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Final 5-Year Outcomes of the Multicenter Randomized Sham-Controlled Trial of a Water Vapor Thermal Therapy for Treatment of Moderate to Severe Lower Urinary Tract Symptoms Secondary to Benign Prostatic Hyperplasia

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Study Need and Importance: The final 5-year results of the Rezūm II study show strong evidence for a minimally invasive surgical treatment (MIST) for BPH that not only offers robust functional outcomes but does so without the historical tradeoffs of limited durability or compromised sexual function. Although many MIST options have been developed over the last several decades, high rates of re-treatment, sexual dysfunction, and/or morphological limitations like an obstructive middle lobe have remained as common barriers to wide adoption.

What We Found: Significant improvement of lower urinary tract symptoms (LUTS) was observed through 5 years with International Prostate Symptom Score reduction of 48%, quality of life increase of 45%, peak urinary flow rate improvement of 44% and a Benign Prostatic Hyperplasia Impact Index decrease of 48%. The surgical re-treatment rate was 4.4% with preserved sexual function. Validating the frequency with which urologists encounter obstructing median tissue, 31% of treated subjects received water vapor treatment to a middle lobe.

Limitations: Study limitations included participant attrition (57% at 5 years) although the statistical significance of the functional results was not negatively impacted. Additionally, the lack of urodynamic testing limits the opportunity to analyze bladder function, the degree of obstruction, bladder contractility and the potential impact on these results therein.

Interpretations for Patient Care: Rezūm™ water vapor therapy is a minimally invasive treatment option that can be performed in a physician's office under local anesthesia that provides long lasting results. It can treat difficult anatomical variants like obstructive middle lobe without advanced training or techniques. This MIST challenges the long-held algorithm of men needing endless medications followed by an invasive surgery if their LUTS progresses. Physicians can now offer an option that removes the obstructive tissue and treats the associated symptoms without permanent implants or prescriptions, while patients no longer have to choose which symptoms or side effects they want to continue to tolerate and can receive definitive treatment in their urologist's office.

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Final 5-Year Outcomes of the Multicenter Randomized Sham-Controlled Trial of a Water Vapor Thermal Therapy for Treatment of Moderate to Severe Lower Urinary Tract Symptoms Secondary to Benign Prostatic Hyperplasia

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Abbreviations and Acronyms

AE = adverse event
BPH = benign prostatic hyperplasia
BPHII = BPH Impact Index
FDA = U.S. Food and Drug Administration
IPSS = International Prostate Symptom Score
ITT = intent-to-treat
LIFT = Prostatic Urethral Lift for the Treatment of LUTS Associated with BPH
LUTS = lower urinary tract symptoms
MIST = minimally invasive surgical therapy
MSHQ-EjD = Male Sexual Health Questionnaire for Ejaculatory Dysfunction
MTOPS = Medical Therapy of Prostatic Symptoms
PSA = prostate specific antigen
PUL = prostatic urethral lift
Qmax = peak urinary flow rate
QOL = quality of life
TUMT = transurethral microwave thermotherapy
TUNA = transurethral needle ablation of the prostate
TURP = transurethral resection of the prostate

Purpose: We present final 5-year outcomes of the multicenter randomized sham-controlled trial of a water vapor therapy (Rezūm™) for treatment of moderate to severe lower urinary tract symptoms due to benign prostatic hyperplasia.

Materials and Methods: A total of 197 subjects >50 years of age with International Prostate Symptom Score ≥13, maximum flow rate ≤15 ml/second and prostate volume 30 to 80 cc were randomized and followed for 5 years. From the control arm of 61 subjects, a subset of 53 subjects requalified and after 3 months received treatment as part of the crossover group and were also followed for 5 years. The total number of vapor treatments to each lobe of the prostate was determined by length of prostatic urethra and included middle lobe treatment per physician discretion.

Results: Significant improvement of lower urinary tract symptoms was observed at <3 months post-thermal therapy, remaining durable through 5 years in the treatment group (International Prostate Symptom Score reduced 48%, quality of life increased 45%, maximum flow rate improved 44%, Benign Prostatic Hyperplasia Impact Index decreased 48%). Surgical re-treatment rate was 4.4% with no reports of device or procedure related sexual dysfunction or sustained de novo erectile dysfunction. Results within the crossover group were similar through 5 years.

