Three-Year Outcomes of the Prospective, Randomized Controlled Rezūm System Study: Convective Radiofrequency Thermal Therapy for Treatment of Lower Urinary Tract Symptoms Due to Benign Prostatic Hyperplasia

Kevin T. McVary and Claus G. Roehrborn

OBJECTIVE To report 3-year outcomes of a prospective, multicenter, randomized, blinded control trial after treatment with convective radiofrequency (RF) water vapor thermal therapy for moderate to severe lower urinary tract symptoms due to benign prostatic hyperplasia (BPH).

MATERIALS AND METHODS Fifteen centers enrolled and randomized 197 men ≥50 years old with International Prostate Symptom Score (IPSS) ≥13, maximum flow rate (Qmax) ≤15 mL/s, and prostate volume 30 to 80 cc to thermal therapy with Rezūm System or control (2:1). Rigid cystoscopy with simulated active treatment sound effects served as the control procedure. Convective RF thermal energy was delivered into obstructive prostate tissue including the median lobe as needed. After randomized comparison at 3 months, thermal therapy subjects were followed annually for 3 years.

RESULTS Convective RF thermal therapy yielded IPSS improvement of 160% compared with control subjects at 3 months (P <.0001). Maximal symptom relief of at least 50% improvement in IPSS, quality of life, Qmax, and BPH Impact Index remained durable throughout 3 years (P <.0001). Subjects with a treated median lobe had similar responses. No late-related adverse events occurred, and no de novo erectile dysfunction was reported. The surgical retreatment rate was 4.4% over 3 years.

CONCLUSION The minimally invasive convective RF thermal therapy is an office or ambulatory outpatient procedure with minimal transient perioperative side effects. It provides early effective and durable relief of BPH symptoms with preservation of sexual function in subjects followed up for 3 years and is applicable to treatment of the median lobe and hyperplastic central zone tissue. UROLOGY 111: 1–9, 2018. © 2017 The Author(s). Published by Elsevier Inc.

The emergence of minimally invasive treatment for bothersome lower urinary tract symptoms/benign prostatic hyperplasia (LUTS/BPH) adds to the armamentarium of available therapies before or after initial medical management. This is particularly true in men who cannot tolerate side effects of medication, have unrealized expectations for symptom relief, may not be compliant with long-term use of costly drugs, or wish to avoid potential complications of invasive surgical procedures. Traditional thermal therapies such as conductive transurethral needle ablation of the prostate (TUNA) and transurethral microwave thermotherapy (TUMT) as alternatives to surgical intervention have declined in use.[1] A novel technology utilizing convective radiofrequency (RF) water vapor thermal therapy (Rezūm System; NxThera, Inc.,

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From the Division of Urology, Southern Illinois University School of Medicine, Springfield, IL; and the Department of Urology, University of Texas Southwestern Medical Center, Dallas, TX

Address correspondence to: Kevin T. McVary, M.D., Division of Urology, Southern Illinois University School of Medicine, St. John's Pavilion, 301 North Eighth Street, PO Box 19665, Springfield, IL 62794-9665. E-mail: kmcvary@gmail.com

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Maple Grove, MN) received Food and Drug Administration clearance in 2015. The principles of the technology and effective ablation of prostate adenomas were validated in histologic and magnetic resonance imaging studies.[2,3] The advantage of the Rezūm System is the use of convective heat energy compared with tissue ablation using conductive heat transfer (TUNA or TUMT). The latter induces molecular agitation within a tissue mass after direct contact between 2 surfaces at different temperatures; this causes a thermal gradient. Consequently, higher temperatures and longer periods of heating are required to achieve a therapeutic temperature in the target tissue through conduction vs convection. In the case of convective heating, there is instead a phase change of water vapor (steam) to liquid such that the energy moves through the tissue confined only by natural collagen barriers (adenoma pseudocapsule) inducing cell death without desiccation, limited to the McNeal's transitional prostatic zone,[4] and a temperature no more than 103°C.

The convective RF thermal therapy has been shown to provide rapid and significant improvements in bothersome LUTS, preserve erectile and ejaculatory function, and enhance quality of life in patients with moderate to severe symptoms.[5-7] The reproducibility of responses and sustained relief of LUTS with minimal side effects and no delayed adverse events was demonstrated over 2 years.[8,9] Similar responses were reported for 1-year outcomes from consecutive cases by community urologists.[10] Continued scrutiny and assessment of durability is important to understand the role of the convective RF thermal therapy in management of patients with LUTS/BPH. This report provides the 3-year results of the multicenter randomized controlled trial (RCT) of the thermal therapy and improvements based on initial severity of LUTS, and demonstrates the ability to treat all zones of the prostate.

