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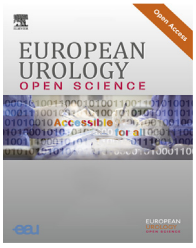

European Association of Urology

Benign Prostatic Hyperplasia

Prospective Trial of Water Vapor Thermal Therapy for Treatment of Lower Urinary Tract Symptoms Due to Benign Prostatic Hyperplasia in Subjects with a Large Prostate: 6- and 12-month Outcomes

Henry Woo [a,*], *Richard Levin* [b], *Christopher Cantrill* [c], *Shaw Zhou* [d], *Donald Neff* [e], *Mark Sutton* [f], *James Bailen* [g], *Michael Darson* [h], *John Horgan* [i], *Paul Zantek* [j], *Robyn Marty-Roix* [j], *on behalf of the Rezūm Clinical Trials Group*

[a] *College of Health and Medicine, Australian National University and SAN Prostate Centre of Excellence, Sydney Adventist Hospital, Sydney, Australia;* [b] *Chesapeake Urology, Baltimore, MD, USA;* [c] *Urology of San Antonio, San Antonio, TX, USA;* [d] *Pinellas Urology, South Pasadena, FL, USA;* [e] *University of Kansas Medical Center, Kansas City, KS, USA;* [f] *Houston Metro Urology, Houston, TX, USA;* [g] *First Urology, Louisville, KY, USA;* [h] *Arizona Urology Specialists, Scottsdale, AZ, USA;* [i] *Adult & Pediatric Urology, Omaha, NE, USA;* [j] *Boston Scientific Corporation, Marlborough, MA, USA*

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Abstract

Background: Current guidelines recommend Rezūm water vapor thermal therapy for the treatment of benign prostatic hyperplasia (BPH) for prostate glands ranging in volume from 30 to 80 cm^3. Few prospective studies have specifically evaluated the use of Rezūm for larger prostates.
Objective: To evaluate the safety and efficacy of water vapor thermal therapy in patients with a prostate gland >80 cm^3 and ≤150 cm^3.
Design, setting, and participants: In this prospective, single-arm study at seven centers in the USA, subjects were males aged >50 yr with symptomatic BPH and prostate volume of >80 cm^3 and ≤150 cm^3.
Intervention: Rezūm was used to deliver sterile water vapor via a transurethral approach to ablate targeted areas of prostate tissue.
Outcome measurements and statistical analysis: The primary efficacy outcome was response to therapy, defined on a per-patient basis as a ≥30% improvement in International Prostate Symptom Score (IPSS) from baseline to 6 mo. The primary safety outcome was a composite of serious device-related safety events. Secondary outcomes included catheterization for device-related retention. IPSS outcomes over time were analyzed via generalized estimating equations.
Results and limitations: Among 47 eligible patients, prostate volume ranged from 80.8 to 148.1 cm^3. All patients completed 6-mo follow-up, and 40/47completed 12-mo follow-up. At 6 mo, 83% were treatment responders according to the primary efficacy endpoint. The mean IPSS improvement at 6 mo was 11.9 ± 7.5 points, reflecting significant improvement. The primary safety outcome was met, with no

* Corresponding author. Sydney Urological Associates, San Clinic, 185 Fox Valley Road, Wahroonga, NSW 2076, Australia. Tel. +61 2 90527586.
E-mail address: hwoo@urologist.net.au (H. Woo).

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occurrence of device-related composite safety events. The study is limited by the nonrandomized design and early termination, unrelated to safety or effectiveness.
Conclusions: Our results are consistent with previous findings for prostate glands of up to 80 cm^3, and indicate the safety and efficacy of Rezūm for BPH in patients with a larger prostate.
Patient summary: Rezūm therapy, in which water vapor is used to treat targeted areas of the prostate, is currently recommended for patients with benign enlargement of the prostate and a prostate size of up to 80 cm^3. We found that this treatment was also effective and safe in patients with a larger prostate of 80–150 cm^3.

1. Introduction

Benign prostatic hyperplasia (BPH) is a histologic condition in which smooth muscle and epithelial cells proliferate within the prostatic transition zone surrounding the urethra. BPH is a common chronic medical condition often associated with progressive development of voiding and storage-related lower urinary tract symptoms (LUTS). The bother factor of symptoms associated with LUTS/BPH increase in severity in proportion to age [1,2]. Between 50% and 70% of men suffer from LUTS associated with BPH after the age of 50 yr, and evidence suggests that the prevalence of LUTS/BPH is as high as 80–90% among males older than 80 yr [3,4]. The global prevalence of LUTS/BPH, the impact of BPH on patients and their partners, and the economic burden of this condition confirm the need for appropriate medical care.