Conclusions: Minimally invasive treatment with water vapor thermal therapy provides significant and durable symptom relief as well as flow rate improvements through 5 years, with low surgical re-treatment rates and without

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impacting sexual function. It is a versatile therapy, providing successful treatment to obstructive lateral and middle lobes.

Key Words: prostate; prostatic hyperplasia; minimally invasive surgical procedures; urologic surgical procedures, male

THE prevalence of benign prostatic hyperplasia (BPH) rises drastically as age advances. Between 50% and 70% of men suffer from lower urinary tract symptoms (LUTS) associated with BPH after the age of 50 years, while evidence suggests that the prevalence of LUTS/BPH is as high as 80% by the eighth decade.[1]

The available treatment options for moderate to severe LUTS/BPH range from oral medications to surgical treatments.[2] Most commonly, the first line of treatment is medication, via alpha blocker and/or 5alpha-reductase inhibitor prescribed as either monotherapy or combination therapy. Evidence suggests, however, that due to adverse events (AEs), poor medication adherence, and/or disease progression, many men seek secondary treatment.[3] Common AEs associated with alpha blocker include abnormal ejaculation due to reduced or absent seminal fluid, dizziness and postural hypotension. With 5alpha-reductase inhibitors, AEs include erectile dysfunction, reduced libido and less commonly ejaculation failure, retrograde ejaculation and gynecomastia.[4] Transurethral resection of the prostate (TURP) has traditionally been considered the gold standard surgical treatment option.[2] While TURP has demonstrated its efficacy in improving urinary symptoms, acute safety concerns and long-term negative impacts such as erectile and ejaculatory dysfunction, possible incontinence as well as other associated complications have been well documented.[5]

As an alternative to TURP, minimally invasive surgical therapies (MISTs) have emerged as options to relieve symptoms while minimizing or eliminating hospital stays and complications.[2] Rezūm™ water vapor thermal therapy (Rezūm System, Boston Scientific, Marlborough, Massachusetts) is an innovative MIST cleared by the U.S. Food and Drug Administration in 2015 to reduce prostate tissue volume associated with BPH, including hyperplasia of the central zone and/or a middle lobe.[6] This therapy transfers stored thermal energy (540 calories/ml H_2O) as vapor to the prostatic tissue. No thermal effects occur outside the targeted treatment zone,[7] thus addressing limitations of conductive heat transfer experienced with other MISTs such as transurethral needle ablation of the prostate (TUNA) and transurethral microwave thermotherapy (TUMT), where cell kill gradient was noted.[8]

The most unique feature of this thermal therapy is that it can treat lateral and central zones without morphological limitation or learning an advanced technique. Difficult anatomical variants, such as intravesical prostatic protrusion, can be treated without effects on sexual function.[9] In the 5 years following FDA clearance, the system has been embraced by urology practices, health technology assessment bodies, and urological societies throughout the U.S. and Europe.[10,11] This adoption is attributed to the evidence of its clinical advantages, including sustained relief of LUTS, enhanced quality of life, and durability of treatment response.[12–14] In this manuscript, we report final 5-year clinical results for the treatment and crossover arms for the multicenter, prospective, blinded, controlled trial of water vapor thermal therapy (Rezūm II Study, NCT01912339).

MATERIALS AND METHODS

The pivotal study was conducted at 15 centers in the United States with a followup period of 5 years. In total, 384 subjects were screened and 197 subjects entered the study. All participants signed a written informed consent form prior to participation, and approval of the protocol was granted by an institutional review board (IRB No. 2105-001) for each participating investigational site. Subjects >50 years of age who had moderate to severe symptomatic BPH were included in the study. A complete list of inclusion and exclusion criteria for this clinical trial has been previously published.[15] Key inclusion criteria consisted of International Prostate Symptom Score (IPSS) $\geq$13 and prostate volume 30 cm^3 to 80 cm^3 without restrictions on the presence of a middle lobe. Subjects were randomized to treatment and control in a 2:1 ratio using a permuted-block randomization schedule with varying block size, stratified on center and baseline IPSS. Unblinded at the 3-month followup visit, 53 control subjects requalified for inclusion in the study and elected to receive thermal therapy. Crossover treatment occurred within 3 to 6 months post-enrollment date.

Statistical Method

The study was powered at 80% with 0.025 one-sided type I error to evaluate the hypothesis that the reduction in IPSS from baseline to 3 months for the active treatment exceeds 125% of that for the control. This hypothesis was assessed using a Student t-test on the intent-to-treat (ITT) populations to compare the mean changes in treatment and control arms. For the primary efficacy end point, subjects who chose alternate treatments other than the assigned treatment prior to the 3-month followup period were considered failures and their baseline value

was used for the primary end point analysis. Summary results for quantitative variables were presented as mean±standard deviation.