MATERIALS AND METHODS

Study Protocol

The prospective, multicenter, double-blinded study of the safety and effectiveness of the Rezūm System convective RF thermal therapy was conducted in 15 centers in the United States (Clinicaltrials.gov: NCT01912339) with intent to follow-up annually for 5 years. The protocol was approved by institutional review boards at each enrolling center, and written informed consent was obtained from all subjects. Enrollment criteria included men with moderate to severe symptomatic BPH, those at least 50 years of age with an International Prostate Symptom Score (IPSS) ≥13, a prostate volume of 30 cc to 80 cc, maximum urinary flow rate (Qmax) of ≤15 mL/s, and a measured postvoid residual (PVR) urine <250 mL. Exclusion criteria included a prostate specific antigen >2.5 ng/mL with a free prostate specific antigen <25% (unless prostate cancer was ruled out by biopsy) and any active urinary tract infection. There were no morphological contraindications for use of this thermal therapy procedure in subjects with an intravesical median lobe or hyperplasia of the central zone. A total of 197 subjects stratified by IPSS severity were randomized 2:1 to thermal therapy with the Rezūm device (n = 136) or sham or control procedure with rigid cystoscopy (n = 61). Participants were required to undergo a washout and discontinue use of any medications for LUTS/BPH before treatment.[5] A second aspect of the RCT included a crossover design trial of the RF thermal therapy after the control procedure. After unblinding at 3 months, control subjects who elected to proceed were requalified for the crossover study.[9]

Statistical Methods

Randomization was conducted before treatment with electronic programming using permuted blocks of various sizes chosen at random, stratified by investigational site. Subjects were allocated in a 2:1 ratio to thermal treatment and control arms, respectively. To ensure balance between the randomized arms at each study site, subjects were first stratified by severity of symptoms, with baseline IPSS 13 to 18 (moderate) and IPSS ≥19 (severe) to ensure equal distribution in both arms. The study was powered at 80% with 0.025 1-sided type I error for the primary end point of IPSS reduction at 3 months, using a Student *t* test on the intent-to-treat populations to compare mean changes in treatment and control arms. Descriptive statistics were used to describe baseline and follow-up values for all variables. To evaluate longitudinal change from baseline, a general estimation equation model was fit to each outcome parameter using an exchangeable working correlation structure.[11] The general estimation equation model takes into account the correlation within a subject over time and uses that information to adjust the estimates and confidence intervals. Change from baseline is the dependent variable; visit and baseline score are used as independent variables. The model was used to calculate *P* values for each follow-up evaluation compared with baseline.

Procedures

Descriptions of the convective RF thermal therapy technology, device, and treatment procedural techniques have been reported in detail.[5,7,10] Briefly, the system utilizes RF-generated water vapor (~103°C) thermal energy based on the thermodynamic properties of convective vs conductive heat transfer to ablate prostate tissue. The handheld transurethral delivery device with a standard reusable 4-mm, 30° rigid lens allows placement of the retractable needle under direct cystoscopic visualization; a saline flush irrigation is used to enhance visualization and cool the urethra. The treatment needle has a total of 12 small emitter holes spaced around its tip to allow circumferential dispersion of thermal energy to create an approximate 1.5- to 2.0-cm lesion which is confined within the prostate zone in which the treatment is delivered. For treatment, the needle tip is positioned and inserted starting approximately 1 cm distal from the bladder neck into the transition and central prostate adenoma. Intravesical prostatic protrusions are injected starting 1 cm from the edge of the protrusion. The total number of treatments in each lobe of the prostate is determined by the length of the prostatic urethra and can be customized to the configuration of the gland including the median lobe or enlarged central zone. The treatment requires repositioning the retractable needle after each water vapor injection approximately 1 cm distal from the previous site to the end of the prostatic urethra proximal to the verumontanum. The thermal therapy creates contiguous, overlapping lesions running parallel to the natural slope of the urethra. The control procedure involved rigid cystoscopy and activation of the system generator outside the subject's body to mimic the sound of the active procedure. A surgical barrier prevented subject visualization of the treating physician and device.

Study Assessments

The double blind was maintained through the 3-month comparison of the active and sham or control groups for the primary efficacy end point, after which all subjects were unblinded. Outcome assessments were performed by an assessor blinded to the procedures. Control subjects who requalified by inclusion criteria were eligible to participate in a crossover study to receive thermal therapy.[9] The RF thermal therapy subjects were followed for 3 years and assessed for symptom relief (IPSS), quality of life measures (IPSS-QOL, BH Impact Index [BPHII]), peak urinary flow rate (Qmax), incontinence (Overactive Bladder Questionnaire-Short Form [OAB-q SF], International Continence Society Male Incontinence Scale Questionnaire-Short Form [ICS male IS-SF]), sexual function (International Index of Erectile Function [IIEF-15], Male Sexual Health Questionnaire for Ejaculatory Dysfunction [MSHQ-EjD]), and acute and late-occurring adverse events. Any subject who received RF thermal therapy is included in annual follow-up evaluations for 5 years. Independent data monitoring and clinical events committees reviewed safety and adjudicated adverse events.