Pharmaceutical, surgical, and minimally invasive treatments for BPH are available. BPH treatments recommended for patients with a large prostate include transurethral resection of the prostate (TURP), laser ablation, and simple open or laparoscopic prostatectomy [5–7]. Current practice guidelines recommend Rezūm system water vapor thermal therapy (Boston Scientific, Marlborough, MA, USA) for prostate glands of 30–80 cm^3 in volume [4,5,7,8]. Treatment recommendations are based on the level of evidence available. High-quality evidence on Rezūm use for larger prostates is limited, and some regions have labeling indications limiting Rezūm to prostate volumes of 30–80 cm^3. Despite the lack of published evidence, patients with a larger prostate may benefit from Rezūm. The aim of this study was to assess Rezūm therapy as a treatment option for men with a larger prostate gland.

Few prospective studies have specifically evaluated the role of Rezūm therapy for larger prostates. The global prevalence of LUTS indicates further study is warranted in this field to guide treatment recommendations. This study will allow systematic evaluation of the treatment algorithm (eg, placement and number of treatments, and post-treatment catheterization) using the Rezūm system to treat BPH in men with a large prostate. Here we report on the safety and efficacy of Rezūm therapy for BPH treatment in men with a prostate >80 cm^3 and ≤150 cm^3 at 6 and 12 mo after the procedure.

2. Patients and methods

2.1. Study design

This prospective, single-arm study was conducted at seven centers in the USA. Each site had ethics committee approval (Clinicaltrials.gov NCT03605745).

2.2. Patients

Complete inclusion and exclusion criteria are listed in Supplementary Table 1. Enrolled subjects were males aged >50 yr with symptomatic BPH, International Prostate Symptom Score (IPSS) ≥13, maximum flow rate (Qmax) ≥5 to ≤12 ml/s, voided volume of ≥125 ml, postvoid residual volume (PVR) ≤300 ml (measured via bladder ultrasound), and prostate volume >80 cm^3 and ≤150 cm^3. Key exclusion criteria were prostate-specific antigen (PSA) >2.5 ng/ml with free PSA <25% (unless a negative biopsy excluded prostate cancer) and active urinary tract infection. Concomitant medications affecting BPH symptoms could not be taken, except the dose at baseline was allowed for up to 120 d after treatment (maximum number of days for the 3-mo follow-up visit window). Medications not restricted by the exclusion criteria could be used during the study for treating or preventing disease or to maintain good health.

2.3. Procedures

Antibiotic prophylaxis was a 5-d course of oral antibiotics starting up to 2 d before the procedure. The device description and technical procedure for Rezūm therapy have previously been published [9–11]. In brief, the Rezūm system delivers sterile water vapor via a transurethral approach for ablation of targeted areas of prostate tissue in men with moderate to severe BPH. Water vapor is injected into prostate tissue via a retractable needle and are varied in number, depending on prostate size and shape. Treatment is typically performed as a day-case procedure and lasted up to 5 h.

Each subject had an indwelling catheter for at least 7 d after the procedure before attempting a voiding trial. Subjects were treated with antibiotics for 2 d before and 3 d after catheter removal. Four subjects had acute urinary retention within 24 h of catheter removal.

2.4. Outcomes

Data were collected before the procedure to establish baseline status and at follow-up visits at 2 and 6 wk and 3, 6, and 12 mo after the procedure. The primary efficacy endpoint was treatment response, defined on a per-subject basis as a composite of freedom from retreatment for BPH and IPSS improvement ≥30% after treatment in comparison to baseline. A 30% IPSS improvement was estimated to be the minimum required to

yield patient satisfaction with treatment in a previous study that included baseline IPSS ≥12 [12]. The present study was designed to evaluate the hypothesis that the proportion of patients with a response to treatment exceeds 50%. The 50% criterion was set at a margin of approximately 15 percentage points above the percentage that responded to sham treatment (34.4%) in a randomized trial of Rezūm therapy [9].

The primary safety endpoint was device-related serious complications, predefined as rectal or gastrointestinal tract perforation; fistula formation between the rectum and urethra; permanent damage to the bladder, trigone, or ureteral orifices requiring intervention; or grade 2 hydronephrosis.

Secondary endpoints included device-related catheterization, defined as de novo acute severe urinary retention lasting more than 30 cumulative days after treatment, and IPSS improvement at 6 mo. The 30-d limit aligns with the maximum cumulative catheterization time in the Rezūm II trial for smaller glands. Ancillary endpoints provided additional characterization of the safety and effectiveness of the Rezūm system and included a variant of the treatment response endpoint, with ≥30% IPSS improvement from baseline replaced by ≥8-point IPSS improvement, Qmax and PVR changes from baseline, treatment of the median lobe, and changes in quality of life (QoL) from baseline at each follow-up visit. QoL change was measured using the QoL questions from the IPSS and the BPH Impact Index (BPHII) [13,14].