Procedure

The technology, device description and technical details of the procedure for water vapor thermal therapy have been published in detail in earlier reports.[12] The basic principle of the system is to apply a controlled level of radiofrequency power to an inductive coil heater in the delivery device through which a predetermined amount of sterile water is delivered to selected areas of the prostate. Using a transurethral approach, the heat generated by the radiofrequency power transforms the sterile water from liquid to vapor state (stored thermal energy). The vapor is convectively delivered directly into the tissue interstices of the hyperplastic tissue in the transition zone of the prostate when treating the lateral lobes, or in the central zone of the prostate in the case of treatment for an obstructive middle lobe. Each vapor injection lasts for 9 seconds. The number of injections varies from case to case depending on the size of the prostate and whether the physician chooses to treat the median tissue. Subjects in the control arm underwent a sham procedure with 19Fr to 21Fr rigid cystoscopy.

Study Assessment

The efficacy end point comparing the treatment and sham/control arms was measured at 3 months post-procedure via IPSS. Subjects were unblinded following completion of their 3-month followup visit, and participants in the control arm were offered the option of treatment with the system if they still met the initial study inclusion criteria. Crossover treatment occurred within 3 to 6 months after the enrollment date. Subjects in the treatment and crossover arms were followed at 3, 6 and 12 months, and then annually until 5 years. At each followup visit, subjects were evaluated by measuring peak urinary flow rate (Qmax), post-void residual volume, voided volume, and prostate specific antigen (PSA), and by administration of the IPSS, IPSS quality of life (QOL) and BPH Impact Index (BPHII) surveys. Incontinence was assessed using the Overactive Bladder Questionnaire-Short Form and International Continence Society Male Incontinence Scale Questionnaire-Short Form. Sexual function was assessed using the International Index of Erectile Function-erectile function domain and the Male Sexual Health Questionnaire for Ejaculatory Dysfunction (MSHQ-EjD). The protocol prespecified a responder end point defined as freedom from re-treatment for BPH and 30% reduction of IPSS from baseline. AEs were captured and adjudicated by independent data monitoring and clinical events committees. To prevent loss to followup and minimize attrition, patients were closely followed as per clinical trial protocol. Re-treatment of BPH, by medical or surgical management, was recorded and followup of the subject discontinued.

RESULTS

A total of 136 subjects were randomized to the treatment arm and 61 subjects were randomized to the control arm. Of the control subjects 53 requalified for crossover, received treatment, and participated in followup through 5 years (see table).

Baseline characteristics of treatment and crossover subjects

	Treatment Group (mean±SD)*	Crossover Group (mean±SD)
No. pts	135	53
Age at screening (yrs)	63.0±7.1	62.9±7.0
PSA (ng/ml)	2.1±1.5	2.1±1.6
IPSS	22.0±4.8	20.0±6.6
IPSS QOL	4.4±1.1	3.9±1.4
Prostate vol (cm^3)	45.9±12.9	44.5±13.3
Qmax (ml)	9.9±2.2	10.1±3.7
Post-void residual vol (ml)	82.4±51.5	93.9±77.2

* One subject from treatment cohort opted out immediately from the study without being treated with the water vapor thermal therapy procedure, and consequently that subject was not considered while calculating average baseline values.

All of the water vapor thermal therapy treatments were completed in the office or ambulatory surgery center. Of these 188 treated subjects, 170 (90.4%) received oral pain medication, 39 (20.7%) received a prostate block/epidural and 19 (10.1%) subjects received intravenous sedation (1 subject opted out of the study after preparation for the procedure, but prior to treatment). The mean±SD number of vapor injections per subject was 4.5±1.8 (135) and 5.1±1.9 (53) across the treatment and crossover groups, respectively. Middle lobe was noted and treated in 58 of 188 subjects (30.9%). These subjects received an additional mean±SD 1.6±0.7 injections to the median tissue. The average±SD procedure time (initial insertion of device until complete removal) for subjects in the treatment arm was 5.3±3.5 minutes, and 4.4±1.7 minutes in the crossover arm.

