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The PINNACLE Study: A Double-blind, Randomized, Sham-controlled Study Evaluating the Optilume BPH Catheter System for the Treatment of Lower Urinary Tract Symptoms Secondary to Benign Prostatic Hyperplasia

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Study Need and Importance: The percentage of men who suffer annually from urinary tract symptoms secondary to benign prostatic hyperplasia (BPH) remains high (70% of men >70 years); however, less than 3% of drug therapy or watchful waiting patients move to surgical intervention, likely due to unwanted side effects and diminished sexual function. Minimally invasive BPH therapies have done well minimizing these effects, but they have failed to achieve their goal of replacing maximum urinary flow rates (Qmax) associated with transurethral prostatectomy—until now.

What We Found: We randomized 148 men (100 active, 48 sham) at 18 centers in North America. Subjects receiving Optilume BPH saw a mean±SD reduction in International Prostate Symptom Score of 11.5±7.8 points at 1 year, as compared to a reduction of 8.0±8.3 points at 3 months in the sham arm. Qmax improved dramatically after treatment with Optilume BPH, with an improvement of +10.3 mL/s from baseline to 1 year (+125%; see Figure). Treatment with Optilume BPH provides immediate and sustained improvements in obstructive symptoms and flow rate while preserving erectile and ejaculatory function. Treatment is well tolerated and can be done in an office or ambulatory setting.

Limitations: Eligibility criteria for this study limited enrollment to those men with prostates below 80 g and with moderate or severe symptoms and restricted flow; results may not be generalizable to all men with lower urinary tract symptoms secondary to BPH.

Interpretation for Patient Care: Treatment of lower urinary tract symptoms secondary to obstructive BPH with Optilume BPH results in significant and clinically meaningful improvements immediately postprocedure, which are sustained through 1 year of follow-up. The improvement seen for Qmax and postvoid residual through 1 year represents the largest seen for this product class. This minimally invasive treatment represents an attractive option to patients looking to maintain sexual function while achieving durable symptom relief and improved flow.

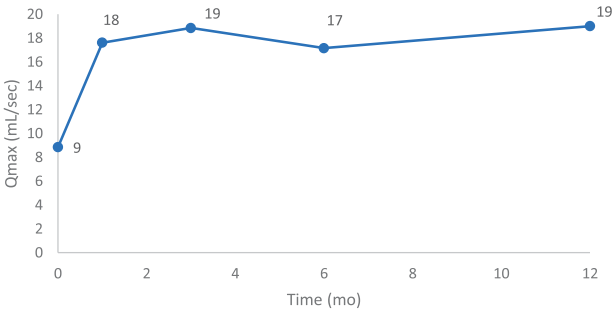

Figure. Peak urinary flow rate (Qmax) after treatment with Optilume BPH (as observed).

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The PINNACLE Study: A Double-blind, Randomized, Sham-controlled Study Evaluating the Optilume BPH Catheter System for the Treatment of Lower Urinary Tract Symptoms Secondary to Benign Prostatic Hyperplasia

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Purpose: The Optilume BPH Catheter System is a novel drug/device combination minimally invasive surgical therapy for the treatment of lower urinary tract symptoms secondary to benign prostatic hyperplasia. The PINNACLE study is a prospective, randomized, double-blind, sham-controlled clinical trial evaluating the safety and efficacy of Optilume BPH against a sham surgical procedure.

Materials and Methods: Eligible patients were men 50 years or older with symptomatic benign prostatic hyperplasia and a prostate size between 20 and 80 g. Subjects were randomized 2:1 to receive treatment with Optilume BPH or a sham surgical procedure. Blinding was maintained for subjects in both arms and evaluating personnel through 1 year postprocedure. Follow-up assessments included

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Conflict of Interest: OP: Gulf Coast: clinical research; BM: Teleflex, Boston Scientific, Proverum: consultant. The remaining Authors have no conflicts of interest to disclose.

Ethics Statement: This study received Institutional Review Board approval (IRB No. PR1087) prior to initiation, and written informed consent was obtained from all study subjects.

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the International Prostate Symptom Score, uroflowmetry, and other quality-of-life and sexual function assessments.

Results: A total of 148 men were randomized (100 active, 48 sham) at 18 centers in the U.S. and Canada. Subjects randomized to receive Optilume BPH saw a reduction in International Prostate Symptom Score of 11.5±7.8 points at 1 year posttreatment, as compared to a reduction of 8.0±8.3 points at 3 months in the sham arm. Flow rate was dramatically improved after treatment with Optilume BPH, with an improvement of +10.3 mL/s from baseline to 1 year (+125%).

Conclusions: Treatment with Optilume BPH provides immediate and sustained improvements in obstructive symptoms and flow rate while preserving erectile and ejaculatory function. Treatment is well tolerated and can be done in an office or ambulatory setting.