2.5. Statistical analysis

A sample size of 88 subjects was required to provide 90% power for the primary efficacy endpoint, assuming 67.5% of patients in the population would be treatment responders. Continuous variables are summarized as the mean and standard deviation or median and interquartile range (IQR) and range. Categorical variables are summarized using frequency distributions. Binary endpoints are summarized using proportions and corresponding two-sided 95% Clopper-Pearson confidence intervals (CIs). The mean 6-mo IPSS improvement was estimated using a two-sided 95% CI. The IPSS change from baseline across visits was analyzed in a linear model using generalized estimating equations. Missing data for continuous variables were imputed via linear interpolation of the last observation before the missing value and the next observation after the missing value. If a subject was surgically retreated for BPH or took medication for BPH after 120 d postprocedure, the IPSS at all time points after such retreatment was replaced by the subject's baseline score to avoid confounding the response to the index treatment with the response to other therapies received; this replacement was applied to indicate that the subject's response to the study treatment was inadequate. Analyses were conducted using SAS v9.4 (SAS Institute, Cary, NC, USA).

3. Results

Of 105 patients who provided consent, 47 were enrolled and treated with Rezūm between July 2018 and August 2020 (Fig. 1). Fifty-seven subjects did not qualify and were excluded before treatment (Supplementary Table 2). The 47 subjects who received treatment completed 6-mo follow-up, and 40 completed 12-mo follow-up. One subject undergoing screening during site closure was not enrolled.

3.1. Patient demographics and procedural characteristics

Table 1 reports patient characteristics. Prostate volume ranged from 80.8 to 148.1 cm^3 (median 92.9). The median Qmax was 9 ml/s (IQR 7–10) and the median PVR was 72 ml (IQR 38–177). Most subjects (95.7%, 45/47) had managed their BPH symptoms using medication, with 85.1% (40/47) using BPH treatment medication at baseline. Procedures had a median duration of 6 min (IQR 5–8) and delivered a median of 11 injections (IQR 9–12) per patient. Injection was delivered to the central zone or median lobe in 96.2% (25/26) of subjects with median lobe prominence noted at baseline and 66.7% (14/21) of subjects without median lobe prominence. A mandatory indwelling catheter was placed for 7–10 d after the procedure.

3.2. Outcome measures

The proportion of subjects with a 6-mo IPSS improvement ≥30% after treatment in comparison to baseline (primary efficacy endpoint) was 83% (95% CI 69.2–92.4). The mean 6-mo IPSS improvement from baseline was 11.9 ± 7.5 points (n = 47) with a 95% CI lower bound of 9.7 points (baseline: 20.6 ± 5.2; 6 mo: 8.7 ± 7.4).

The mean change in IPSS from baseline gradually improved over time (Fig. 2 and Supplementary Table 3). By 12 mo, 69.0% of patients (95% CI 52.9–82.4%) had an improvement in IPSS of at least 8 points in comparison to baseline (Table 2).

Other longitudinal outcomes are detailed in Figure 3 and Supplementary Table 4. Qmax was higher than at baseline at each visit up to 12 mo, with a mean improvement at 12 mo of 7.1 ± 7.0 ml/s (95% CI 4.9–9.3). Mean PVR was lower than at baseline at each visit and a durable improvement up to 12 mo by a mean of 32.1 ml, with an upper 95% confidence bound (minimum reduction) of 2.9 ml. The mean IPSS-QoL score improved in comparison to baseline at each visit, with a durable reduction up to 12 mo by a mean of 3.0 points, with an upper 95% confidence bound (minimum reduction) of 2.4 points. Similarly, the mean BPHII score improved in comparison to baseline at each visit, with a durable reduction up to 12 mo by a mean of 5.0 points, with an upper 95% confidence bound (minimum reduction) of 4.1 points.

3.3. BPH retreatment within 6 mo

There were no surgical retreatments within 6 mo. Three subjects (6.4%) were considered nonresponders to treatment because they continued α-blocker medication beyond the 3-mo visit window (120 d). One of these subjects exited the trial after his 6-mo visit (6 d after stopping medication) because his symptoms had not sufficiently improved from baseline. He reported urgency onset a few days before stopping BPH medication that was ongoing at the time of study exit.

3.4. Safety outcomes

No primary safety endpoint events (0/47, 95% CI 0.0–7.5%) occurred within 6 mo after treatment. No catheters were placed for de novo acute severe urinary retention lasting more than 30 cumulative days after treatment (0/47). No serious adverse events (SAEs) were related to the device. Two SAEs were associated with the treatment procedure: acute prostatitis (n = 1; (Clavien-Dindo grade II) and gross hematuria with clots and retention (n = 1; Clavien-Dindo grade IIIb). Acute prostatitis was treated with antibiotics, and gross hematuria with clots and retention was treated with cystourethroscopy with clot irrigation/evacuation.

