Convective RF Water Vapor Energy Ablation Effectively Treats LUTS due to BPH, Preserves Erectile and Ejaculatory Function

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Minimally Invasive Prostatic Vapor Ablation - Multicenter, Randomized, Controlled Study for the Treatment of BPH (Rezūm II)

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BPH Treatments

- Minimally-Invasive Surgical Therapy (MIST) for LUTS due to BPH
  - TUNA
  - TUMT
  - Prostatic Urethral Lift
  - Others

- Limited adoption historically
  - Lack durability, high retreatment rates
  - Restricted patient selection (prostate size, median lobe)
Convective RF Water Vapor Energy Ablation

- Rezūm® (NxThera Inc.)

- Radiofrequency generates wet thermal energy – water vapor (steam)

- Steam travels between cells, not beyond collagen barriers

- Disrupts cell membranes – cell death and necrosis
The Rezūm System

Intended to relieve symptoms, obstructions, and reduce prostate tissue associated with BPH.
**Heat Transfer Mechanism**

**Convective RF Thermal Energy**
- Transition Zone Boundary
- .42 mL RF Water Vapor Injection
- RF vapor convectively dispersed through interstices
- Condensation releases stored thermal energy
- Cell membranes denatured, causing cell death

**Conductive RF Thermal Energy**
- Heat Source
- RF heat conductively transferred from cell to cell
- Conductive heating of prostate tissue occurs
- Temp gradient results in cells near heat source substantially more than those further away
Methods

- Men ≥ 50 years old
- IPSS ≥ 13
- Peak flow rate between 5-15 mL
- Prostate size 30-80cc
- PVR < 250cc
- Middle lobe/Median bar not excluded
- Randomized 2:1 – Rezūm vs sham
  - Sham – cysto, simulated sounds
- Blinded comparison at 3 months
  - Treatment arm followed for 12 months
  - At 3 months, sham subjects given option for Rezūm
Methods

• Primary endpoint – Improvement in IPSS 125% greater in treatment than control group
• Questionnaires
  • IPSS
  • IIEF-15
  • MSHQ-EjD
  • MCID
    • 2 for mild ED, 5 for moderate ED, 7 for severe ED
• Uroflow
• Pain – Visual Analog Scale
Results

• 197 subjects
  • 136 treatment group
  • 61 control group

<table>
<thead>
<tr>
<th></th>
<th>Treatment (SD)</th>
<th>Control (SD)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>63 (7.1)</td>
<td>62.9 (7.0)</td>
<td>0.914</td>
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<tr>
<td>BMI</td>
<td>28.7 (4.4)</td>
<td>28.1 (5.0)</td>
<td>0.363</td>
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<tr>
<td>Prostate vol</td>
<td>45.8 (13.0)</td>
<td>44.5 (13.3)</td>
<td>0.525</td>
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<tr>
<td>PSA</td>
<td>2.1 (1.5)</td>
<td>2.0 (1.6)</td>
<td>0.695</td>
</tr>
<tr>
<td>IPSS</td>
<td>22 (4.8)</td>
<td>21.9 (4.7)</td>
<td>0.857</td>
</tr>
<tr>
<td>Qmax</td>
<td>9.9 (2.3)</td>
<td>10.4 (2.1)</td>
<td>0.187</td>
</tr>
<tr>
<td>PVR</td>
<td>82 (51.5)</td>
<td>85.5 (51.6)</td>
<td>0.658</td>
</tr>
<tr>
<td>IPSS QoL</td>
<td>4.4 (1.1)</td>
<td>4.4 (1.1)</td>
<td>0.800</td>
</tr>
<tr>
<td>IIEF15</td>
<td>17.2 (10.3)</td>
<td>16.5 (9.8)</td>
<td>0.693</td>
</tr>
<tr>
<td>MSHQ-EjD</td>
<td>7.8 (4.1)</td>
<td>9.0 (3.8)</td>
<td>0.050</td>
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</tbody>
</table>
**IPSS, QoL and Qmax**

- **IPSS**:}
  - **Baseline**: Treatment 22.0, Control 21.9
  - **1 Month**: Treatment 14.5, Control 15.1
  - **3 Months**: Treatment 10.6, Control 17.5
  - **6 Months**: Treatment 9.8, Control —
  - **12 Months**: Treatment 10.3, Control —

- **IPSS-QoL**:}
  - **Baseline**: Treatment 4.4, Control 4.4
  - **1 Month**: Treatment 3.3, Control 3.4
  - **3 Months**: Treatment 2.3, Control 3.5
  - **6 Months**: Treatment 2.1, Control —
  - **12 Months**: Treatment 2.1, Control —

- **Qmax (ml/sec)**:}
  - **Baseline**: Treatment 9.9, Control 10.4
  - **1 Month**: Treatment 13.1, Control 12.0
  - **3 Months**: Treatment 16.1, Control 10.8
  - **6 Months**: Treatment 15.4, Control —
  - **12 Months**: Treatment 15.1, Control —

* Denotes significant difference of the treatment group from baseline (>3 months) P<.05
† Denotes significant differences of the treatment group from the control group (≤3 months) P<.05
Results

- Voiding change at 3 months

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<th></th>
<th>Treatment</th>
<th>Control</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>IPSS</td>
<td>-11.2</td>
<td>-4.3</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Qmax</td>
<td>6.2</td>
<td>0.5</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>PVR</td>
<td>-10.6</td>
<td>7.2</td>
<td>0.108</td>
</tr>
<tr>
<td>IPSS QoL</td>
<td>-2.1</td>
<td>0.9</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