Key Words: prostatic hyperplasia, lower urinary tract symptoms, minimally invasive surgical procedures

THE development of benign prostatic hyperplasia (BPH) is nearly universal as men age, with approximately 80% of men developing BPH by age 80.[1] Lower urinary tract symptoms (LUTS) also increase in frequency and severity with the progression of BPH due in large part to bladder outlet obstruction from enlarged prostatic lobes. In one epidemiological study, nearly 25% of men aged 70 or older had received some form of treatment for BPH over 6 years of follow-up.[2]

The continuum of treatments for BPH range from less invasive lifestyle modification and medical management to more invasive transurethral or radical prostatectomy. Front-line therapy includes medical management, including α-adrenergic antagonists (α-blockers), 5-α reductase inhibitors (5-ARIs), or a combination of the two. Although this approach is the least invasive, patient adherence to long-term therapy can be as low as 30% and recent publications have called attention to potential negative effects of long-term medication usage.[3,4] Transurethral resection of the prostate has long been considered the gold standard for endoscopic treatment of BPH, offering significant improvement in symptoms and flow. However, the more invasive nature of surgical resection leads to the risk of perioperative and longer-term procedure-related morbidity.[5-7] Numerous minimally invasive surgical therapy (MIST) devices have been developed to bridge the gap between medications and resection, however attempts at developing this type of technology have had mixed results.[8]

The Optilume BPH Catheter System is a minimally invasive paclitaxel-coated dilation system and the first MIST device with a dual mechanical and pharmacological mechanism of action. Paclitaxel is an antiproliferative agent that is intended to maintain luminal patency of the prostatic urethra after dilation. Early experience with Optilume BPH has shown significant and durable improvement in symptoms and flow.[9] Treatment with paclitaxel-coated balloons has also been shown to significantly reduce the rate of stricture recurrence in men with urethral strictures.[10,11] This study compares the safety and efficacy of Optilume BPH to a sham surgical procedure for the treatment of LUTS secondary to BPH with outcomes reported through 12 months of follow-up.

MATERIALS AND METHODS

Study Protocol and Objectives

A prospective, randomized, controlled, double-blind study of Optilume BPH titled PINNACLE was conducted in men with symptomatic BPH (NCT04131907). One hundred forty-eight subjects were randomized in a 2:1 fashion to receive treatment with Optilume BPH or a sham procedure at 18 investigational centers in North America. Institutional Review Board approval was obtained at each center prior to initiation and written informed consent was obtained from all study subjects.

Eligible subjects included men between 50-80 years with an International Prostate Symptom Score (IPSS) of ≥13, peak urinary flow rate (Qmax) between 5-12 mL/s, prostate volume 20-80 g, and a prostatic urethral length of 32-55 mm. Key exclusions included prior minimally invasive or surgical intervention on the prostate, prostate specific antigen >10 ng/mL without negative biopsy, diagnosis or suspicion of prostate or bladder cancer, active urinary tract infection, postvoid residual urine volume (PVR) >300 mL, and confounding bladder or urinary tract diagnoses that could impact urinary function (neurogenic bladder, stricture, etc).

Subjects were required to wash out of BPH medications prior to baseline assessments, with a washout of 2 weeks for α-blockers and phosphodiesterase type 5 inhibitors, 3 months for 5-ARIs specifically targeting the type 2 isoenzyme, and 6 months for nonspecific 5-ARIs.

Optilume BPH Treatment Procedure

The objective of the Optilume BPH procedure is to create an anterior commissurotomy while simultaneously delivering paclitaxel to the prostatic adenoma to prevent continued growth and refusion of the lateral lobes (Figure 1). The proprietary balloon design overcomes limitations of previous dilation systems, with a double-lobe balloon design that "locks" onto the bladder neck to prevent migration of the balloon during inflation.

The Optilume BPH Catheter System is comprised of 2 dilation balloon catheters: 1 uncoated predilation catheter and 1 drug-coated balloon (DCB) catheter. The Optilume BPH DCB is available in 4 sizes, all 90F in diameter and