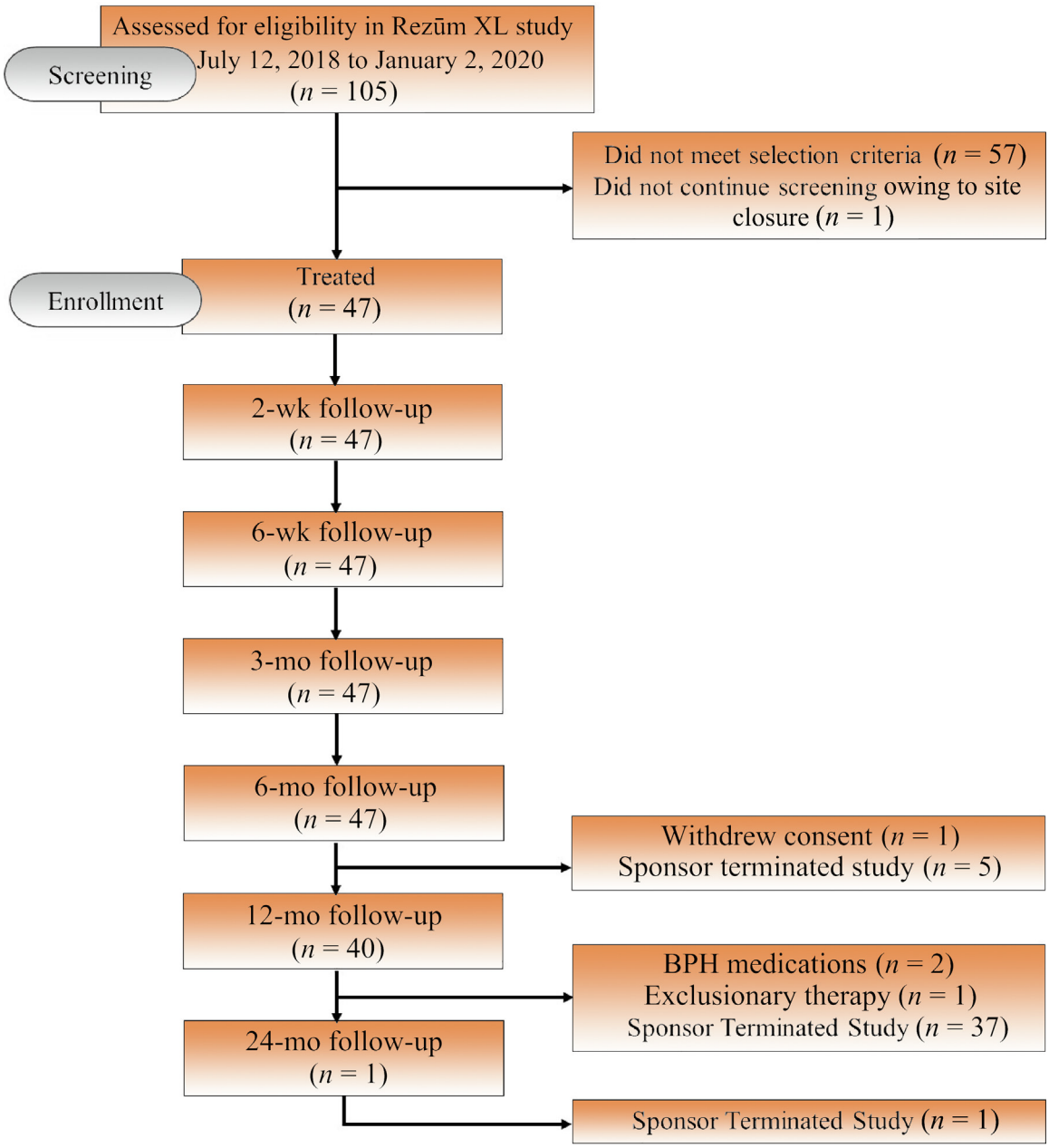

Fig. 1 – Study enrollment and follow-up.

Two additional SAEs were unrelated to the device or treatment procedure.

Up to the last follow-up visit, 164 nonserious AEs were reported in 43 (91.5%) subjects (Table 3). Of these AEs, 34 were device-related and 117 were related to the treatment. The most common AEs were urinary tract infections, gross hematuria, urinary urgency, bladder spasms, and dysuria. Most of the nonserious AEs occurred during the first 6 mo (145 events in 80.9% of subjects, 38/47).