- ≥8 point improvement IPSS in >70% of treatment group at 3 months and through end of study
**IIEF-EF, MSHQ-EjD Function, MSHQ-EjD Bother**

### IIEF-EF

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>3 Months</th>
<th>6 Months</th>
<th>12 Months</th>
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<tbody>
<tr>
<td>Treatment</td>
<td>22.6</td>
<td>22.7</td>
<td>22.7</td>
<td>22.9</td>
</tr>
<tr>
<td>Control</td>
<td>21.2</td>
<td>21.0</td>
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### MSHQ-EjD Function

<table>
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<tr>
<th></th>
<th>Baseline</th>
<th>3 Months</th>
<th>6 Months</th>
<th>12 Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment</td>
<td>9.3</td>
<td>9.7</td>
<td>9.7</td>
<td>9.3</td>
</tr>
<tr>
<td>Control</td>
<td>9.8</td>
<td>9.6</td>
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### MSHQ-EjD Bother

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>3 Months</th>
<th>6 Months</th>
<th>12 Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment</td>
<td>2.2</td>
<td>1.8</td>
<td>1.8</td>
<td>1.5</td>
</tr>
<tr>
<td>Control</td>
<td>2.0</td>
<td>1.8</td>
<td></td>
<td></td>
</tr>
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</table>

* p<.05
IIEF Domains for Sexually Active Subjects

Erectile Function
- Baseline: Treatment, Control
- 3 Months: Treatment, Control

Orgasmic Function
- Baseline: Treatment, Control
- 3 Months: Treatment, Control

Sexual Desire
- Baseline: Treatment, Control
- 3 Months: Treatment, Control

Intercourse Satisfaction
- Baseline: Treatment, Control
- 3 Months: Treatment, Control

Overall Satisfaction
- Baseline: Treatment, Control
- 3 Months: Treatment, Control

P-values:
- Erectile Function: P=0.795
- Orgasmic Function: P=0.425
- Sexual Desire: P=0.153
- Intercourse Satisfaction: P=0.603
- Overall Satisfaction: P=0.321
Minimal Clinically Important Difference (MCID)*

- MCID for the EF domain represents the smallest difference in score that patients perceive as a benefit, or clinically meaningful
- Changes needed: Mild ≥ 2; Moderate ≥ 5; Severe ≥ 7

Results

• Ejaculatory bother improved 31% over baseline (p=0.0011)

• MCID (mild-2, moderate-5, severe-7)

<table>
<thead>
<tr>
<th></th>
<th>n/N (3 month)</th>
<th>MCID (3 month)</th>
<th>n/N (12 month)</th>
<th>MCID (12 month)</th>
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</thead>
<tbody>
<tr>
<td>Severe (1-10)</td>
<td>2/7</td>
<td>12.5</td>
<td>2/3</td>
<td>11.5</td>
</tr>
<tr>
<td>Moderate (11-16)</td>
<td>9/15</td>
<td>10.1</td>
<td>6/13</td>
<td>11.2</td>
</tr>
<tr>
<td>Mild (17 – 25)</td>
<td>18/68</td>
<td>4.0</td>
<td>13/61</td>
<td>5.3</td>
</tr>
<tr>
<td>Improved scores (%)</td>
<td>29/90 (32%)</td>
<td></td>
<td>21/77 (27%)</td>
<td></td>
</tr>
</tbody>
</table>
Results

• 42 subjects w median lobe
  • Treatment of median lobe at discretion of physician

• 30 subjects had treatment of median lobe
  • Outcomes similar to subjects without median lobe
  • Symptom scores (p = 0.33)
  • Flow rates (p = 0.52)
Treatment of Obese Subjects

Percentage of Patients with IPSS ≥ 50% Improvement

- Similar improvement in obese and non-obese subjects
- Obese subjects with severe LUTS – earlier and slightly higher percentage of response
Treatment of Obese Subjects

- Obesity associated with more moderate/severe ED
- MCID achievement rate similar regardless of weight or ED severity

<table>
<thead>
<tr>
<th>IIEF-EF Severity</th>
<th>BMI ≤30 (n=54)</th>
<th>BMI ≥30 (n=30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe (1-10)</td>
<td>1</td>
<td>13</td>
</tr>
<tr>
<td>Moderate (11-16)</td>
<td>11</td>
<td>27</td>
</tr>
<tr>
<td>Mild (17-30)</td>
<td>87</td>
<td>60</td>
</tr>
<tr>
<td><strong>Achieved MCID</strong></td>
<td><strong>11/54 (20%)</strong></td>
<td><strong>8/30 (27%)</strong></td>
</tr>
</tbody>
</table>

**MCID** (minimal clinically important difference): minimal increase in IIEF-EF
Mild ED ≥2; Moderate ED ≥ 5; Severe ED ≥ 7
Obesity Effects Response to Medical Treatment?

- Obese (>30 BMI) had the greatest improvement in IPSS total and storage and voiding sub-scores compared with baseline.

- This group also had the largest placebo response among the groups.
Central obesity is predictive of persistent storage LUTS after surgery for BPH: results of a multicenter prospective study

Mean and 95% confidence interval of the mean of postoperative IPSS storage score, stratified according to the number of MetS parameters (age adjusted wald 1.090, p=0.009)
Figure 1: a) total International Prostatic Symptoms Score (IPSS) before (PRE) and after (POST) surgery for BPH; b) Storage IPSS subscore before and after surgery for BPH. WC = waist circumference. Adapted from: Gacci M et al, BJU Int 2015 [29]
Conclusions

- Rezūm® significantly improves symptoms due to BPH in patients with moderate to severe LUTS
- Erectile function is not affected by treatment
- Obese patients experience similar improvements as non-obese patients