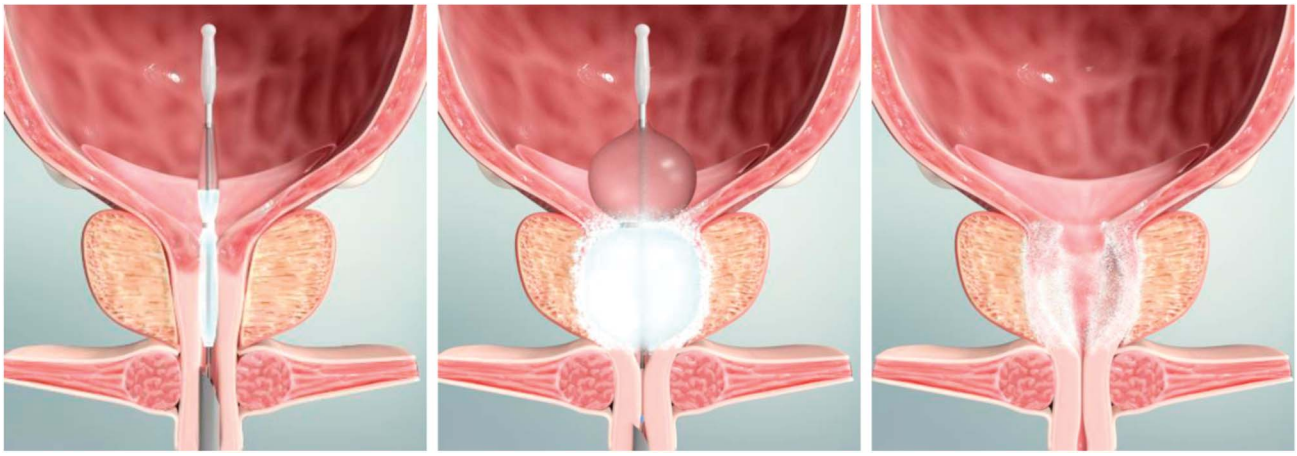

Figure 1. Optilume BPH combines mechanical dilation using a proprietary double-lobe balloon with concurrent delivery of paclitaxel to limit continued growth and refusion of the lateral lobes after achievement of the anterior commissurotomy.

ranging from 30 mm to 45 mm in treatment length. Size selection is precision matched to every individual prostate based on prostatic urethral length as measured by transrectal ultrasound performed preprocedure.

During the Optilume BPH procedure, cystoscopy is performed with a 20F rigid scope, followed by insertion of the uncoated predilation catheter which is then positioned under direct visualization. A blue mark on the catheter shaft aids with precision placement of the device and is positioned at the distal end of the external sphincter and monitored cystoscopically throughout the procedure. The predilation balloon is inflated and held for approximately 1 minute to initiate an anterior commissurotomy. The DCB is inserted, positioned in a similar manner, and inflated for at least 5 minutes to further propagate the anterior commissurotomy and deliver paclitaxel to the prostatic urothelium. After the procedure a Foley catheter is placed for 2 days.

Sham Treatment Procedure

The sham treatment utilized rigid cystoscopy followed by insertion of a sheathed (21F) Optilume BPH Predilation Catheter that was not inflated. The sham device was held in place for approximately 5 minutes and a script was provided to study staff to mimic the discussion and procedure steps of the Optilume BPH procedure. Both devices were required to be visible in the operating room during the procedure and a sheet was placed to block the subject's view of the treatment area. The study required that treatment location, analgesia and anesthesia protocols, and catheterization protocols must not differ between arms. All subjects receiving the sham procedure had a Foley catheter placed for 2 days.

Assessments and Follow-up

Follow-up assessments were conducted at 14 days, 30 days, 3 months, 6 months, and 1 year after treatment in both arms. Self-administered questionnaires included the IPSS, BPH Impact Index (BPH-II), International Index of Erectile Function, Male Sexual Health Questionnaire for Ejaculatory Dysfunction, and the EQ-5D-5L. Uroflowmetry and PVR assessments were conducted at each follow-up, with a minimum voided volume of 150 mL required to qualify as a valid reading.

Subjects and evaluating personnel were blinded to treatment received through the 1-year time point in both arms. Subjects initiating alternative BPH therapy were discontinued from further follow-up at the time therapy was received. Subjects randomized to the sham arm were allowed to cross over to receive treatment with Optilume BPH after the 3-month visit, however this was only allowed after the subject had discussed general treatment options in a blinded manner with blinded site personnel and had opted to break the blind and pursue alternative therapy. Subjects opting to cross over were required to continue to meet study eligibility criteria.

Table 1. *Subject Demographics and Baseline Characteristics*

Characteristic	Optilume BPH (n = 100)	Sham (n = 48)	*P* value[a]
Age, mean ± SD, y	64.5 ± 6.4	65.5 ± 5.6	.4
BMI, mean ± SD, kg/m^2	29.3 ± 4.5	29.1 ± 4.7	.7
Prostate-specific antigen, mean ± SD, ng/mL	2.42 ± 2.0	2.2 ± 1.8	.5
Prostate volume, mean ± SD, mL	44.9 ± 14.5	45.0 ± 13.2	> .9
Intravesical prostatic protrusion			
No./total No. (%)	28/100 (28.0)	16/48 (33.3)	.5
Size, mean ± SD, mm	5.1 ± 2.2	5.3 ± 1.5	.7
IPSS, mean ± SD	23.4 ± 5.5	24.3 ± 5.8	.4
Qmax, mean ± SD, mL/s	8.9 ± 2.2	9.0 ± 1.8	.8
Postvoid residual volume, mean ± SD, mL	84.1 ± 70.2	89.4 ± 73.9	.7

Abbreviations: BMI, body mass index; BPH, benign prostatic hyperplasia; IPPS, International Prostate Symptom Score; Qmax, peak urinary flow rate; SD, standard deviation.
[a] Calculated using 2-sample *t* test for continuous variables and χ^2 test for categorical variables.