4. Discussion

This multicenter prospective trial adds to the growing body of evidence supporting the safety and effectiveness of Rezūm therapy for men with a prostate gland >80 cm^3. At 6 mo after treatment, 83% of subjects (39/47) had a ≥30% reduction in IPSS in comparison to baseline. IPSS improved over time and was durable up to 12 mo. There were no device-related SAEs and no device-related catheterizations (0/47) due to de novo acute severe urinary retention more than 30 cumulative days after treatment.

One ancillary endpoint was comparison of AE rates between this study and the Rezūm II trial, a 5-yr prospective, randomized controlled trial on the safety and efficacy of Rezūm for BPH [15]. The SAE rate within 180 d (6.4%, 3/47) was similar to the rate in the Rezūm II trial (6.7%, 9/135). The nonserious AE rate was lower in the Rezūm II trial (80.9%, 38/47 vs 47.4%, 64/185), and the device-related event rate (number of device-related events/total

Table 1 – Patient demographics and treatment characteristics

Parameter	Result
Median age, yr (IQR) {range}	68 (63–73) {51–82}
Median body mass index, kg/m^2 (IQR {range}	29 (26.2–33) {23–45.8}
Race/ethnicity, % (*n*/*N*)	
White	85.1 (40/47)
Hispanic or Latino	8.5 (4/47)
Black or African American	6.4 (3/47)
Other	0 (0/47)
Median prostate volume, cm^3 (IQR) {range}	92.9 (85.1–115.6) {80.8–148.1}
Median prostatic lobe, % (*n*/*N*)	55.3% (26/47)
Intravesical prostatic protrusion, % (*n*/*N*)	80.9% (38/47)
Grade I (≤5 mm)	14.9% (7/47)
Grade II (>5 to 10 mm)	17% (8/47)
Grade III (>10 mm)	46.8% (22/47)
Median prostate-specific antigen, ng/dl (IQR {range}	3.3 (2.3–5.5) {0.3–11.2}
Median Qmax, ml/s (IQR) {range}	9 (7–10) {6–12}
Median postvoid residual volume, ml, *n* (IQR) {range}	72 (38–177) {0–297}
Prior BPH management, % (*n*/*N*)	
Medication	95.7 (45/47)
Active surveillance	10.6 (5/47)
Other	2.1 (1/47)
Current BPH medication use, % (*n*/*N*)	85.1 (40/47)
Median length of procedure, min (IQR) {range}	6 (5–8) {4–30}
Median number of treatments, *n* (IQR) {range}	
Right lobe	5 (4–5) {3–7}
Left lobe	4 (4–5) {3–7}
Median lobe	1 (0–2) {0–3}
Central zone	0 (0–0) {0–2}
Intravesical protrusions	0 (0–0) {0–3}
Total	11 (9–12) {6–15}
Median number of treatments per cm^3 prostate volume, *n* (IQR) {range}	0.1 (0.1–0.1) {0.1–0.2}

BPH = benign prostatic hyperplasia; IQR = interquartile range; Qmax = maximum flow rate.

Table 2 – Longitudinal International Prostate Symptom Score responder rate up to 12 mo

Time	Responders (*n*/*N*)	Response rate, % (95% CI)
6 wk	31/47	66.0 (50.7–79.1)
3 mo	34/47	72.3 (57.4–84.4)
6 mo	33/47	70.2 (55.1–82.7)
12 mo	29/42	69.0 (52.9–82.4)

CI = confidence interval.
[a]A response was defined as an improvement of ≥8 points in International Prostate Symptom Score from baseline.

number of events) did not exceed that in Rezūm II (69.7%, 129/185 vs 23.4%, 34/145). Study protocol differences in the reporting of nonserious AEs may explain the higher AE rate. Worsening or de novo LUTS, dysuria, nonobstructive hematuria that occurred and resolved within 14 d of treatment that did not require intervention beyond catheterization, prophylactic antibiotics, anti-inflammatory medication, and pain medication were not considered reportable AEs in Rezūm II, as these are expected during the healing process after vapor ablation or cystoscopy. The protocol for the present study recorded these events as AEs. In addition, more injections were necessary because of the larger prostates in this study (4.5 ± 1.8 vs. 10.6 ± 2.3) [15]. A greater number of injections may proportionally affect postprocedural event rates. Moreover, flexible cystoscopy and an indwelling catheter were mandatory for 7–10 d after treatment in the present study, versus only 2–4 d in Rezūm II. A longer catheterization time could cause increased postprocedure irritative symptoms.