As noted in figure 1, after 5 years, data from 77 subjects from the treatment arm were analyzed. There were no study withdrawals attributed to any procedure or device-related AEs. Eighteen subjects were lost to followup, while an additional 13 withdrew consent. Five subjects were censored for protocol noncompliance, and 2 were withdrawn for prostate cancer treatment. Within the crossover group, 21 subjects completed 5 years of followup. Ten subjects withdrew consent and an additional 5 were lost to followup. One subject was censored for noncompliance, 1 due to cancer diagnosis, and 1 subject died due to unrelated causes.

Device and procedure related AEs were similar between groups. A total of 151 related AEs were reported in 53 subjects in the treatment arm and 59 events in 23 subjects in the crossover group. As expected, the most common AEs related to the device or procedure were dysuria (16.9% and 18.9%), gross hematuria (12.5% and 11.3%), hematospermia (7.4% and 3.8%), urinary frequency (5.9% and 5.7%), acute urinary retention (4.4% and 5.7%),

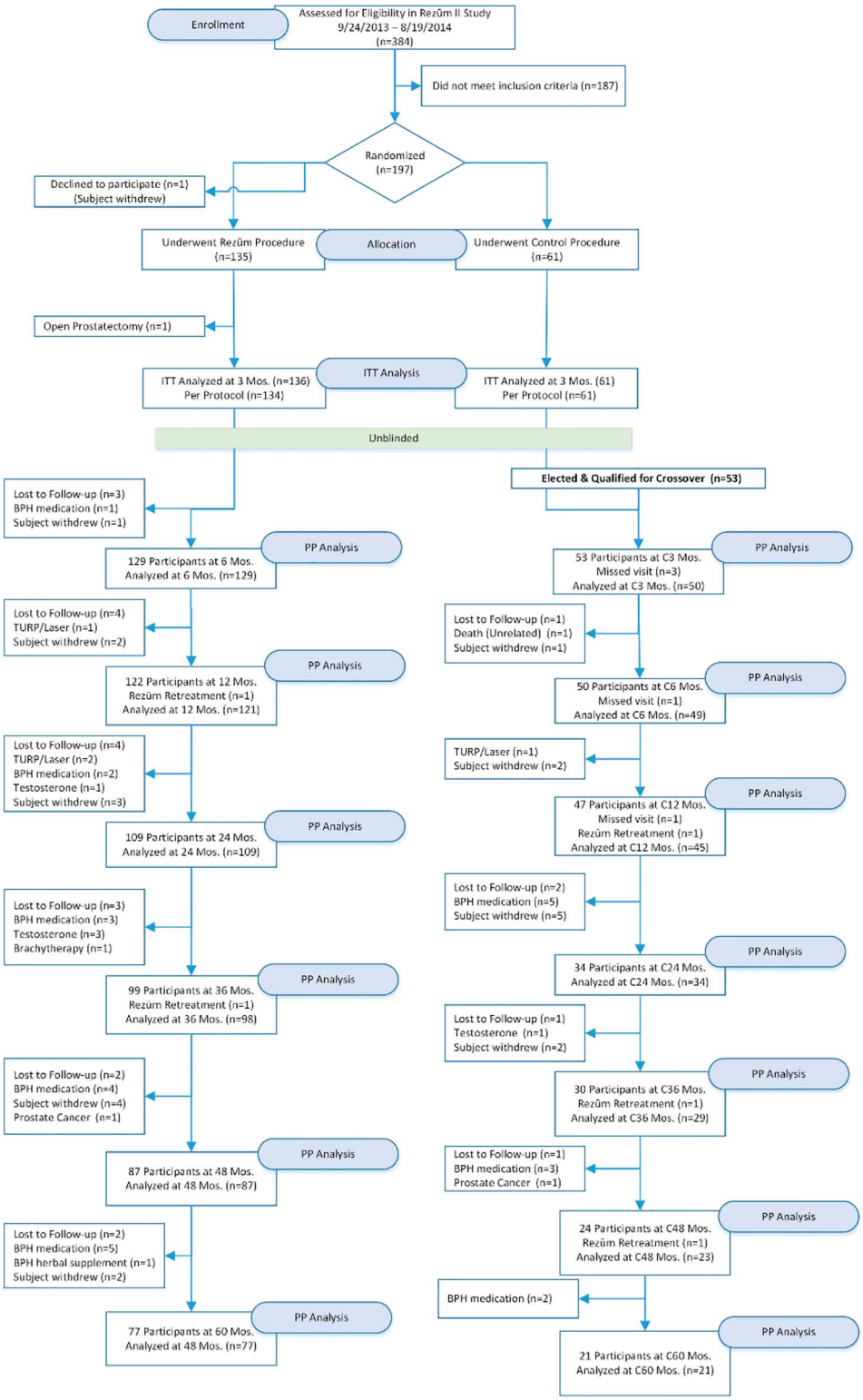

Figure 1. CONSORT (Consolidated Standards of Reporting Trials) diagram of subject disposition in water vapor thermal therapy study, including thermal therapy, control and crossover (*C*) groups. Subjects re-treated with water vapor thermal therapy procedures were excluded from analysis. *PP*, per protocol analysis.