RESULTS

Study enrollment between September 2013 and August 2014 included 197 subjects, of whom 136 were randomized to convective RF thermal therapy and 61 were randomized to the sham or control procedure (Fig. 1). For the active treatment cohort, the mean age was 63 ± 7.1 years, mean prostate volume was 45.8 ± 13 cc, and mean baseline IPSS was 22.0 ± 4.8. The control subjects had similar characteristics.[5] After the 3-month blinded comparison, 53 of 61 control subjects who again met IPSS and Qmax eligibility criteria elected to participate in a crossover active treatment study. Results of the per protocol analysis with a 2-year follow-up and a crossover study were reported previously.[5,9] RF thermal therapy treatments were performed on the median lobe or enlarged central zone of 58 of 188 subjects (30.9%) in the original randomized and crossover studies. The total number of RF water vapor treatments in each lobe of the prostate was determined by the length of the hyperplastic prostatic tissue and customized to the configuration of the gland. The number of treatments to prostate zones was a mean of 4.7 ± 1.7 and 1.6 ± 0.7 to the median lobe when present. All procedures were performed in an office or ambulatory surgery center and successfully completed without perioperative device or procedure-related adverse events. Management of pain and anxiety was controlled at investigator discretion. Anesthesia was variable; 69% of patients received oral sedation only, 21% of patients received prostate block, and 10% of patients received intravenous sedation.[5]

The IPSS improvements after thermal therapy at the primary end point analysis (intention-to-treat) at 3 months were significant (−11.2 ± 7.6 points reduction) compared with the control group (−4.3 ± 6.9 points), P <.0001.[5] The early response of the 50% improvement in IPSS (baseline 22.0 ± 4.8) was consistently sustained at this level throughout 3 years of follow-up (Table 1). The longitudinal profile of IPSS improvements is shown in Figure 2A; it is closely replicated in a cumulative total of 384 subjects treated with convective RF thermal therapy in this RCT and in previously published studies.[8-10] Without exception, the 7 individual domains of the IPSS for voiding and storage functions indicated significant relief of symptoms at 1 month to 2 years after convective RF thermal therapy[9] and remained significant throughout 3 years, P <.0001 (Fig. 2B,C).

Corresponding and durable improvements in urinary flow rate (Qmax), quality of life, and incontinence assessments were significant compared with baseline, P <.0001 (Table 1). The increased urinary flow of >50% from 3 to 24 months fell off slightly to 39% at 36 months. Symptomatic relief reflected in IPSS and Qmax outcomes was achieved in subjects with moderate and severe LUTS (Supplementary Figs. S1, S2). The percentage of symptom improvement is commensurate with symptom severity at baseline, that is, higher improvement with higher baseline scores, but not dependent on baseline Qmax. Subjects who were not sexually active (reported "did not attempt intercourse") on the IIEF-15 before treatment were censored from sexual function analyses.[6] The sexually active subjects had no negative changes in IIEF-EF and MSHQ-EjD function scores throughout 3 years of follow-up; however, the ejaculatory bother score (MSHQ-EjD) improved over baseline from 12 to 36 months (P <.03). Further evaluation of the minimal clinically important differences in erectile function, perceptible as a benefit to the patient,[12] showed improvements in 29 of 90 subjects (32%) at 3 months and 21 of 77 subjects (27%) at 12 months after treatment,[5] which remained durable in 10 of 62 subjects (16%) at 36 months (Supplementary Table S1).

Of the 135 subjects, 42 (31%) had a median lobe or central zone enlargement identified and 30 of 42 (71%) received thermal therapy (Table 2). Subjects with a treated median lobe and those without a median lobe (93 of 135) had similar significant improvements in IPSS and urinary flow rate throughout 36 months. After ablation of the median lobe, these 30 subjects had significantly decreased PVR from 24 to 36 months (P <.04, adjusted for baseline PVR). At 36 months, the decrease in PVR was 54.8 mL (61% of the baseline mean of 90.2 ± 57.2) compared with 14.2 mL (18% of the baseline mean of 77.7 ± 49.0) in subjects without a treated median lobe, P = .0109.

Adverse events reported were infrequent and of short duration. The most common were dysuria (16.9%), hematuria (11.8%), frequency and urgency (5.9%), acute urinary retention (3.7%), and suspected urinary tract infection (3.7%); all were treated routinely or resolved without treatment within 3 weeks.[9] There were no late-occurring–related adverse events. No de novo erectile dysfunction was reported.

A total of 97 of 135 subjects (72%) treated with convective RF thermal therapy were available for the 3-year evaluations. Of the 38 subjects excluded from analysis, 14 were lost to follow-up, 7 withdrew consent (1 with a cancer