There are a growing number of studies on Rezūm therapy for prostates >80 cm^3. A retrospective review by Bole et al. [16] revealed similar symptom and voiding improvements in groups of men with large (>80 ml, *n* = 47) and small glands (*n* = 140) 3 mo after Rezūm treatment. Another retrospective analysis by Garden et al. [17] found similar symptomatic relief and durable voiding improvements for groups with small (<80 cm^3) and large (≥80 cm^3) glands after Rezūm treatment at follow-up exceeding 3 mo. A recent prospective registry study by Elterman et al [18,19] demonstrated the safety and efficacy of Rezūm treatment in men with a prostate ≥80 ml. BPH symptom improvement was similar to that described here. IPSS improved by 59% by

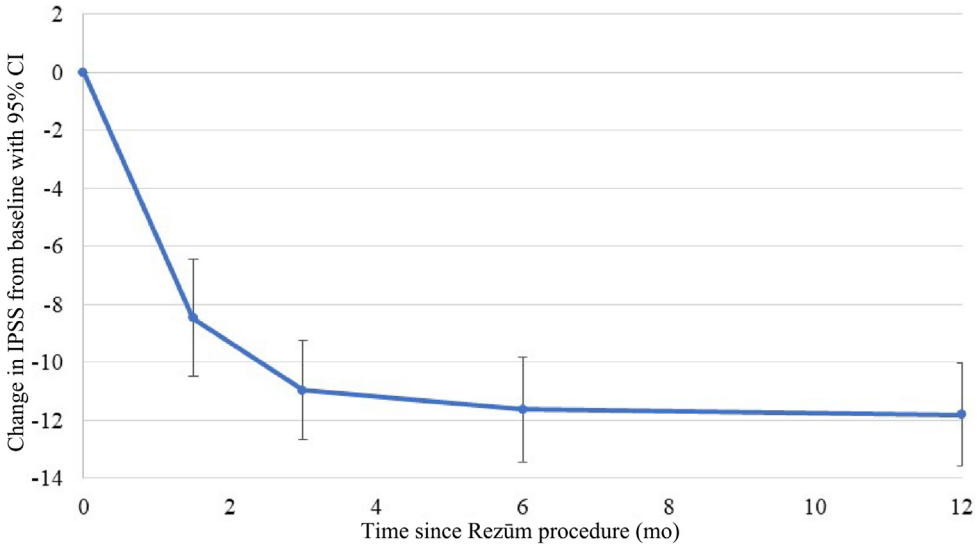

Fig. 2 – Change in International Prostate Symptom Score (IPSS) from baseline over time with 95% confidence interval (CI).