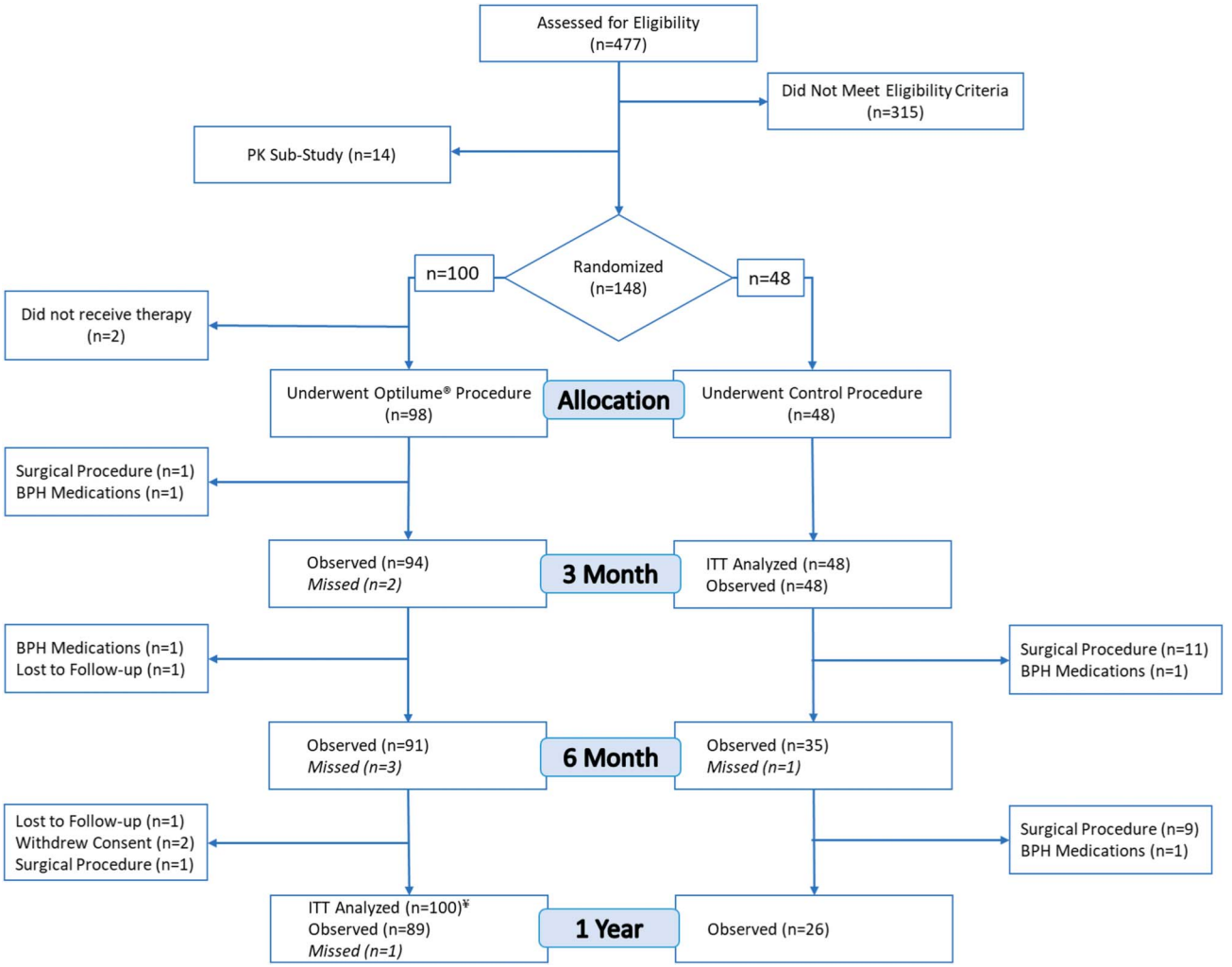

Figure 2. CONSORT (Consolidated Standards of Reporting Trials) flow diagram of subject disposition in both study arms through the 12-month time point. ¥Subjects missing data for the intent-to-treat (ITT) analysis of the primary end point were imputed using multiple imputation; subjects receiving additional medical or surgical therapy for benign prostatic hyperplasia (BPH) were considered as having no improvement from baseline. PK indicates pharmacokinetic.

Adverse events were prospectively collected, and all events were adjudicated by a blinded, independent clinical events committee for relatedness and event severity utilizing the Common Terminology Criteria for Adverse Events. A separate Data Monitoring Committee reviewed study progress and ongoing safety outcomes.

Statistical Methods

Randomization was conducted in an electronic system utilizing permuted blocks stratified by center and by baseline IPSS severity ($\leq$19 vs $>$19). The primary end point compared the improvement in IPSS from baseline to 3 months in the sham arm against the improvement from baseline to 1 year in the Optilume BPH arm. Key secondary end points included a comparison of improvement in Qmax between arms at the same time points (2-sample t test), the proportion of subjects experiencing a clinically meaningful improvement in symptoms in each arm (Fisher's exact test), and a comparison of the percent improvement in IPSS seen in the Optilume arm at 12 months against a performance goal of $\geq$30% (1-sample t test). Sample size was calculated for 90% power (2:1 allocation, 0.025 1-sided type I error) for a comparison of mean values using a 2-sample t test. For the intent-to-treat (ITT) analysis, any subject who received alternative BPH therapy prior to the scheduled time point was considered as having no improvement from baseline. IPSS values missing for reasons other than treatment failure (eg, missed visit, loss to follow-up) were imputed using multiple imputation under the "missing at random" assumption. Descriptive statistics are used to present study variables, with continuous data presented as mean ($\pm$SD), and categorical data presented as proportion (percent). P values presented are nominal and are not adjusted for multiple comparisons.