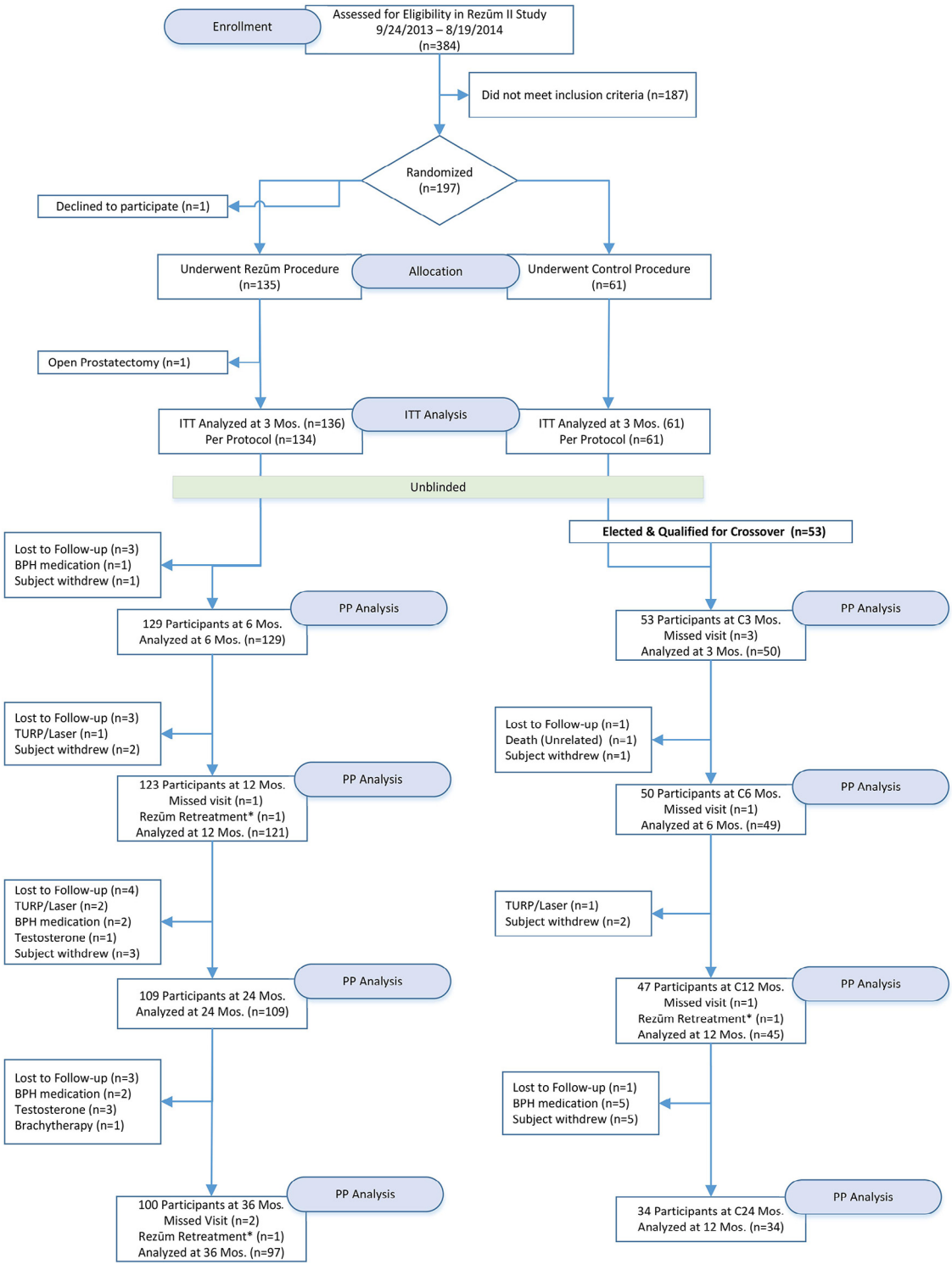

Figure 1. CONSORT (Consolidated Standards of Reporting Trials) diagram of subject disposition in convective RF thermal therapy, control, and crossover (C) groups. *Subjects retreated with Rezūm procedures were excluded from analysis. ITT, intent-to-treat analysis; PP, per protocol analysis; RF, radiofrequency; TURP, transurethral resection of prostate.

diagnosis), 5 were censored for use of BPH medications, and 4 were censored for use of testosterone at the time of follow-up, 2 missed a clinic visit, and 6 underwent a secondary treatment for LUTS (1 subject had open prostatectomy, 3 had a plasma-button transurethral vaporization of the prostate, and 2 were retreated with Rezūm). Thus, the retreatment rate with a surgical or minimally invasive procedure was 4.4% (6 of 135 subjects) over 3 years of follow-up. Four of these 6 secondary interventions were related to the presence of a median lobe, identified but not

Table 1. Paired outcome measures after convective RF thermal therapy from baseline through 36 months