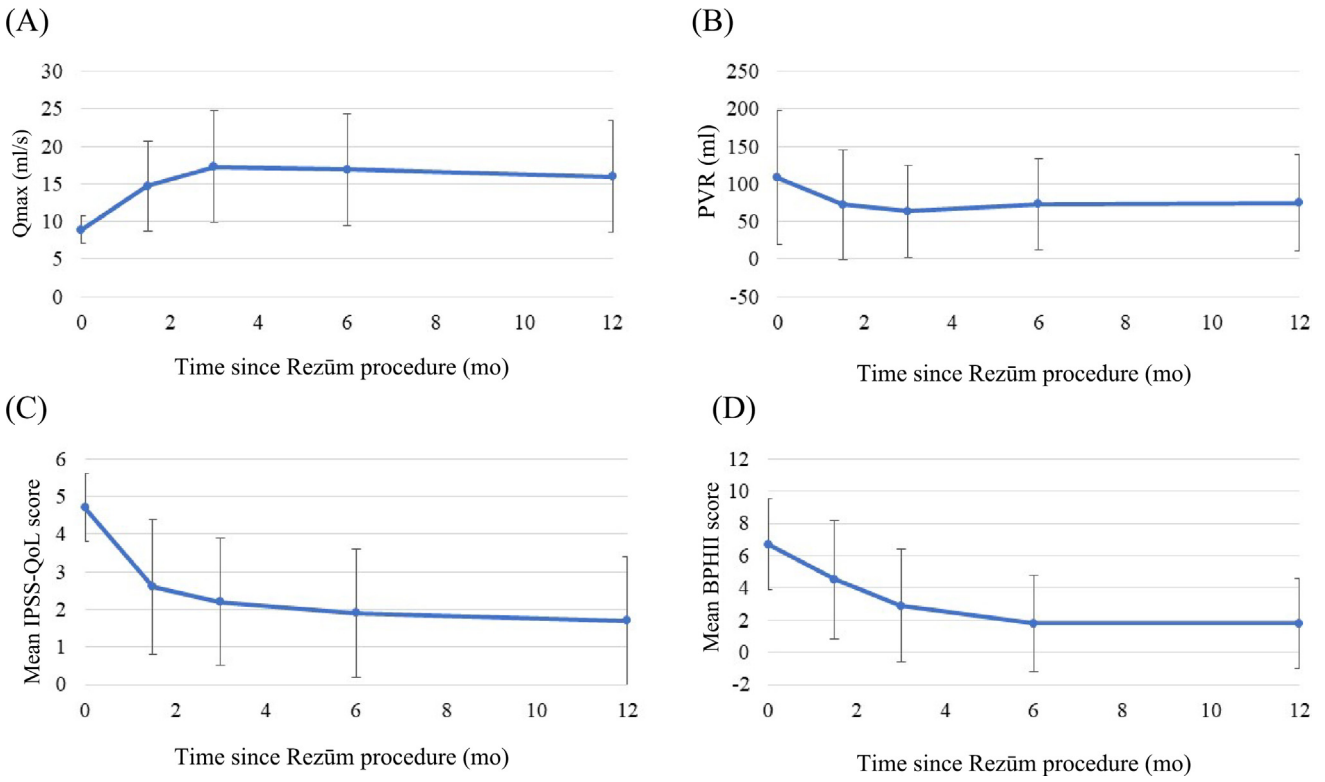

Fig. 3 – Longitudinal analysis of (A) maximum flow rate (Qmax), (B) postvoid residual volume (PVR), (C) International Prostate Symptom Score-quality of life (IPSS-QoL), and (D) Benign Prostate Hyperplasia Impact Index (BPHII) up to 12 mo. Data are reported as the mean and standard deviation.

12 mo with a change of −12.2 ± 7.7 from baseline, which is similar to the change reported here (−11.9 ± 7.5). At 6 mo, Qmax had improved by 67% to 6.2 ± 8.3 ml/s, which is comparable to the improvement in this study (8.0 ± 7.5 ml/s). In addition, the 12-mo BPHII score improved by 4.5 ± 3.0 points in comparison to baseline, similar to the improvement here (5.0 ± 3.1).

Additional studies in patients with a large gland include both prospective and retrospective cohorts. A retrospective study by Campobasso et al. [20] included patients with a gland >80 ml and the authors concluded that prostate volume is not a predictive factor for urinary and sexual outcomes after Rezūm. A single-site prospective registry study of 24 patients treated with Rezūm included five patients with a gland of 80–120 ml, with favorable safety and effectiveness outcomes for the entire cohort [21]. A retrospective study (n = 211) that included 42 patients with a prostate ≥80 ml revealed that prostate volume ≥80 ml was associated with a higher risk of reoperation (odds ratio 4.29, 95% CI 1.15–15.1; p = 0.024), with 9.5% of the large-gland cohort undergoing retreatment (4/42) [22]. However, a multisite prospective observational study of 461 patients (n = 83 with prostate ≥80 ml) by Whiting et al [23] found no significant difference in the retreatment rate at 1 yr between groups with small and large glands (2.7% vs 3.6%; p = 0.07).

In our study, no subjects (0/47) needed surgical retreatment within 6 mo of Rezūm; three patients (6.4%) continued α-blocker medication beyond the 3-mo visit window and were counted as treatment failures. This is less than the surgical retreatment rate of 8.33% (3/25) for the large-gland cohort in the study by Garden et al [17], and the 2.2% in the Rezūm II trial up to 12 mo [15]. Although retreatment was followed up to 6 mo in this study, the surgical retreatment rate was not higher for patients with a large gland.

Although there is an absence of head-to-head comparisons between Rezūm and other minimally invasive procedures for BPH, a recent network meta-analysis of four randomized controlled trials compared functional and perioperative outcomes for Aquablation, Rezūm, and UroLift to a pooled control group (TURP) [24]. None of the procedures was associated with greater improvements across the board, highlighting the tradeoffs to be considered for factors such as anesthesia, complications, and preservation of sexual and urinary function. TURP outperformed Rezūm for outcomes that included Qmax and PVR, but was associated with higher incidence of AEs and longer hospital stay, versus same-day discharge for Rezūm. Rezūm performance was variable in comparison to the other minimally invasive procedures, with the shortest return to preoperative activity and comparable sexual function outcomes. These comparisons did not take into account the presence of patients with a large gland. In a narrative review of minimally invasive therapies including Aquablation, Rezūm, and transperineal laser prostate ablation, Nguyen and colleagues [25]