RESULTS

Demographics and Procedure

A total of 148 subjects were randomized to receive Optilume BPH (100) or sham (48) between January 2020 and September 2021. Subject demographics were well matched between arms (Table 1). All subjects were

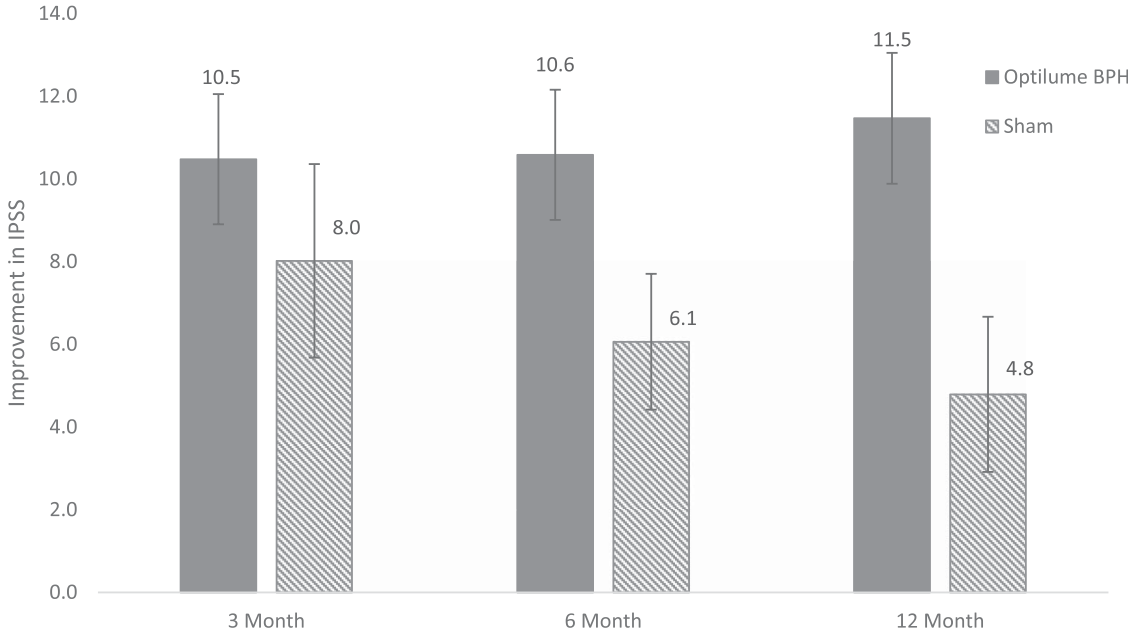

Figure 3. Improvement in International Prostate Symptom Score (IPSS) from baseline to the stated time point in the intent-to-treat population (mean±95% CI).

included in the ITT primary end point analysis, including 5 subjects imputed as having no improvement from baseline, 4 receiving alternative BPH therapy, and 1 subject who withdrew consent due to perceived lack of effectiveness (Figure 2).

Procedures were done in an outpatient setting, including both ambulatory surgical center and office-based locations. Most patients in each arm were treated under deep sedation or general anesthesia (84.7% vs 87.5%, $P = .9$), while moderate ("conscious") sedation and local prostate block were also used at a similar rate in each arm. The Optilume BPH procedure was well tolerated in those subjects utilizing prostate block. The average procedure time (scope in to scope out) was 26 minutes in the Optilume BPH group and 8 minutes in the sham group ($P < .01$). The duration of catheterization was similar between arms (3.0 vs 2.5 days, $P = .15$). Blinding procedures were very successful, with 100% of the sham arm subjects believing they underwent treatment with Optilume BPH or were not sure what treatment they received at the time of Foley removal 2-5 days posttreatment. This rate remained at 62.5% at the 3-month time point.

Efficacy

In the ITT analysis, the average improvement in IPSS from baseline to 12 months in the Optilume BPH arm (11.5±7.8) was significantly greater than that seen in the sham arm at 3 months (8.0±8.3), with an estimated difference of 3.4 between the groups (95% CI 0.6 to 6.2, $P = .008$). This significance was not maintained when a 25% super-superiority margin was incorporated ($P = .18$). IPSS improvement was maintained over time in the Optilume BPH arm while the magnitude of improvement in the sham arm deteriorated over time (Figure 3). Subject IPSS improved an average of 49% (95% CI 42.7% to 55.4%) from baseline to 1 year in the Optilume BPH arm, which easily met the prespecified performance goal of 30% ($P < .001$). Significantly more subjects experienced a ≥30% improvement in IPSS at 1 year in the Optilume BPH arm when compared to the sham arm at 3 months (66/96 [76.6%] vs 25/48 [52.1%], $P = .003$). The change in Qmax from baseline also significantly favored Optilume at 12 months over sham at 3 months (+9.7±10.1 vs +5.5±7.4 mL/s, $P = .009$).