Outcome Measure	3 mo	6 mo	12 mo	24 mo	36 mo
IPSS*					
N (paired values)	134	129	121	109	97
Baseline	22.0 ± 4.8	22.0 ± 4.8	21.8 ± 4.8	21.4 ± 4.5	21.4 ± 4.6
Follow-up	10.6 ± 6.4	9.8 ± 6.2	10.3 ± 6.7	10.2 ± 6.2	10.4 ± 6.1
Change	–11.3 ± 7.6	–12.2 ± 7.6	–11.6 ± 7.3	–11.2 ± 7.3	–11.0 ± 7.1
% Change	–50	–54	–52	–51	–50
P value (GEE)	<.0001	<.0001	<.0001	<.0001	<.0001
IPSS QoL*					
N (paired values)	134	129	121	109	97
Baseline	4.4 ± 1.1	4.4 ± 1.1	4.4 ± 1.1	4.3 ± 1.0	4.3 ± 1.0
Follow-up	2.3 ± 1.5	2.1 ± 1.5	2.1 ± 1.5	2.1 ± 1.4	2.1 ± 1.3
Change	–2.1 ± 1.6	–2.3 ± 1.6	–2.2 ± 1.6	–2.2 ± 1.5	–2.2 ± 1.6
% Change	–46	–51	–50	–50	–49
P value (GEE)	<.0001	<.0001	<.0001	<.0001	<.0001
Qmax (mL/s)† (voided vol ≥125 mL)					
N (paired values)	125	119	112	99	80
Baseline	10.0 ± 2.2	10.0 ± 2.2	10.0 ± 2.2	10.0 ± 2.2	9.7 ± 2.0
Follow-up	16.4 ± 7.3	15.7 ± 6.3	15.5 ± 6.7	14.7 ± 6.1	13.2 ± 4.8
Change	6.4 ± 7.2	5.7 ± 6.2	5.5 ± 6.4	4.8 ± 6.1	3.5 ± 4.7
% Change	69	62	59	53	39
P value (GEE)	<.0001	<.0001	<.0001	<.0001	<.0001
PVR volume (mL)*					
N (paired values)	133	125	118	106	92
Baseline	82.4 ± 51.8	83.4 ± 51.9	82.5 ± 51.2	84.9 ± 54.0	81.5 ± 53.4
Follow-up	71.8 ± 72.2	75.0 ± 81.8	78.6 ± 79.9	84.6 ± 92.0	55.1 ± 61.9
Change ± SD	–10.6 ± 68.3	–8.4 ± 75.8	–3.9 ± 82.7	–0.3 ± 85.3	–26.4 ± 63.9
% Change	56	78	51	9	–21
P value (GEE)	.3459	.3721	.8943	.6549	.0004
BPHII*					
N (paired values)	134	129	121	109	97
Baseline	6.3 ± 2.8	6.3 ± 2.8	6.2 ± 2.8	6.1 ± 2.8	6.1 ± 2.9
Follow-up	2.9 ± 2.9	2.2 ± 2.6	2.3 ± 3.0	2.3 ± 2.7	2.4 ± 2.9
Change	–3.4 ± 3.5	–4.1 ± 3.0	–3.9 ± 3.3	–3.8 ± 3.1	–3.7 ± 3.3
% Change	–46	–65	–61	–61	–57
P value (GEE)	<.0001	<.0001	<.0001	<.0001	<.0001
IIEF-EF†					
N (paired values)	90	84	77	71	62
Baseline	22.7 ± 7.5	23.0 ± 7.4	23.3 ± 6.9	22.9 ± 7.3	23.2 ± 7.4
Follow-up	22.7 ± 8.4	22.7 ± 8.8	23.0 ± 8.4	21.8 ± 8.7	21.3 ± 9.1
Change	0.1 ± 7.4	–0.3 ± 6.4	–0.3 ± 7.5	–1.2 ± 7.6	–1.9 ± 8.2
% Change	7	2	4	–1	–3
P value (GEE)	.8927	.8816	.8709	.4080	.1119
MSHQ-EjD Function*					
N (paired values)	90	83	78	70	63
Baseline	9.3 ± 3.1	9.6 ± 3.0	9.6 ± 3.0	9.6 ± 3.0	9.9 ± 3.0
Follow-up	9.7 ± 4.5	9.7 ± 4.0	9.3 ± 4.0	9.1 ± 4.4	8.5 ± 4.5
Change	0.3 ± 4.3	0.1 ± 3.6	-0.3 ± 3.5	–0.5 ± 4.2	–1.4 ± 3.8
% Change	11	6	0.4	0.3	–14
P value (GEE)	.5612	.7451	.2778	.3505	.0033
MSHQ-EjD Bother*					
N (paired values)	90	84	79	70	63
Baseline	2.2 ± 1.7	2.2 ± 1.6	2.2 ± 1.6	2.2 ± 1.6	2.0 ± 1.6
Follow-up	1.8 ± 1.7	1.8 ± 1.5	1.5 ± 1.5	1.7 ± 1.7	1.6 ± 1.5
Change	–0.3 ± 1.9	–0.4 ± 1.9	–0.7 ± 1.8	–0.5 ± 1.7	–0.5 ± 1.6
% Change	–14	–6	–18	–25	–18
P value (GEE)	.0776	.0951	.0015	.0129	.0060