suspected urinary tract infection (3.7% and 7.5%), and decrease in ejaculatory volume (3.7% and 7.5%) between the treatment and crossover arms, respectively. These AEs were mild to moderate in severity and resolved either spontaneously or with routine treatment. No late related AEs occurred from years 1 to 5. Details of all other AEs, including serious AEs, were previously reported.[12–14]

Outcome measures for the original treatment arm are as follows: IPSS decreased from 22.0 points at baseline to 10.6 at 3 months for a change of −11.3±7.6. The primary end point analysis demonstrated that the IPSS reduction in the active treatment exceeded 125% of that in the control arm ($p < 0.0001$). IPSS score improvement remained consistent throughout the study as the value at 5 years showed near 48% reduction (mean±SD 11.1±7.8) from baseline. Similarly, the improved IPSS QOL score remained consistent from baseline reducing from a mean±SD value of 4.4±1.1 to 2.3±1.5 at 3 months and to 2.2±1.4, or 45% reduction at 5 years. Flow rate as measured by Qmax (voided volume ≥125 ml) exhibited similar sustained improvement: increasing from a mean±SD baseline of 9.9±2.2 to 15.5±6.7 at the end of year 1 and remaining at 14±5.4 (49%) through year 5 of followup. Additionally, 5-year BPHII results, which peaked at a 51% decrease 6 months post-treatment (mean±SD 2.1±1.5), showed similarly durable improvement with a mean decline of 45% at 5 years (2.2±1.4; fig. 2). Furthermore, 61% of subjects in the treatment arm (82 of 135) were both free from retreatment and had a 30% or greater reduction from baseline IPSS at 5 years.

There were no reports of de novo device or procedure-related erectile dysfunction throughout the duration of the study. Five-year results corresponded well with prior time points. Mean PSA value remained stable through 5 years of followup. Modest changes were observed in International Index of Erectile Function-erectile function domain and MSHQ-EjD function domain at 5 years consistent with the aging of the treated cohort, with mean±SD changes of −2.4±9.2 and −2.0±3.9, respectively.[16] MSHQ-EjD bother score improvement remained consistent through the length of followup, with a 16% improvement at 60 months (supplementary Appendix, https://www.jurology.com).

As displayed in figure 3, the total surgical retreatment rate for the treatment arm at the end of the study was 4.4%. Within that group, 83% of the surgical re-treatments occurred in the first 2 years of followup, with no treatment arm subjects receiving surgical re-treatment after year 3. As was noted in a prior manuscript, of the 6 subjects retreated surgically, 4 had identified obstructive

