OPTILUME® BPH Catheter System

Instructions for Use

Caution: Federal law restricts this device to sale by or on the order of a physician.

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1 DEVICE DESCRIPTION

1.1 Optilume BPH Catheter System

The Optilume BPH Catheter System is a combination drug/device minimally invasive surgical therapy (MIST) comprised of an uncoated pre-dilation balloon catheter and a separate drug coated balloon (DCB) catheter. The distal end of each catheter has a semi-compliant, inflatable, double lobe balloon that is used to dilate the prostate. The double-lobe DCB catheter is coated with a proprietary coating containing the active pharmaceutical agent paclitaxel. The drug coating covers the working length of the balloon body.

Each Optilume BPH Catheter is a single inflation lumen balloon catheter that terminates in an atraumatic tip. The folded balloon has a 14.5Fr profile. The device is inserted through the outer sheath of a rigid cystoscope and then visualized procedurally in a side-by-side fashion with a cystoscope. The balloon has a double lobe design with a neck separating the two sections. The balloon neck is reinforced preventing diameter growth during the inflation process. The double lobe design allows the balloon neck to seat in the bladder neck during inflation and helps prevent migration of the balloon into the bladder. The distal lobe of the balloon inflates in the bladder and aids in anchoring the device, while the proximal lobe of the balloon is positioned in the prostatic urethra to dilate the prostate and create an anterior commissurotomy. Both the pre-dilation and the drug coated balloon catheters are identical, the only difference being the DCB is coated with the drug paclitaxel as shown in Figure 2.

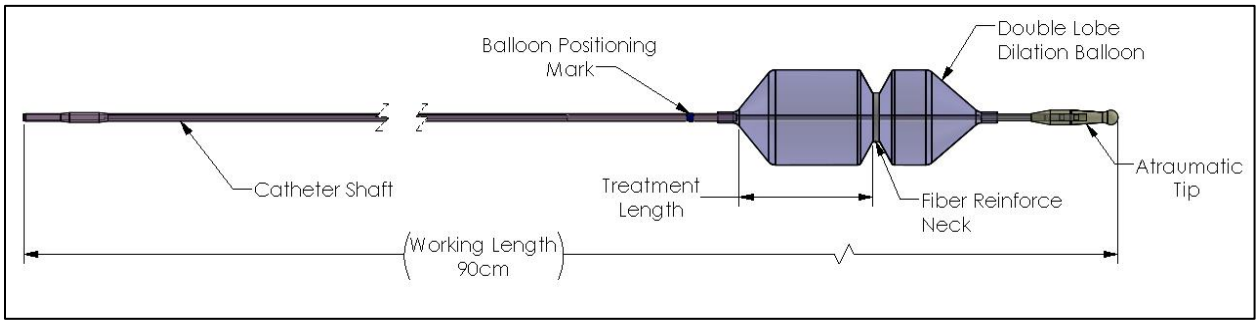


Figure 1. Inflated Pre-dilation Balloon Catheter

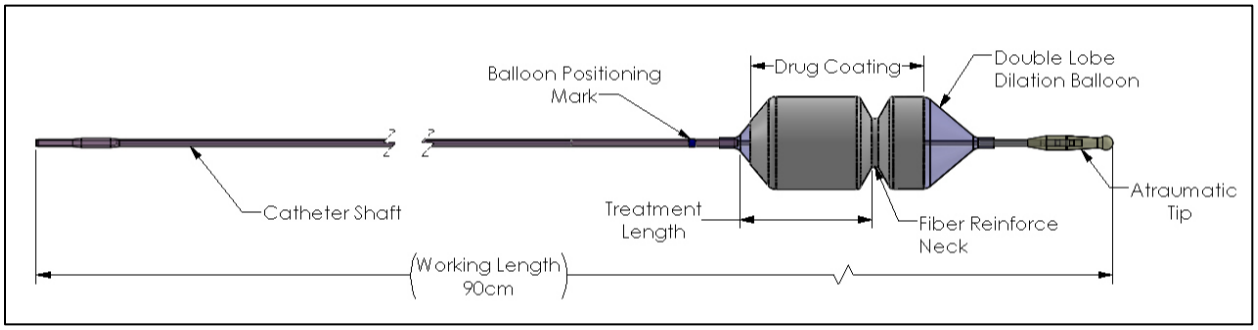


Figure 2. Inflated Drug Coated Balloon Catheter

The Optilume BPH Catheter System is provided as a convenience kit, containing one pre-dilation balloon catheter, one DCB catheter, and the accessories needed to complete a procedure. Catalogue numbers for the different kit configurations are provided in Table 1.