Continued

Table 1. Continued

Outcome Measure	3 mo	6 mo	12 mo	24 mo	36 mo
ICS Male IS Score*					
N (paired values)	133	129	120	109	97
Baseline	4.4 ± 2.9	4.3 ± 2.8	4.3 ± 2.7	4.2 ± 2.4	4.1 ± 2.3
Follow-up	3.2 ± 2.7	2.7 ± 2.6	3.0 ± 2.8	3.0 ± 2.6	3.0 ± 2.6
Change	−1.2 ± 2.7	−1.6 ± 2.8	−1.2 ± 2.5	−1.2 ± 2.6	−1.1 ± 2.6
% Change	−16	−26	−24	−19	−18
P value (GEE)	<.0001	<.0001	<.0001	<.0001	<.0001
OAB HRQL Score†					
N (paired values)	132	128	120	106	95
Baseline	64.4 ± 20.0	64.7 ± 19.8	65.8 ± 18.9	66.6 ± 18.3	66.7 ± 18.2
Follow-up	82.0 ± 17.5	84.8 ± 16.2	83.7 ± 18.2	85.6 ± 15.1	84.6 ± 15.4
Change	17.6 ± 18.8	20.1 ± 18.9	17.9 ± 18.6	18.9 ± 16.9	17.9 ± 17.3
% Change	39	53	48	51	53
P value (GEE)	<.0001	<.0001	<.0001	<.0001	<.0001
OAB Symptom Score*					
N (paired values)	133	129	121	109	97
Baseline	39.4 ± 17.8	39.5 ± 18.1	39.0 ± 17.5	38.2 ± 17.2	37.5 ± 16.2
Follow-up	24.9 ± 18.0	20.3 ± 15.4	20.6 ± 18.4	20.9 ± 16.6	21.6 ± 16.2
Change	−14.5 ± 18.3	−19.1 ± 18.8	−18.4 ± 17.8	−17.2 ± 14.3	−15.8 ± 16.0
% Change	−31	−40	−45	−45	−40
P value (GEE)	<.0001	<.0001	<.0001	<.0001	<.0001
PSA*					
N (paired values)	133	126	120	109	96
Baseline	2.1 ± 1.6	2.1 ± 1.6	2.1 ± 1.6	2.1 ± 1.6	2.0 ± 1.6
Follow-up	2.0 ± 1.7	1.8 ± 1.3	1.9 ± 1.6	1.8 ± 1.6	1.8 ± 1.7
Change	−0.1 ± 1.2	−0.3 ± 0.9	−0.3 ± 1.0	−0.3 ± 1.1	−0.2 ± 1.1
% Change	7	−7	−9	−9	−1
P value (GEE)	.1574	<.0001	.0003	.0015	.0947

GEE, general estimating equation; HRQL, Health-Related Quality of Life; ICS, International Continence Society; IIEF-15, International Index of Erectile Function; IPSS, International Prostate Symptom Score; LUTS, lower urinary tract symptoms; MSHQ-EjD, Male Sexual Health Questionnaire for Ejaculatory Dysfunction (EjD); OAB, overactive bladder; PVR, postvoid residual urine volume; Qmax, peak urinary flow; QOL, quality of life; RF, radiofrequency.

Analysis population includes all treatment arm subjects who underwent treatment with Rezūm System procedure. Only subjects who were sexually active are included for IIEF-EF, MSHQ-EjD Function, and Bother evaluations. Data presented as mean ± SD and compared with baseline using paired Student *t* test; *P* values from Wald test for whether GEE estimate of change from baseline is different from 0.

* Decrease indicates improvement.

† Increase indicates improvement.

previously treated. At the time of study exit, 26 of 36 of excluded subjects (72%) had a ≥7 points improvement in IPSS. No study withdrawals were due to related adverse events.

COMMENT

This report presents the longest term follow-up to date of a randomized trial for convective RF thermal therapy for treatment of bothersome LUTS. The significant improvements in symptoms, both storage and voiding functions, quality of life measures, urinary flow rates, and incontinence measures are durable throughout 3 years. Sexual function was preserved; erectile function remained improved and durable in the subset of sexually active subjects. Notable is the reproducibility of symptom relief with profiles of improvements in IPSS that mirror results in published studies including a real-world experience with community urologists.[8-10] This corroboration of nearly identical outcomes in a variety of patient cohorts and settings is significant in meeting expectations for care of a variety of patients beyond the realm of a randomized clinical trial involving strict enrollment criteria. This tight correlation speaks to a strong sense generalizability of the technology as it transitions from experimental to standard treatment option. Baseline severity of symptoms is known to influence treatment outcomes.[13] As shown in Supplementary Figures S1 and S2, IPSS outcomes based on severity of LUTS indicate that subjects with both moderate and severe LUTS had significant symptomatic relief.