Table 3 – Nonserious adverse events among the 47 patients

Adverse event	Events	Patients,	Relatedness		
	(*n*)	*n* (%)	Device	Treatment	Unrelated
Other	17	8 (17.0)	0	0	17
Urinary tract infection – culture-proven	13	11 (23.4)	4	13	0
Hematuria – gross	12	12 (25.5)	6	12	0
Urinary urgency	11	10 (21.3)	3	10	1
Bladder spasms	10	10 (21.3)	5	9	1
Dysuria	10	10 (21.3)	6	9	1
Acute urinary retention	7	7 (14.9)	2	7	0
Urinary incontinence – urge	6	5 (10.6)	2	6	0
Pain/discomfort – other	5	4 (8.5)	0	2	3
Pain/discomfort – penile	5	4 (8.5)	3	5	0
Poor stream	5	5 (10.6)	0	5	0
Terminal dribbling	4	4 (8.5)	0	4	0
Urinary incontinence – not specified	4	3 (6.4)	0	3	1
Constipation	3	3 (6.4)	0	1	2
Diarrhea	3	3 (6.4)	0	0	3
Erectile dysfunction – worsening	3	3 (6.4)	0	3	0
Nocturia	3	3 (6.4)	0	3	0
Pain/discomfort – leg	3	2 (4.3)	0	0	3
Anejaculation	2	2 (4.3)	0	2	0
Decrease in ejaculatory volume	2	2 (4.3)	0	2	0
Epididymitis	2	2 (4.3)	1	2	0
Fever	2	2 (4.3)	0	1	1
Hematospermia	2	2 (4.3)	1	2	0
Hesitancy	2	2 (4.3)	0	2	0
Incomplete voiding	2	2 (4.3)	0	2	0
Pain/discomfort – arm	2	2 (4.3)	0	0	2
Pain/discomfort – back	2	2 (4.3)	0	0	2
Rising prostate-specific antigen	2	2 (4.3)	0	0	2
Sloughing	2	2 (4.3)	0	2	0
Urinary frequency	2	2 (4.3)	0	1	1
Cancer – other	1	1 (2.1)	0	0	1
Catheter malfunction	1	1 (2.1)	0	1	0
Dizziness	1	1 (2.1)	0	0	1
Erectile dysfunction – de novo	1	1 (2.1)	0	1	0
Headache	1	1 (2.1)	0	1	0
Hematuria – intermittent uncomplicated	1	1 (2.1)	1	1	0
Hematuria – gross with clots and retention	1	1 (2.1)	0	1	0
Hypertension	1	1 (2.1)	0	0	1
Pain/discomfort – abdominal	1	1 (2.1)	0	1	0
Pain/discomfort – body aches	1	1 (2.1)	0	0	1
Pain/discomfort – pelvic	1	1 (2.1)	0	1	0
Pain/discomfort – suprapubic	1	1 (2.1)	0	1	0
Retrograde ejaculation – confirmed	1	1 (2.1)	0	1	0
Syncope	1	1 (2.1)	0	0	1
Urinary tract infection – suspected	1	1 (2.1)	0	0	1
Upper respiratory tract infection	1	1 (2.1)	0	0	1
Total	164	43 (91.5)	34	117	47

highlighted the rapid treatment and recovery times and promising safety profile for Rezūm, including men with a large gland.

It has previously been shown that the Rezūm system is safe and effective when treating men with a prostate $\leq$80 cm^3, and this study provides additional data suggesting it is also effective in treating prostates >80 cm^3 and <150 cm^3. Rezūm therapy is a minimally invasive option for men who want to avoid the risks of more invasive treatments. Data from this study suggest that Rezūm has significant therapeutic benefit and manageable nonserious AEs that resolve over time. In addition, clinicians treated larger prostates in an office setting under local anesthesia, allowing treatment of men who would not otherwise be able to undergo treatment for their BPH symptoms.

A critical strength of this study is that it is a data-rich, prospective, multicenter trial with a preplanned protocol. The study adds to the growing body of literature on treating glands $\geq$80 cm^3 with water vapor thermal therapy, with good patient compliance with follow-up visits.

A major study limitation is the lack of a randomized comparison. In addition, the original plan was to follow subjects for 3 yr, but the study was terminated early. Early study closure precluded 3-yr follow-up and achievement of the planned enrollment number. The shorter follow-up limits conclusions regarding efficacy. Subject enrollment was a challenge because of the ambitious protocol, the decision by many urologists to start treating larger glands, and the negative impact of COVID-19 on enrollment and protocol-specified follow-up visits. The study was not closed for safety or effectiveness reasons.

5. Conclusions

Our prospective study corroborates previous findings indicating that Rezūm water vapor therapy is a safe and effective option for men with a larger prostate who desire minimally invasive treatment for their BPH.

Author contributions: Henry Woo had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Woo.
Acquisition of data: Levin, Cantrill, Zhou, Neff, Sutton, Bailen, Darson, Horgan.
Analysis and interpretation of data: Zantek, Woo.
Drafting of the manuscript: Woo, Marty-Roix.
Critical revision of the manuscript for important intellectual content: Woo, Levin, Zantek, Marty-Roix, Cantrill, Zhou, Neff, Sutton, Bailen, Darson, Horgan.
Statistical analysis: Zantek.
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Appendix A. Supplementary data

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