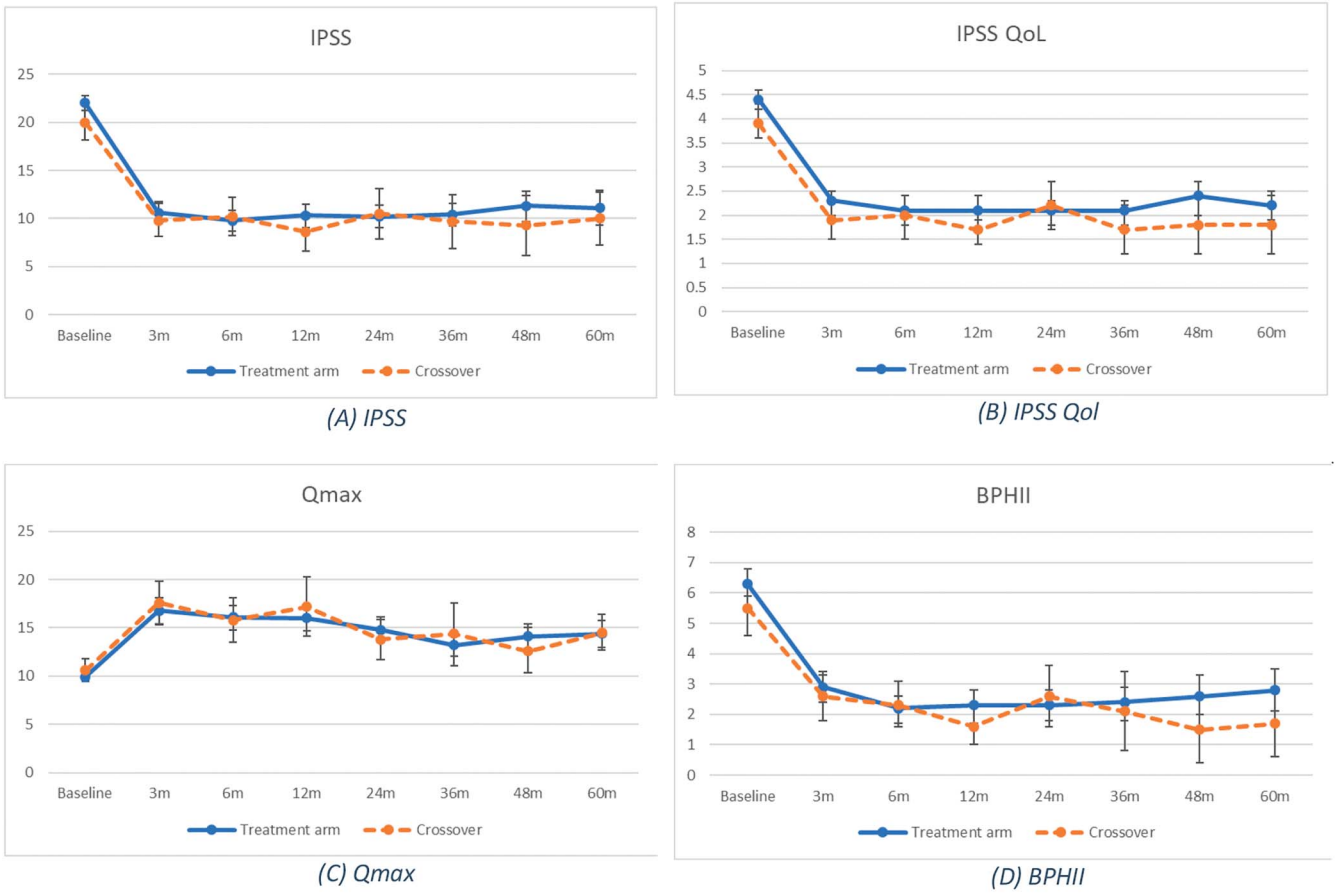

Figure 2. Graphical representation of outcomes at end of 5-year study for water vapor thermal therapy shows results of both treatment and crossover arms. *A*, IPSS. *B*, IPSS QOL. *C*, Qmax. *D*, BPHII. Values are means, and error bars represent 95% CI.

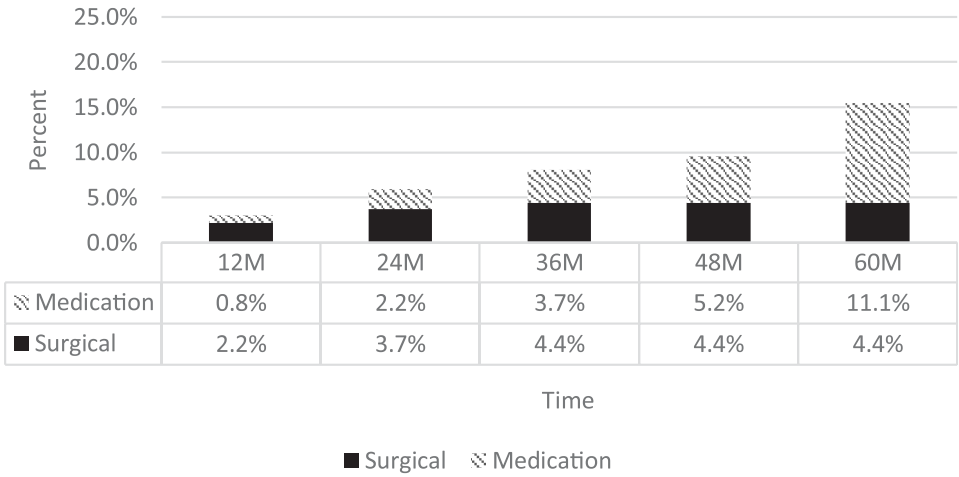

Figure 3. Treatment arm re-treatment rates through 5 years.

median tissue that was initially left untreated.[12] An additional 11.1% of treatment arm subjects were re-treated with BPH medication through 5 years. Four crossover arm subjects were re-treated surgically (3 for previously untreated obstructive median tissue) and 10 received BPH medication.