The convective RF thermal therapy is unique among other minimally invasive thermal therapies. The procedure is a TUNA approach, but with considerably more efficient convective delivery of thermal energy to heat and ablate tissue compared with conductive delivery using currently available traditional TUNA and TUMT systems. The convective RF thermal procedure has several advantages: It is a very efficient procedure that can be performed in an outpatient setting using oral sedation or local anesthesia in most cases. Ablation can be targeted

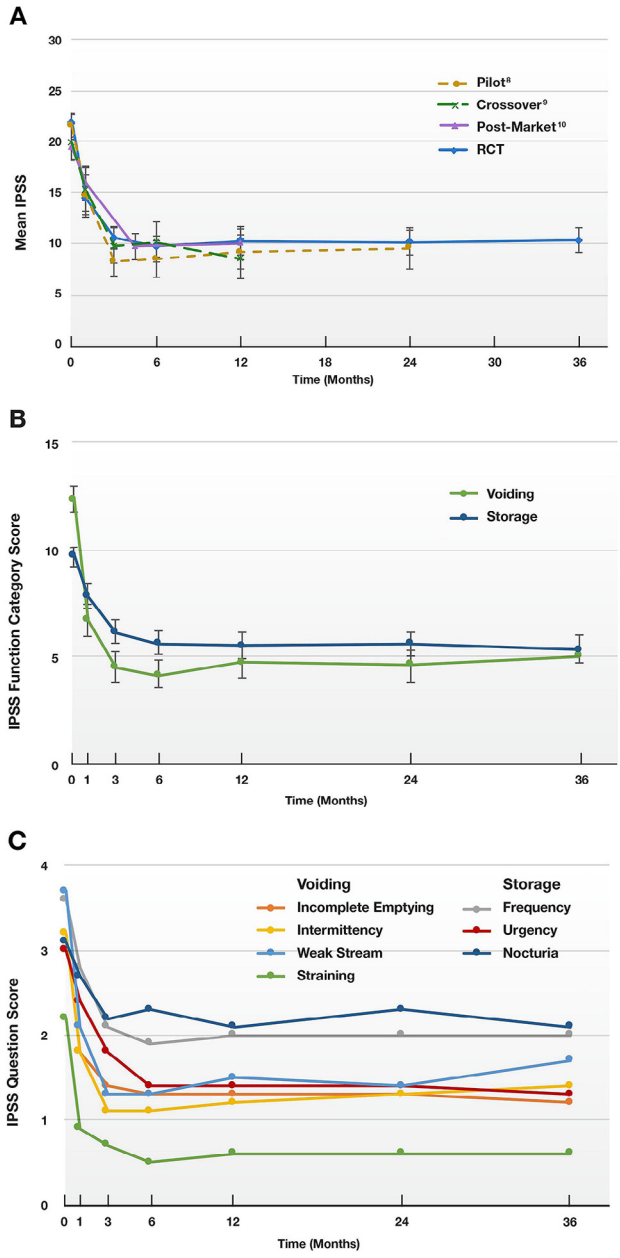

Figure 2. IPSS improvements shown for patients throughout 36 months after convective RF thermal therapy in this RCT **(A)**. The profile of IPSS improvements is closely replicated among subjects treated with thermal therapy in previously published pilot,[8] crossover,[9] and postmarket experience studies.[10] IPSS improvements relative to baseline are significant at all time points, P <.001-.0001. Mean changes in IPSS functional domains after convective RF water vapor thermal therapy including voiding and storage category responses **(B)**, and 7 questions related to storage and voiding symptoms **(C)**. Improvements relative to baseline were significant at all time points, P <.0001. Values are the means, and errors bars represent the 95% CI. CI, confidence interval; IPSS, International Prostate Symptom Score; RCT, randomized controlled trial; RF, radiofrequency.

precisely to those zones of the prostate with obstructive tissue, and customized to the configuration of individual prostate glands including intravesical prostatic protrusions of either lateral or median lobes. In this RCT, subjects with a median lobe or central zone hyperplasia achieved similar significant relief of symptoms as those without this anatomic hyperplasia.

The BPH surgical retreatment was low at 4.4% over 3 years and primarily related to the failure to initially treat the median lobe in 4 of 135 subjects (3%). This rate is considerably less than the variable reoperation rates for TUNA and TUMT followed up for 5 years[14-18]; however, a direct temporal comparison cannot be made with convective RF thermal therapy. The retreatment rate is similar to that reported in a study of more than 6000 transurethral surgical patients: rate of 4% after resection and 6% after laser vaporization patients at 3 years and new BPH oral medications were started among 22% of initial responders to surgery.[19] A reoperation rate of 4% occurred up to 3 years after plasma-button enucleation of the prostate.[20] The surgical retreatment rate for LUTS/BPH after a mechanical procedure of a prostatic urethral lift was 10.7% (15 of 140) at 3 years.[21]

Symptomatic men with moderate to severe LUTS/BPH who wish to move beyond watchful waiting could consider convective RF water vapor thermal therapy as a low-risk treatment in the continuum between medical management and more invasive surgical approaches. The one-time procedure provides rapid, significant, and durable relief of LUTS/BPH in contrast to a lifetime commitment of pharmaceutical agents and their undesirable side effects and lower-than-desired symptom improvement.

