TRUS Biopsy, MRI, and PROMIS Trial

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January 24, 2019
Disclosure

- Co-Founder and Chief Science Officer, Precision Biopsy Inc., Aurora, CO
1. **PROstate MR Imaging Study** (or **PROMIS**) showed mpMRI performed better than expected diagnosing clinically significant prostate cancer with sensitivity **93%** and the negative predictive value **89%** compared to TRUS biopsy with sensitivity **48%** and negative predictive value **74%**. What is the definition of clinically significant cancer used here?

   A. Gleason score $\geq 3+4$ or cancer core length $\geq 4$ mm
   B. Any Gleason score 7 ($\geq 3+4$) cancer
   C. Gleason score $\geq 4+3$ or cancer core length $\geq 6$ mm
   D. Gleason score $\geq 3+4$ or tumor volume $\geq 0.5$ cc
   E. None of the above
### PROMIS Trial Results for Clinically Significant Cancer

<table>
<thead>
<tr>
<th>N= 576</th>
<th>GS ≥ 4+3 or cancer core ≥ 6 mm</th>
<th>GS ≥ 3+4 or cancer core ≥ 4 mm</th>
<th>GS ≥ 3+4</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n = 230 (40%)</td>
<td>n = 331 (57%)</td>
<td>n = 308 (53%)</td>
</tr>
<tr>
<td></td>
<td>mpMRI</td>
<td>TRUS</td>
<td>mpMRI</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>87% (83-90%)</td>
<td>48% (42-55%)</td>
<td>87% (83-90%)</td>
</tr>
<tr>
<td>Specificity</td>
<td>47% (40-53%)</td>
<td>96% (94-98%)</td>
<td>47% (40-53%)</td>
</tr>
<tr>
<td>PPV</td>
<td>69% (64-73%)</td>
<td>90% (83-94%)</td>
<td>69% (64-73%)</td>
</tr>
<tr>
<td>NPV</td>
<td>72% (65-79%)</td>
<td>74% (69-78%)</td>
<td>72% (65-79%)</td>
</tr>
<tr>
<td>AUC</td>
<td>0.67 (0.63-0.71)</td>
<td>0.72 (0.63-0.71)</td>
<td><strong>0.67 (0.63-0.71)</strong></td>
</tr>
</tbody>
</table>

- Study results did not provide AUC information
- Our estimates of AUC are given in the table
- AUC of TRUS is better than mpMRI (0.79 vs 0.67) for diagnosis of GS ≥ 3+4 or cancer core ≥ 4 mm (this result may be statistically significant)
Comparison of ROC curves

- 0.90-1.0 = excellent
- 0.80-0.90 = good
- 0.70-0.80 = fair (TRUS)
- 0.60-.70 = poor (mpMRI)
- 0.50-.60 = fail (F)

mpMRI performance is highly dependent on:
- Expertise of radiologist
- Methods used (ex: PIRADS)
- Quality of scans
- Types of scanners
PROMISed Benefits

- mpMRI to triage men allow 27% of patients avoid a primary biopsy
- mpMRI diagnose 5% fewer clinically insignificant cancers
- If TRUS-biopsies directed by mpMRI findings, up to 18% more cases of clinically significant cancer might be detected compared to standard TRUS-biopsy
Limitations of PROMIS Trial

- mpMRI used a 1.5T rather than 3T which may be more contemporary
- UK cohort is “symptomatic” - May harbor large lesions (≥ 0.5cc) easily visible on mpMRI whereas US cohort is largely “asymptomatic” and may harbor smaller clinically significant
- No use of the now standardized PIRADS score for MRI reporting
- No ROC reported for dozen or so radiologists
- No AUC data reported to compare mpMRI versus TRUS
- Economic data is yet to be reported. The reality of implementing this new pathway will depend on service availability, local expertise, wait times and cost.
- Absence of Lesion-Level Analysis – No information whether mapping biopsy detected cancer lesions identified on mpMRI
A cohort of 47 patients at the University of Colorado Hospital (UCH) chose template-guided transperineal mapping biopsy (MB)

All patients had 3T endorectal-coil mpMRI prior to MB

Histopathology of MB was independently read by a pathologist

Prostate divided to 12 segments (apex, mid, base; anterior, posterior; left, right)

PI-RADS scores assigned to each segment by two radiologists independently, with any discordance resolved by a third radiologist

MB data co-registered to each segment without the knowledge of mpMRI data

Clinically significant lesion defined as a tumor with volume $\geq$ 0.5cc and/or Gleason score $\geq$ 7 without extra-capsular extension
Template-Guided Transperineal Mapping Biopsy

![Image of medical equipment and diagram showing biopsy process]
PI-RADS Scores for 12 Segments of the Prostate

Assignment of PI-RADS scores to 12 prostate segments

Lesion is considered detected if PI-RADS score \( \geq 3 \) associates with histopathology in at least one segment

Co-registration of histopathology data to segments
UCH Study: mpMRI miss CS tumors

- 47 patients had mapping biopsy after MRI
  - 34 had clinically significant cancer

- mpMRI missed **6/34 (18%)** patients with CS cancer (table)

- mpMRI missed **10/25 (40%)** tumors with Gleason Score ≥ 7 and **27/60 (45%)** CS cancer (table)

- Some patients may harbor more than one CS lesion (figure)

<table>
<thead>
<tr>
<th>Indication to Biopsy by PIRADS Score ≥ 3</th>
<th>Patient Level</th>
<th>Lesion Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Statistics</td>
<td>N = 47 (CS=34)</td>
<td>N = 122 (CS=60)</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>82%</td>
<td>55%</td>
</tr>
<tr>
<td>Specificity</td>
<td>54%</td>
<td>74%</td>
</tr>
<tr>
<td>PPV</td>
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<td>67%</td>
</tr>
<tr>
<td>NPV</td>
<td>54%</td>
<td>63%</td>
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mpMRI Invisible Patients

GS = 8 (4+4) tumor, volume > 0.5 cc

GS = 7 tumor, volume >0.5 cc

GS = 7 tumor, volume >0.5 cc
Comparison of PROMIS and UCH Study

<table>
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<th>CS Cancer: Gleason score ≥ 4+3 or cancer core length ≥ 4 mm</th>
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<td>UCH Results</td>
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<td><strong>AUC</strong></td>
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<td>0.68 (0.53-0.81)</td>
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UCH Study: mpMRI diagnosed all Gleason score ≥ 4+3 cancer with 100% sensitivity and NPV
Conclusions

1. Depending on the definition, some clinically significant cancer MRI invisible

2. Prostate MRI costs vary $500 to $2,500 in US

3. 1 million American men sent for prostate biopsy every year. If all of those received mpMRI instead, costs could reach $3 billion annually

4. Lack of expertise to read mpMRI - prostate MRI results from community hospitals only agree with high-volume, expert facilities only 54% of the time

5. Scaling up prostate MRI capabilities at hospitals throughout the country will take time and significant expense

6. “PROMIS works as advertised if: you do not expect to find every millimeter of significant disease; if you accept that results depend on your definition of clinical significance; and if you quality assure ever scanner, optimize the sequences iteratively, quality control scans and have robust training for radiologists” - Dr. Jochen Walz (France), EAU 2017