Table 1. Catalogue Number Identification of the Optilume BPH Kits

Catalogue Number	Description	Pre-dilation Catheter Size	DCB Catheter Size
1189-30030	Optilume BPH Prostatic Dilation Kit 30x30	90Fr x 30mm	90Fr x 30mm
1189-30035	Optilume BPH Prostatic Dilation Kit 30x35	90Fr x 30mm	90Fr x 35mm
1189-30040	Optilume BPH Prostatic Dilation Kit 30x40	90Fr x 30mm	90Fr x 40mm
1189-30045	Optilume BPH Prostatic Dilation Kit 30x45	90Fr x 30mm	90Fr x 45mm

1.2 Available Sizes and Nominal Paclitaxel Dose

The Optilume BPH Catheter System is available with one pre-dilation balloon size (90Fr x 30mm) and four DCB sizes which are selected based on prostatic urethral length (Table 2). The drug coating covers the working length of the balloon component of the DCB and is evenly distributed across the balloon surface at a nominal paclitaxel dose density of 2.4 µg/mm^2. The drug coating is released from the balloon and transferred to the prostatic urothelium during balloon inflation.

Table 2. DCB Sizes and Nominal Paclitaxel Dose

Balloon Diameter	Balloon Treatment Length (mm)			
90Fr (30mm)	30	35	40	45
	Paclitaxel Dose (µg)			
	10,262	11,433	12,567	13,661

2 INDICATIONS FOR USE

The Optilume BPH Catheter System is indicated for the treatment of obstructive urinary symptoms associated with Benign Prostatic Hyperplasia (BPH) in men ≥ 50 years of age.

3 CONTRAINDICATIONS

The Optilume BPH Catheter System is contraindicated for use in:

- Patients with known hypersensitivity to paclitaxel or structurally related compounds
- Patients with an active urinary tract infection
- Patients with an artificial urinary sphincter
- Patients with a penile prosthesis

4 WARNINGS

- The Optilume BPH Catheter System should be used only by physicians who are experienced and knowledgeable with the clinical and technical aspects of transurethral endoscopic treatment of BPH.
- Urotronic requires physician training on the Optilume BPH Catheter System prior to use. Please contact Urotronic for more information.
- The Optilume BPH Catheter is supplied for single use only. Do not reprocess or re-sterilize. Reprocessing and re-sterilizing could increase the risk of patient infection and risk of compromised device performance.
- Each balloon catheter is supplied sterile. Do not use the catheter if the sterile barrier is damaged or opened.
- The foil pouch and the outer surface of the inner Tyvek pouch are non-sterile. The

contents of the inner Tyvek pouch are sterile. Use proper sterile technique to transfer the device from the inner Tyvek pouch to the sterile field.

- Do not use after the “Use By” date on the package label.
- Men should abstain from sex or use barrier contraception (wear a condom) for 30 days post treatment to avoid exposure of sexual partner to paclitaxel. Paclitaxel may still be present at low levels after 30 days.
- The Optilume BPH DCB contains paclitaxel, a known genotoxic aneugen capable of causing chromosomal abnormalities in sperm. Paclitaxel is present in semen for an extended duration after treatment with Optilume BPH. The total duration of time that paclitaxel remains in the semen post-procedure varies, but some men have had trace amounts detected up to 1 year after treatment. The risks associated with paclitaxel in semen are unknown. For this reason, men with partners of child-bearing potential should use highly effective contraceptive (to avoid fathering children) for at least 12 months post-procedure. Urologists should engage in a discussion with prospective patients regarding this risk and their individual family planning situation, with consideration of longer duration contraceptive use or other precautions based on a shared decision making process.

  Paclitaxel was detectable (i.e., equal to or greater than lower limit of quantitation of 0.1 ng/mL) in semen in 4/5 (80.0%), 5/7 (71.4%), 4/10 (40.0%), and 1/3 (33.3%) of evaluable subjects at 1 month, 3 months, 6 months, and 12 months post-treatment, respectively.

  Maximum paclitaxel concentrations in semen were 8.9, 7.5, 1.8, and 0.16 ng/mL at 1 month, 3 months, 6 months, and 12 months post-treatment, respectively, while group mean (SD) paclitaxel concentrations in semen at those same timepoints were 2.3 (3.7), 1.3 (2.8), 0.29 (0.53), and 0.09 (0.06) ng/mL. Of the three subjects who had evaluable data at 12 months post-treatment, one had detectable paclitaxel concentration in semen (0.16 ng/mL).

  The risks associated with these paclitaxel concentrations in semen are unknown. The effect of treatment with the Optilume BPH DCB on sperm and spermatogenesis is also unknown.

- Always inflate with a sterile liquid. Never inflate with air, carbon dioxide, or any other gas.
- The balloon catheters should not be inflated in excess of the rated burst pressure (RBP). Inflation to pressures above RBP may cause the balloon to rupture.
- During use, each balloon catheter of the Optilume BPH Catheter System should be manipulated under direct visualization via cystoscopy.
- If resistance is encountered at any time during insertion or removal, do not force passage. Resistance may cause damage to device or urethra. Ensure the balloon is fully deflated and under negative pressure during withdrawal.
- Monitor for signs of anaphylaxis or hypersensitivity to paclitaxel.