As reimbursement for patient care moves from volume-based services to value-based services, cost-effectiveness coupled with appreciable symptom relief for LUTS/BPH plays an important role. For example, the TUNA procedure with conductive heat delivery system compared favorably with combination medical therapy when viewed over a 5-year period.[22] Similarly, the cost-effectiveness of convective RF heat delivery (Rezūm System) compares favorably with the spectrum of BPH treatment options including drugs, minimally invasive therapies, and invasive surgeries (TURP and photovaporization of prostate).[23] Utilization of the convective RF thermal therapy procedure could lead to a reduction in inpatient hospitalization required with TURP. Furthermore, although generic combination drugs are the least expensive therapy for LUTS and branded combination drugs the most expensive, both are less effective than any minimally invasive therapy, including convective RF thermal therapy, over a 2-year period. Surgical intervention provides slightly greater relief of LUTS than minimally invasive modalities, however, at nearly twice the cost over a 2-year horizon. Typically, these more invasive and aggressive surgeries are reserved for larger prostate glands and subjects with underactive bladder function. With consideration of the profiles of safety, no reported occurrences of erectile dysfunction, and durability of LUTS relief as well as cost-effectiveness, convective RF water vapor

Table 2. IPSS, Qmax, and PVR changes in subjects with either no median lobe or a median lobe after treatment with convective RF thermal therapy

Outcome Measure	No Median Lobe Present (No. of paired values)		Median Lobe Treated (No. of paired values)		*P* Value (GEE)
	Time Point	Change	Time Point	Change	
IPSS*					
Baseline	21.7 ± 5.0 (91)	N/A	22.4 ± 4.0 (30)	N/A	N/A
1 mo	14.2 ± 6.9 (90)	–7.5 ± 7.8	15.4 ± 7.6 (29)	–6.8 ± 9.2	.7140
3 mo	10.9 ± 6.7 (90)	–10.8 ± 7.5	9.9 ± 4.6 (30)	–12.5 ± 7.0	.2643
6 mo	9.2 ± 5.9 (87)	–12.6 ± 7.3	10.8 ± 6.2 (29)	–11.5 ± 7.9	.4853
12 mo	9.8 ± 6.7 (82)	–11.9 ± 7.6	10.4 ± 5.5 (27)	–11.6 ± 6.4	.8786
24 mo	9.9 ± 6.1 (73)	–11.3 ± 7.5	10.6 ± 6.1 (26)	–11.6 ± 7.7	.8671
36 mo	9.9 ± 6.0 (65)	–11.2 ± 7.1	11.8 ± 6.6 (24)	–10.3 ± 8.0	.6104
Qmax (mL/s)† (voided volume ≥125 mL)					
Baseline	10.3 ± 2.3 (91)	N/A	9.3 ± 2.0 (30)	N/A	N/A
1 mo	14.1 ± 5.1 (79)	3.7 ± 5.1	13.0 ± 6.2 (26)	3.7 ± 6.0	.9638
3 mo	16.4 ± 6.8 (87)	6.2 ± 6.6	16.5 ± 8.0 (27)	7.0 ± 8.0	.5807
6 mo	16.0 ± 6.1 (82)	5.7 ± 5.9	15.8 ± 7.0 (26)	6.4 ± 7.4	.6126
12 mo	15.8 ± 6.0 (77)	5.5 ± 5.7	15.6 ± 5.9 (25)	6.2 ± 6.0	.5911
24 mo	14.7 ± 5.5 (67)	4.4 ± 5.4	14.9 ± 7.2 (25)	5.5 ± 7.3	.4376
36 mo	13.5 ± 3.9 (51)	3.5 ± 3.7	13.6 ± 6.4 (22)	4.2 ± 6.7	.6491
PVR volume (mL)*					
Baseline	77.7 ± 49.0 (91)	N/A	90.2 ± 57.2 (30)	N/A	N/A
1 mo	67.8 ± 56.9 (90)	–9.5 ± 58.9	90.9 ± 74.7 (28)	1.3 ± 75.4	.4317
3 mo	59.2 ± 52.7 (90)	–18.0 ± 58.3	75.0 ± 63.5 (29)	–16.5 ± 51.5	.9010
6 mo	68.3 ± 65.5 (84)	–8.6 ± 67.7	71.3 ± 79.2 (28)	–22.4 ± 63.2	.3444
12 mo	76.9 ± 81.3 (81)	–0.2 ± 88.4	71.4 ± 69.1 (25)	–17.5 ± 64.7	.3660
24 mo	82.7 ± 88.4 (71)	5.8 ± 81.5	68.2 ± 70.3 (25)	–33.2 ± 75.7	.0388
36 mo	59.5 ± 66.3 (61)	–14.2 ± 59.9	43.7 ± 54.1 (23)	–54.8 ± 73.5	.0109

N/A, not applicable.
Data presented as mean ± SD.
* Decrease indicates improvement.
† Increase indicates improvement.

thermal therapy warrants use as a first line of treatment for moderate to severe LUTS/BPH, and within the armamentarium of available treatments, it also represents a legitimate alternative to transurethral removal of obstructed tissue in select patients.

CONCLUSION

Convective RF water vapor thermal therapy of benign prostate adenomas represents a unique minimally invasive and durable modality for men with bothersome moderate to severe LUTS. The thermal therapy warrants positioning as a procedure for LUTS relief, both as an initial therapy vs medications and as an alternative to transurethral surgery for select patients.

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APPENDIX

Supplementary Data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.urology.2017.10.023.