5 – 75%
    – Mertan FV (Pinto PA) et al, J Urol 2016
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- Dr. Perlis – will you biopsy PiRAD 3 or only 4 and/or 5?
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†

Lancet 2017; 389:815
PROMIS


- **Brief summary and highlights:**
  - Paired validation cohort of patients undergoing mpMRI (index test), TRUS bx (current standard), and template prostate mapping (reference)
  - MRI outperformed systematic biopsy in sensitivity (93%) and negative predictive value (89%)
  - Potentially avoided biopsy in men at low risk of harbouring clinically significant cancer (27% negative MRI), and probable cost-effectiveness
PROMIS – Issues

1. No actual MRI guided or MRI targeted biopsies were performed!!! Instead, PROMIS compared MRI imaging results with transperineal template bx assuming that theoretically $MRI = MRI \text{ bx}$
   
   – Correct comparison would be MRI bx vs TRUS bx
   
   – Completely omits the issue of hitting these lesions / accuracy which is subject to centre-specific factors, patient, and learning curve
   
   – If MRI bx was (performed and) compared, would likely underperform
PROMIS – Issues

2. Are these rates of PIRADS 4/5 consistent with our practice?
PROMIS – Issues

• 3. Reproducibility of MRI results

  – Assessed by two trained expert uro-radiologists, kappa 0.5 (moderate agreement)

  – Unknown number of “scans of insufficient quality” repeated
PROMIS – Issues

• 4. Cost effectiveness analysis
  – Minimal difference between “most cost effective threshold” = mpMRI + up to two targeted biopsies (sensitivity 0.95, £807/patient) versus systematic biopsy followed by MRI (sensitivity 0.91, £709/patient)
    • Completely dependent on assumptions
  
  – Cost effectiveness strategy changed between MRI and TRUS based on sensitivity of MRI targeted bx (not assessed in PROMIS)
  
  – Effect in a Canadian context (vs. UK) unknown
MRI-Targeted or Standard Biopsy for Prostate-Cancer Diagnosis

The NEW ENGLAND JOURNAL of MEDICINE

MRI-Targeted or Standard Biopsy for Prostate-Cancer Diagnosis


PRECISION is not to be confused with Accuracy
**PRECISION**

- Multicentre, randomized, non inferiority trial
- 500 men randomized across academic and community sites with 1.5T and 3.0T MRI machines, endorectal coil and without, cognitive and fusion biopsy
- Positive MRI proceeded to targeted biopsy of their lesion and those without were not offered biopsy versus systematic TRUS bx
- MRI increased detection of CSPC 38% vs. 26%
- MRI had fewer clinically insignificant PC 9% vs 22%
- Avoided biopsy in 28%
PRECISION – Issues

- Are these rates representative of disease in Canada?
PRECISION – Issues

- Did the young Dr. Perlis read the ENTIRE paper??
Let’s start with Table 1 like every good journal club.

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<th>Standard-Biopsy Group (N=248)</th>
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<td>Age — yr</td>
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<td>PSA level — ng/ml</td>
<td>Median 6.75</td>
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<td>Interquartile range 5.16–9.35</td>
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<td>Family history of prostate cancer — no. (%)</td>
<td>48 (19)</td>
<td>40 (16)</td>
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<td>Abnormal digital rectal examination — no. (%)</td>
<td>36 (14)</td>
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**Table 1. Characteristics of the Participants at Baseline.***

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How many 64 y.o. in your practice with PSA 6.7 at presentation or will you order MRI earlier?
How about the Supplementary tables??