DISCUSSION

The results of this randomized controlled trial revealed that the thermal therapy for BPH has clinically meaningful outcomes and proven durability. The inclusion of patients with obstructive median tissue underscores the rare versatility of water vapor thermal therapy, especially among MISTs, as this system is capable of ablating tissue from lateral lobes as well as tissue of an enlarged central zone (ie middle lobe or median bar) without advanced training or learning a complex technique.[17]

The 5-year responder analysis end point (30% improvement of IPSS and freedom from re-treatment) is also of particular importance given the recent draft guidance proposed by FDA as the basis for minimal clinical improvement following device therapy for BPH,[18] as reported in the analysis from Roehrborn et al.[19] Without a predefined measure for clinically significant difference, this IPSS responder analysis provides a reliable surrogate.

Other MISTs like prostatic urethral lift (PUL) or other implantable devices provide relief from symptoms without removing tissue. It is perhaps less surprising then that the 5-year surgical re-treatment rate of 4.4% for the treatment arm herein compares so favorably to the 13.6% reported in the 5-year LIFT (Prostatic Urethral Lift for the Treatment of LUTS Associated with BPH) Study.[20] These results also compare well to other MISTs such as TUNA and TUMT, where 5-year study surgical re-treatment rates ranged from 14% to 51% and 8.9% to 21%, respectively.[21–23] This is noteworthy when considering that 7 of the 10 subjects re-treated surgically in this study had identified middle lobes that were previously untreated, supporting a more durable impact on LUTS if an obstructive middle lobe is addressed when noted.

Despite the majority of subjects in this study presenting with severe LUTS at enrollment (72.5% with IPSS 19–35), outcomes as measured by storage and voiding function, urinary flow rates, and quality of life improved from the first visit 3 months post-procedure through the final visit at 60 months after a single water vapor thermal therapy treatment, without negatively impacting sexual function. In order to produce outcome measures with similar results to this study, pharmacotherapy requires patients to adhere to a combination of interminable prescription regimens, which often have undesirable sexual side effects.[9,24,25] To achieve similar results with PUL, permanent implants are required, but the re-treatment rates appear much higher.[26] The Rezūm II Study results aid in establishing water vapor therapy as a first-line treatment for BPH. Patients who may be candidates for water vapor thermal therapy are often referred for more invasive surgical techniques such as TURP, holmium laser enucleation of the prostate, or other laser treatments that can involve greater bleeding risks, longer recovery time, declines in measures of sexual function, and other undesirable side effects.[27]

Study limitations included participant attrition, but that is unique neither to this trial nor to studies within this disease state. As was the case with the LIFT Study, a similar percentage of participants from the treatment arm were evaluated at 5 years

per protocol (62%) as this study (57%), and in each study the statistical significance of the functional results was not negatively impacted.[20] Attrition rates are also similar for prospective studies with other modalities like TURP and TUNA,[23,28] photoselective vaporization of the prostate,[29] and TUMT.[30] Additionally, the lack of urodynamic testing limits the opportunity to analyze bladder function, the degree of obstruction, and bladder contractility, and the potential impact on these reported results.

CONCLUSIONS

Water vapor thermal therapy for BPH is a treatment that combines the properties of a MIST with the functional outcomes expected from other ablative therapies. There is a short learning curve without the need for advanced techniques to treat various zones of the prostate, including an obstructive middle lobe. The positive safety profile, long-term durability, and maintenance of sexual function make water vapor thermal therapy an optimal treatment choice for patients with moderate to severe LUTS.

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EDITORIAL COMMENTS

Treatment of symptomatic BPH may be reaching an inflection point: newer minimally invasive procedures appear to offer appropriately selected men the benefits of significant, durable symptom relief and a side effect profile that competes well with medical therapy. Is the newest wave of MIST here to stay?