Other outcomes showed a trend toward durable improvement with Optilume BPH, with significant improvements in IPSS–Quality of Life, BPH-II, Qmax, and PVR in the Optilume BPH arm from baseline through 1 year (Table 2). A significant increase in Qmax was observed immediately postprocedure, increasing from an average of 8.9 mL/s at baseline to 17.6 mL/s at 1 month postprocedure and maintained at 19.0 mL/s at 1 year ($P < .001$ for both). A concurrent decrease was observed in PVR, improving from 82 mL at baseline to 58 mL at 1 year ($P = .004$).

Safety and Tolerability

Five serious adverse events were adjudicated as possibly related to the study device; 4 events of post-procedural hematuria requiring cystoscopic management or extended observation which resolved without sequelae and 1 event of urethral false passage that required extended catheterization. Common nonserious adverse events in the Optilume BPH arm,

Table 2. *Changes in Outcomes for Optilume BPH From Baseline Through 12 Months of Follow-up*

Outcome	1 Mo	3 Mo	6 Mo	12 Mo
IPSS				
No. (paired)	97	94	91	89
Baseline, mean±SD	23.4±5.5	23.3±5.5	23.1±5.5	23.0±5.4
Follow-up, mean±SD	13.4±7.0	12.6±7.2	12.2±7.1	10.9±6.6
Change, mean±SD	−10.0±7.5	−10.7±7.8	−10.9±7.7	−12.1±7.5
% Change (95%CI)	−41.7 (−35.7, −47.8)	−44.7 (−38.1, −51.3)	−46.4 (−39.9, −53.0)	−51.7 (−45.5, −57.8)
P value[a]	< .0001	< .0001	< .0001	< .0001
IPSS−quality of life				
No. (paired)	97	94	91	89
Baseline, mean±SD	4.6±1.3	4.6±1.3	4.6±1.3	4.6±1.3
Follow-up, mean±SD	3.0±1.6	2.9±1.7	2.6±1.5	2.2±1.5
Change, mean±SD	−1.6±1.9	−1.7±1.8	−2.0±1.8	−2.4±1.9
% Change (95%CI)	−33.4 (−26.1, −40.7)	−36.2 (−29.2, −43.2)	−33.4 (−34.5, −49.8)	−50.9 (−43.9, −57.9)
P value[a]	< .0001	< .0001	< .0001	< .0001
Qmax				
No. (paired)	79	79	83	82
Baseline, mean±SD	8.9±2.2	8.8±2.1	8.8±2.2	8.7±2.1
Follow-up, mean±SD	17.6±9.0	18.8±9.7	17.2±8.9	19.0±10.3
Change, mean±SD	+8.7±8.9	+10.0±9.5	+8.3±8.7	+10.3±10.2
% Change (95%CI)	104.8 (79.2, 130.3)	120.5 (94.8, 146.1)	101.8 (78.4, 125.1)	125.2 (95.7, 154.7)
P value[a]	< .0001	< .0001	< .0001	< .0001
PVR				
No. (paired)	83	84	84	82
Baseline, mean±SD	82.2±72.1	84.8±73.1	84.8±73.1	83.2±71.1
Follow-up, mean±SD	61.9±55.5	66.8±69.4	58.9±59.3	58.0±51.2
Change, mean±SD	−22.5±85.2	−19.2±89.0	−25.7±87.2	−25.2±81.3
P value[a]	.019	.053	.009	.006
BPH-II				
No. (paired)	96	93	91	89
Baseline, mean±SD	6.9±3.0	6.9±3.0	6.8±3.0	6.8±3.0
Follow-up, mean±SD	5.3±3.2	4.5±3.2	2.9±2.8	2.3±2.5
Change, mean±SD	−1.6±3.8	−2.4±3.8	−3.9±3.8	−4.5±3.2
% Change (95%CI)	−3.0 (−21.1, 15.2)	−17.3 (−36.2, 1.6)	−46.7 (−60.6, −32.9)	−63.2 (−71.8, −54.5)
P value[a]	< .0001	< .0001	< .0001	< .0001

Abbreviations: BPH, benign prostatic hyperplasia; BPH-II, BPH Impact Index; CI, confidence interval; IPSS, International Prostate Symptom Score; PVR, postvoid residual urine volume; Qmax, peak urinary flow rate; SD, standard deviation.
[a] *P* values for change from baseline for each measure were calculated using a paired *t* test.

regardless of relatedness, included hematuria (39/98 [40%]), urinary tract infection (14/98 [14%]), dysuria (9/98 [9.2%]), urge/mixed incontinence (8/98 [8.2%]), mild stress incontinence (7/98 [7.1%]), bladder spasms (6/98 [6.1%]), elevated PSA (6/98 [6.1%]), and urinary urgency (6/98 [6.1%]). These events were typically mild to moderate and resolved within 1 month. One subject died of unrelated causes, as adjudicated by the clinical events committee, 18 months after treatment with Optilume BPH. Systemic exposure to paclitaxel was minimal in the subset of subjects in which pharmacokinetics was measured, with a mean maximum plasma paclitaxel concentration of 0.4 ng/mL reported at a median of 1 hour posttreatment. Average paclitaxel concentration in plasma was below the limit of quantitation of the analytical method by the time of Foley removal.