5 PRECAUTIONS

- Carefully inspect the product prior to use. Do not use the catheter if it is damaged or if the size, shape, or condition is unsuitable for the intended procedure.
- Do not immerse or wipe the Optilume BPH DCB with any fluid prior to use, as the integrity of the drug coating may be damaged or compromised. Replace the DCB if the

balloon has come into contact with fluids prior to use.

- Use dry sterile gloves or dry gauze pads to handle the Optilume BPH DCB prior to use. Care should be taken to minimize contact with the drug coated portion of the device.
- Never inflate the Optilume BPH DCB outside the body or prior to reaching the prostatic urethra as it may disrupt the coating integrity.
- For proper drug delivery to the prostatic urethra, allow the drug coating on the balloon to hydrate while in the urethra for approximately 1 minute prior to inflation. Maintain inflation of the catheter for a minimum of 5 minutes. To optimize the anterior commissurotomy and drug delivery, longer inflation times > 5 minutes may be performed at the discretion of the operator.
- If the balloon catheter has a failure prior to or during inflation, replace the balloon catheter and inflate per procedure. If failure of the Optilume BPH DCB is after inflation to rated burst pressure (RBP), do not repeat/replace with a second DCB.
- Handle and dispose of the used device in accordance with accepted medical practice and applicable local regulations for biohazard waste.

6 DRUG INFORMATION

6.1 Mechanism of Action

The coating of the Optilume BPH DCB contains paclitaxel, an anti-mitotic pharmaceutical agent that specifically binds to and stabilizes microtubules. Paclitaxel has been reported to inhibit smooth muscle cell and fibroblast proliferation and migration as well as secretion of extracellular matrix. The combination of these effects may result in the inhibition of prostatic tissue hyperplasia and re-fusion of the lateral lobes after achievement of the anterior commissurotomy.

6.2 Drug Interactions

Formal drug interaction studies have not been conducted for the Optilume BPH DCB. The respective instructions for use for all drugs used in conjunction with the Optilume BPH DCB should be consulted for interactions with paclitaxel.

Consideration should be given to the potential for systemic and local drug interactions in the prostate in a patient who is taking a drug with known interactions to paclitaxel or when deciding to initiate drug therapy in a patient who has been treated with the Optilume BPH Catheter System.

The metabolism of paclitaxel is catalyzed by cytochrome P450 isoenzymes CYP2C8 and CYP3A4, and it is a substrate of P-glycoprotein. Potential drug interactions may occur with any drug that affects these isoenzymes. In the absence of formal drug interaction studies, caution should be exercised when administering paclitaxel.

6.3 Carcinogenicity, Genotoxicity, and Reproductive Toxicology

The Optilume BPH DCB contains paclitaxel, a known genotoxic aneugen capable of causing chromosomal abnormalities in sperm. Paclitaxel is present in semen for an extended duration after treatment with Optilume BPH. The total duration of time that paclitaxel remains in the semen post-procedure varies, but some men have trace amounts detected up to 1 year after treatment. The risks associated with paclitaxel in semen are unknown. For this reason, men with partners of child-bearing potential should use highly effective contraceptive (to avoid fathering children) for at least 12 months post-procedure. Urologists should engage in a discussion with prospective patients regarding this risk and their individual family planning situation, with consideration of longer duration contraceptive use or other precautions based on a shared decision making process.

Paclitaxel was detectable (i.e., equal to or greater than lower limit of quantitation of 0.1 ng/mL) in semen in 4/5 (80%), 5/7 (71.4%), 4/10 (40.0%), and 1/3 (33.3%) evaluable subjects at 1 month, 3 months, 6 months, and 12 months post-treatment, respectively.

Maximum paclitaxel concentrations in semen were 8.9, 7.5, 1.8, and 0.16 ng/mL at 1 month, 3 months, 6 months, and 12 months post-treatment, respectively, while group mean (SD) paclitaxel concentrations in semen at those same timepoints were 2.3 (3.7), 1.3 (2.8), 0.29 (0.53), and 0.09 (0.06) ng/mL. Of the three subjects who had evaluable data at 12 months post-treatment, one had detectable paclitaxel concentration in semen (0.16 ng/mL).

The risks associated with these paclitaxel concentrations in semen are unknown. The effect of treatment with the Optilume BPH DCB on sperm and spermatogenesis is also unknown.

