Five-year Outcomes from a Prospective Phase I Study of MRI-guided Transurethral Ultrasound Ablation in Men with Localized Prostate Cancer

Shiva Nair, G Hatiboglu, J Relle, J Hafron, M Roethke, M Mueller-Wolf, D Bonekamp, Z Kassam, R Staruch, M Burtynk, HP Schlemmer, S Pahernik, J Chin
MRI-guided transurethral ultrasound ablation (TULSA)

- **Incision-free** procedure for customized ablation of prostate tissue
- Conducted within an MRI, offering high-resolution planning images, **real-time MRI guidance** and closed-loop thermal feedback
- Transurethral directional ultrasound under continuous rotational sweep for precise thermal ablation of small or large regions
- Water cooling of urethra and rectum
Phase I Safety and Feasibility: 5-year Outcomes

Conservative whole-gland ablation (90%)

- Targeted prostate volume defined with **3-mm safety margin** from prostate capsule
- Intentionally sparing 10% viable prostate tissue at periphery

Inclusion Criteria

- Age ≥ 65 years, PSA ≤ 10 ng/ml
- No prior PCa treatment
- Gleason Score 3+3 (3+4 in Canada)
- Eligible for MRI, and anesthesia
- Prostate length ≤ 5 cm, width ≤ 6 cm
Primary Outcomes (1-Year)

Safety

• No intraoperative complications, no rectal injury or fistula, and no severe urinary incontinence
• Urinary tract infection (10 G2), acute retention (3 G1; 5 G2), epididymitis (1 G3). No new serious/severe adverse events between 1y and 5y

Feasibility

• Accuracy ± precision of heating: 0.1 ± 1.3 mm (n=30)
• Prostate volume mean 47 cc (95% CI 41–54, range 21–95)
• Treatment time mean 36 min (95% CI 32–40, range 24–61)
• PSA decreased from 5.8 (3.8-8.0) ng/ml to 0.8 (0.5-1.1) ng/ml at 1 month, stable at 1 year 0.8 (0.6-1.1) ng/ml.

Exploratory Endpoints (1 and 3-Year)

1-Year MRI and Biopsy

- 88% prostate volume reduction, matching 90% planned ablation volume.
- Significant PCa in 9/29, any disease 16/29, 61% reduction in PCa length, risk of residual disease was accepted by conservative treatment protocol

3-Year Biopsy

- 3/22 refused biopsy, 12/22 negative
- Significant PCa in 2/22, any disease in 7/22

5-Year Follow-Up

Salvage-free survival

- 16 men completed 5y follow-up, 3 left with PSA <0.4 ng/ml, 1 died (unrelated)
- 10 underwent salvage treatment: 6 RP, 3 EBRT, 1 laser
- Estimated 5-year salvage free survival: 65% (95CI: 50-85%).

PSA

- Stable to 5y in 16 men with complete follow-up:
  Median 0.6 ng/ml
  (IQR 0.4-1.2 ng/ml)
- Estimated 5-year biochemical failure free survival: 66% (95CI: 50-87%).
5-Year Follow-Up: Quality of Life

In 16 men who completed 5 year follow-up:

• **Continence**: 16/16 leak-free, pad-free at 1 and 5y
• **Erections** sufficient for penetration: 9/16 at baseline, 7/16 at 5y
Salvage Radical Prostatectomy

- 4 salvage RP at 1 site: minimal fibrosis, no complications or rectal injury
- Whole mount histology showed 2 pT2b and 2 pT3a consistent with persistent cancer in untreated peripheral safety region

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<thead>
<tr>
<th></th>
<th>Mean operating time (min)</th>
<th>Blood loss (ml)</th>
<th>Length of stay (days)</th>
<th>Perioperative complications</th>
<th>Tumor Stage</th>
<th>Tumor Grade</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>191 (165-217)</td>
<td>900 (700-1000)</td>
<td>3.5 (2-6)</td>
<td>None</td>
<td>pT2b (2/4), pT3a (2/4)</td>
<td>4+3 (1/4), 3+4 (3/4)</td>
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<td>Stress urinary incontinence</td>
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<td>Mild 2/4, Implant 1/4</td>
<td>2/4</td>
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<td>Erect Dys. unresponsive to PDE-5i</td>
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<td>Biochemical recurrence</td>
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<td>2/4</td>
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</table>

Conclusions

• Five-year follow-up of MRI-guided TULSA in men with localized PCa demonstrates low toxicity, stable quality of life and disease control, while maintaining salvage treatment options.

• Phase I safety and feasibility protocol with only 90% ablation accepted risk of residual disease. Larger pivotal study used intensified treatment parameters for complete whole-gland ablation (AUA Virtual Experience PD17-02).