Sexual function was not significantly impacted by treatment with Optilume BPH, with both arms showing mild improvement in average scores across all International Index of Erectile Function and Male Sexual Health Questionnaire for Ejaculatory Dysfunction subdomains (Table 3). Four subjects in the Optilume BPH arm reported an adverse event of ejaculatory dysfunction, compared to 1 subject in the sham arm (4/98 [4.1%] vs 1/48 [2.1%], $P > .9$). No treatment-related de novo erectile dysfunction was reported.

DISCUSSION

The PINNACLE study provides confirmation that treatment with Optilume BPH leads to significant, immediate symptom relief and increased flow with minimal treatment-related adverse events and no impact of sexual function when compared to a robust sham procedure. Average IPSS decreased significantly from baseline to 3 months (−10.7, −45%), and this decrease was sustained through 12 months follow-up (−12.1, −52%). Improvement was also seen in the IPSS−Quality of Life (−2.4, −51%) and BPH-II (−4.5, −63%), both of which are measures of urinary health−related quality of life. Symptom and quality-of-life improvement was paired with clinically significant improvement in more objective measures such as Qmax (+10 mL/s) and PVR (−25 mL) 12 months after treatment. There was no heterogeneity observed in treatment effect among key clinical subgroups including moderate vs severe baseline symptom

Table 3. *Sexual Function Parameters in All Subjects*

Arm	Baseline mean±SD (n)	3 Mo mean±SD (n) Δbaseline	6 Mo mean±SD (n) Δbaseline	12 Mo mean±SD (n) Δbaseline
Optilume BPH				
IIEF-EF	15.6±10.3 (97)	16.5±10.8 (92) +0.8±8.6	17.3±11.0 (91) +1.5±7.9	17.1±11.1 (87) +0.9±7.7
MSHQ-EjD				
Function	7.6±3.9 (98)	8.5±4.8 (86) +1.1±4.0	8.3±4.5 (87) +0.9±3.4	8.4±4.6 (87) +0.9±3.5
Bother	2.5±1.7 (98)	1.9±1.6 (86) −0.7±1.8	2.1±1.7 (87) −0.5±1.9	2.0±1.7 (87) −0.6±1.7
Sham				
IIEF-EF	16.8±9.3 (48)	17.6±9.8 (47) +1.0±6.7	19.8±8.7 (35) +2.4±9.3	20.1±8.4 (26) +2.7±7.1
MSHQ-EjD				
Function	8.0±3.4 (47)	8.8±3.9 (47) +0.8±1.0	9.1±3.4 (35) +0.8±1.1	9.9±3.5 (26) +0.2±1.9
Bother	2.2±1.7 (47)	2.0±1.5 (47) −0.3±1.8	2.1±1.6 (35) −0.2±1.7	2.0±1.8 (26) −0.5±2.1

Abbreviations: Δbaseline, change from baseline; BPH, benign prostatic hyperplasia; IIEF-EF, International Index of Erectile Function—Erectile Function domain; MSHQ-EjD, Male Sexual Health Questionnaire for Ejaculatory Dysfunction; SD, standard deviation.
No significant differences were noted between arms.

scores, large prostate volume, and the presence of an intravesical prostatic protrusion. These outcomes substantiate previous experience with Optilume BPH, which reported an average Qmax of 18.4 mL/s and PVR improvement of 29.8 mL at 1 year posttreatment.[9] The symptom improvement seen with Optilume BPH is comparable to that reported for other MISTs in similar patient populations, while the improvement seen in flow and PVR represents the best improvements seen for this technology class.[12-18]

Sham procedures have been a fixture in randomized trials evaluating MIST devices; however, no prior studies included blinding and follow-up through 12 months in the sham subjects. Welliver and colleagues evaluated 14 sham-controlled trials and found that sham procedures resulted in statistically and clinically significant improvements in symptoms through 3 months postprocedure, with an average decrease of −6.3 points in studies using IPSS.[19] In the current study a marked sham effect was noted at the 3-month time point (−8.0, −33.3%); however, this effect was not durable through 12 months (−4.8, −21.5%). It is likely that the observed improvement is a combination of placebo effect, dilation from multiple instruments being passed through the urethra, and regression to the mean.[19] Of note, the PINNACLE protocol incorporated a number of best practices for blinding procedures, including requiring that all aspects of the procedure and follow-up (pain management, Foley placement, etc) be identical between arms. This resulted in highly effective blinding in the sham arm immediately postprocedure, potentially contributing to the significant sham effect seen at 3 months.