McVary et al present impressive 5-year outcomes of water vapor thermal therapy, outlining the results of a device that appears rapid (treatment time roughly 5 minutes), broadly applicable to include median lobes, and largely devoid of sustained side effects. Average IPSS decreased by more than 11 points over the initial 3-month period after treatment, and this benefit was sustained for the entirety of the study, with few re-treatments. Sexual side effects were minimal, and rough comparison of other series suggests that these may in fact be less than those experienced by men on medical therapy (reference 9 in article).

Direct comparison to medication, prostatic lift, and transurethral surgery will go a long way to flesh out the best utility of this procedure. This FDA-influenced trial design is unfortunate, as the treated vs sham arms were separate for only 3 months before crossover, hampering comparison. As PSA predicts likelihood of LUTS/BPH progression, the relatively low entry PSA levels in these men suggest a group that was at lower risk for symptomatic deterioration over time.[1] Similarly, we see a surprisingly small decrease in post-treatment PSA, the significance of which is unclear. More work remains, but the authors must be congratulated for presenting a significant data point for this very promising technology.

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This study is the 5-year followup of the original study designed with FDA imposed metrics of protocol development. This trial emulated contemporary MIST trials randomized to sham and offered treatment (MIST/sham) to control subjects in order to provide an “ethical pathway” to patients seeking treatment. For most (57%) of patients available for followup at 5 years, there is durable symptom relief with modest improved urodynamic durability compared to “sham”/control at 3 months. The therapy fills a void prior to prostatectomy, where the number one indication for surgical therapy is medical treatment failure. However, comparison to formal debulking prostatectomy cannot be made without a randomized trial to TURP-like procedures. As an alternative to medical therapy, this study demonstrates reasonable symptom relief durability to 5 years for some who seek a minimally invasive therapy (fast and quick in office) to improve quality of life. Since it is not randomized to TURP like prostatectomy, and only 57% (includes crossovers) were present at 5 years in an industry sponsored trial, it has not proven itself as an effective alternative for medical therapy failure since controls included washouts from medical therapy. These MISTs have only been demonstrated to be better than sham as opposed to true

prostatectomy procedures that have shown non-inferiority to TURP, such as Aquablation®, holmium laser enucleation of the prostate, thulium laser enucleation of the prostate, and 532 nm laser prostatectomy (reference 20 in article).[1,2] MIST/sham trials need to better define indication, and patient selection and position in BPH treatment algorithm. Notably, these MIST/sham trials were designed as alternatives to medical therapy, and have not yet proven to be efficacious options to medical treatment failures, and re-treatment rates may be higher than the 6% rate of surgical re-treatment seen in prostatic urethral lift, another current MIST/sham procedure with similar results.[3]

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REPLY BY AUTHORS

We agree with Lloyd that the FDA mandated sham limits some comparisons. The crossover design is a well-versed model in all U.S.-based MIST investigations. Fortunately, additional studies are planned to investigate the comparison of water vapor thermal therapy to other treatments. We note that the majority of subjects in this study had severe LUTS (72.5% with IPSS 19–35), and thus these enrollees were at risk for progression, particularly when compared to the MTOPS Study. One notes the water vapor thermal therapy cohort compared favorably in all aspects of BPH progression to the MTOPS Study.[1] We again thank Lloyd for acknowledging the significance of the findings herein.

Regarding Te's comments, the design of every MIST trial offers a crossover pathway as a compromise, as patients cannot be "locked into a control arm" for a 5-year trial. Should all MISTs be compared to a TURP? Doing so presents a challenge in design as a key in randomization requires "balanced arms" with equivalent pathways. Given the lack of impact in sexual function with MISTs, does Te really consider these 2 surgeries equivalent? Of course not, and thus MIST vs sham is the most reasonable compromise.

What about the role of MIST vs medications? A cohort analysis at 3 years was conducted against MTOPS, and the results showed that symptom improvement and flow rates were greater with water vapor thermal therapy (reference 24 in article). Importantly, the rates of progression corroborate these outcomes, with 5 times greater progression for medical therapy vs a single water vapor thermal therapy. This is very encouraging for clinicians and their patients.

Consistent with the new American Urological Association guidelines' shared decision process, the adage that patients are best to seek MIST when their medication has failed them has been officially abandoned.[1] Consistent with this now accepted practice, this approach is a challenge to Te's implied failed medication algorithm. Lastly, although we appreciate that there are a number of ways that UroLift® and the LIFT Study can be compared to this device and study, we kindly ask that Te amend the 6% re-treatment rate cited above to more accurately reflect it as an annual re-treatment rate for PUL.[2]

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