S16
- 24/64 (38%) had discordant pathology between local and central review
- Of these, 14/24 (58%) would have changed management
- In particular, 5 cases where it was PIRADS 1-2 versus PIRADS 4 on central review
- Learning curve??
PRÉCISION – Issues

- Supplementary table S15, higher rate of discordant pathology (both upgrading and downgrading) in MRI arm versus final RP pathology

Table S15: Gleason grade concordance with original biopsy after radical prostatectomy

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<th>Concordant</th>
<th>Upgraded</th>
<th>Downgraded</th>
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<td>MRI±TB arm - no. (%)</td>
<td>19 (63.3)</td>
<td>5 (16.7)</td>
<td>6 (20.0)</td>
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<td>TRUS biopsy arm - no. (%)</td>
<td>19 (70.4)</td>
<td>4 (14.8)</td>
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MRI±TB = MRI±targeted biopsy, TRUS = Transrectal ultrasound guided. Results of radical prostatectomy were available for 30 of the 34 men in the MRI±TB arm and 27 of the 30 men in the TRUS biopsy arm. The remainder were lost to follow up.
MRI in Biopsy-naïve Patients is not ready for primetime

- Test performance is not high enough
  - A great deal of PROMIS with questionable PRECISION and accuracy
  - Generalizeability is lacking

- Distribution of PiRAD scores and yield of CSPC unlikely the case in Canada

- High rates of discordance with final pathology remain
MRI in Biopsy Naïve Patients –

CON Rebuttal

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The Impact of Tumor Volume and Multi-focality

- Retrospective study was performed with 122 consecutive men who underwent mp-MRI before RP at a single referral academic center.

  - 39/151 (26%) tumours were missed even though they were > 1cm in diameter

  - 36/239 (15%) with Gleason 3+4 or higher were missed

  - Le JD et al (Marks L), Euro Urol 2015
239 were multifocal and 44 were solitary

Le JD (Marks L) et al, Euro Urol 2015
The Impact of Tumor Volume and Multi-focality

- Of the 122 cases, 44 (36%) had solitary and 78 (64%) had multifocal tumors.

- Overall mp-MRI sensitivity for tumor detection was 47% (132/283), with increased sensitivity for:
  - larger (102/141 [72%] >1.0 cm),
  - higher-grade (96/134 [72%] Gleason 7) tumors, and
  - index tumors (98/122 [80%]).
Other Issues to Consider

- **Learning Curve**
  - Prostate cancer detection rate on mpMRI increased from 42% to 81% over series ($P < 0.001$).
    - The prostate cancer detection rate by targeted biopsy increased from 27% to 63% ($P < 0.001$).
    - The negative predictive value of MRI for significant cancer (>Gleason 3+3) was 88.9% later in the series compared with 66.6% earlier.
      - Gaziev et al, BJUI

- **Cost**
  - MRI utilization, Software and expanding indications
Other Issues to Consider

- **Fusion Technique and room for Error**
  - Software Registration versus Cognitive fusion
  - The overall detection rate of cancer is significantly higher in a software fusion cohort (48.1%) compared with both cognitive fusion (34.6% P = .04) and conventional biopsy (32.0%, P = .03).
    - Oberline D et al, Urol 2016

  - *Is the target registered accurately? Is the target being struck consistently and reliably?*

- **Morbidity**
  - *No data to support lower risk of sepsis because of less cores*
Ontario Specific Data

- The wait time for Priority 4 which is what most prostate MRI's for high PSA and non-staging would be coded is a mean of 59 days with a low of 12 and high of 195.

- Number of magnets in Ontario (2017): 74 sites with 120 units - includes private units 8.49/million.
  - The vast majority of these are 1.5T
How to follow these patients? What next?

- Natural history of MRI unknown
  - Conversion rate
  - Timing for repeat/confirmatory MRI
  - Rate of upgrading/downgrading

- Wide variability in the progression (regression) of lesions and appearance (disappearance) of new lesions in repeat MRI
  - 70% of patients had progression across median 2 yrs (PI-RADS upgrade, new lesions, increase in size)
Who will you order it for?

- What will be the threshold to prompt MRI in this setting??
Urologists

• *Isn’t this reminiscent of the screening enthusiasm associated with the introduction of PSA?*
Urologists

• Isn’t this reminiscent of the screening enthusiasm associated with the introduction of PSA?
MRI in biopsy-naïve men is not ready for prime time!
Thank You