Preservation of sexual function after treatment has emerged as an important issue for men seeking treatment for BPH. Side effects related to sexual function such as ejaculatory dysfunction, loss of libido, and erectile dysfunction are a common reason of noncompliance for BPH medication. Likewise, more invasive treatment with transurethral resection of the prostate can result in sexual dysfunction in the form of retrograde ejaculation in >50% of men.[20] MIST therapies have filled the void as a viable option for men seeking treatment that preserves sexual function yet is still effective at relieving symptoms.[21] Sexual function was prospectively assessed in this study utilizing validated questionnaires. There was no apparent impact on erectile or ejaculatory function using these tools.

Consistent with other minimally invasive technologies, the Optilume BPH procedure is a straightforward procedure that can be conducted in an ambulatory or office outpatient setting with pain management at physician and patient discretion. Perioperative adverse events were generally mild and resolved within several weeks of the procedure. Serious adverse events were rare and generally related to clot blockage of the urethra or Foley catheter secondary to hematuria. The rate of these events was drastically reduced after the implementation of common postprocedure hematuria management practices including mild-to-moderate traction of the Foley catheter and flushing the bladder to remove residual blood postprocedure.

Limitations of this study include the fact that eligibility criteria limited enrollment to those men with prostates below 80 g and with moderate or severe symptoms and restricted flow at baseline; results may not be generalizable to all men with LUTS secondary to BPH. The mechanism of action described above is inferred from established action of paclitaxel in the prevention of smooth muscle cell growth and cystoscopic observations and functional maintenance of flow rate improvement during long-term follow-up from earlier studies; however, direct mechanistic evidence is lacking.[9,22]

CONCLUSIONS

Treatment of LUTS secondary to obstructive BPH with Optilume BPH results in significant and clinically meaningful improvements immediately postprocedure, which are sustained through 1 year of follow-up. The improvement seen for peak flow rate and PVR through 1 year represents the largest seen for this product class. This minimally invasive treatment represents an attractive option to patients looking to maintain sexual function while achieving durable symptom relief and improved flow.

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EDITORIAL COMMENT

The Optilume BPH system is a next-generation dilation balloon that creates an anterior commissurotomy with simultaneous paclitaxel delivery to prevent growth or refusion of the anterior prostatic lateral lobes. The PINNACLE authors describe a rigorously designed sham-controlled study on a large number of patients over a 1-year period, allowing comparison of medium-term outcomes to similar minimally invasive surgical therapy (MIST) technologies.[1] Results indicate an impressive 11-point improvement from baseline International Prostate Symptom Score at 1 year, though this was only 3 points better than sham surgery at 3 months.

Benefits of Optilume BPH include safety, short procedural time under 30 minutes, minimal learning curve, and no effect on either erectile or ejaculatory function. Unlike other MISTs such as water vapor thermal therapy (Rezūm), the majority of patients do still require general anesthesia or moderate sedation, making this procedure optimally suited for the

ambulatory surgical center setting. The urethral catheter, which is a major postoperative source of patient dissatisfaction, remains in place for 2 days, which is not significantly different from water vapor thermal therapy, holmium laser enucleation of the prostate, or laser photovaporization in similar gland sizes.

None of the study patients suffered from chronic urinary retention or neurogenic bladder, and, therefore, future studies may be needed to explore the efficacy in this population as well, given that MIST therapies are ideal not only for uncomplicated patients who prioritize sexual function, but also medically complex bladder outlet obstruction in patients who may not tolerate invasive therapies.

Overall, optimal patient counseling and selection will be critical for this treatment to carve out a niche among comparable MIST therapies. Given the target population, further planned studies on fertility impact and long-term durability will be a welcome addition to the literature.

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REPLY BY AUTHORS

We appreciate the thoughtful commentary by Drs Bole and Bajic. Although the majority of patients were treated using parenteral sedation, those who were treated using oral and local anesthetic in the Optilume BPH cohort tolerated the procedure well and actually had lower postprocedural visual analogue scale pain scores than those with parenteral sedation (2.3 vs 4.3).[1] Utilization of local block has been established as an option for balloon dilation of the prostate[2]; however, the authors suggest that further research is needed to identify the combination of analgesics for optimal patient comfort.

With regard to Optilume BPH International Prostate Symptom Score improvement at 12 months being "only" 3 points better than sham at 3 months, the response seen in the sham group for the PINNACLE represents the most marked sham effect seen in minimally invasive surgical therapy trials to date, and rivals that seen by some active arms.[3] Given that baseline characteristics for the different studies are largely similar, it is likely that the differences in sham effect seen between trials is driven by the choice of sham procedure and blinding controls implemented during the study. Blinding was highly effective in the PINNACLE study (100% postprocedure in the sham arm). With the pipeline of new minimally invasive surgical therapy devices more crowded than ever, the authors suggest that the urology community establish a framework of best practices for sham-controlled trials to ensure appropriate comparability across trials.

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