7 HOW SUPPLIED

The Optilume BPH Catheter System is supplied as a convenience kit containing:

- One (1) Optilume BPH Prostatic Pre-dilation Catheter with Tuohy Borst adapter and 1-way stopcock
- One (1) Optilume BPH Prostatic Dilation Drug Coated Balloon Catheter
- One (1) 60mL Inflation device with pressure gauge and 3-way stopcock

Each component in the Optilume BPH kit is supplied sterile and intended for single use only. Each Optilume BPH Catheter is sterilized by ethylene oxide. Each balloon catheter is in a double pouch packaging system (foil and Tyvek pouches) contained within a single unit box.

8 POTENTIAL ADVERSE EFFECTS

Potential adverse effects after treatment with the Optilume BPH Catheter System are similar to standard cystoscopic procedures and mechanical dilation and include, but are not limited to fever, bleeding, pain, urinary tract infection, false route of the urethra, dysuria, difficult urination, frequency/urgency/irritative urinary symptoms, urinary retention and related symptoms, blood in urine (hematuria), urinary incontinence, urethrorrhagia, blood in semen (hematospermia), ejaculatory dysfunction, bladder perforation, urethral and/or bladder neck strictures, injury or perforation to the urethra, sphincter or prostatic capsule, and inflammation of genitourinary system (prostatitis, orchitis, balanitis).

Although systemic effects from the paclitaxel coating are not anticipated, adverse effects observed during intravenous administration of paclitaxel for chemotherapy include, but are not limited to, allergic reaction, alopecia, anemia, gastrointestinal symptoms, hematological dyscrasia (including leucopenia, neutropenia, thrombocytopenia), hepatic enzyme changes, myalgia/arthralgia, myelosuppression, and peripheral neuropathy. Maximum systemic paclitaxel levels after treatment with the Optilume BPH DCB are more than 100 times lower than with IV administration of paclitaxel for chemotherapy.

9 STORAGE

The Optilume BPH Catheter System should be stored at room temperature between 15°C and 30°C (59°F and 86°F) in a dry location in its original packaging. The device should be used prior to the “Use By” date on the package label.

10 RECOMMENDED ITEMS

Prepare the following items using sterile technique:

- Lubricious surgical gel to aid with device insertion
- 60 mL inflation device with pressure gauge
- One-way stopcock

- Tuohy-Borst adapter
- Rigid cystoscope (minimum sheath size 19.5Fr)
- Sterile saline

11 DIRECTIONS FOR USE

11.1 Perioperative Medications

It is recommended that physicians follow guidelines for pre-procedure medications and preparation for a cystoscopic urethral procedure, including the administration of a pre-procedure antibiotic as appropriate. If a urinary tract infection (UTI) is present at the time of treatment, the patient must be treated until the infection is cleared before the Optilume BPH procedure can take place.

The prostate is a highly vascularized organ and the Optilume BPH procedure, like other transurethral procedures for the treatment of BPH, may cause bleeding within the prostatic urethra. Peri-operative management of anticoagulant and antiplatelet medications is at the discretion of the treating physician and should balance the patient risk of thromboembolic events against the risk of hemorrhagic events.

11.2 Optilume BPH Size Selection

Selection of the appropriate kit for the Optilume BPH procedure is based on the measured prostatic urethral length (PUL) of the patient. Use of transrectal ultrasound (TRUS) to determine the PUL is recommended. The PUL measurement should be taken in the mid-sagittal plane as a direct line from the base of the bladder neck to the proximal edge of the external urethral sphincter.

Note: If an intravesical prostatic protrusion (IPP) is present, the measurement should be from the base of the bladder neck, NOT the tip of the IPP.

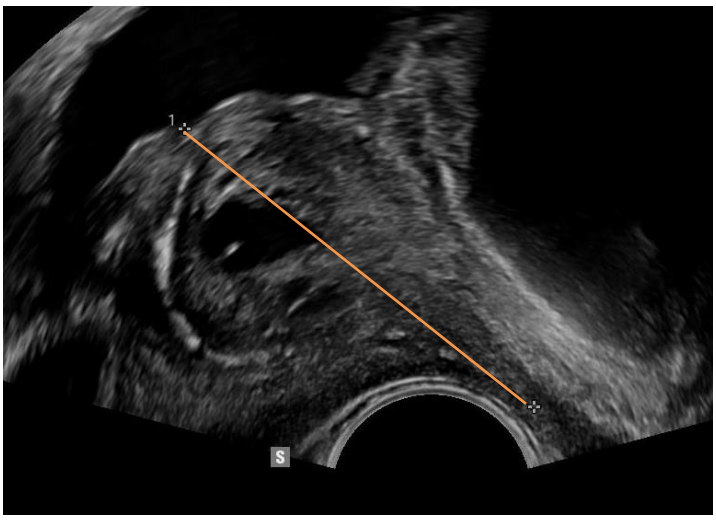


Figure 3. Mid-sagittal TRUS Image Showing PUL Measurement

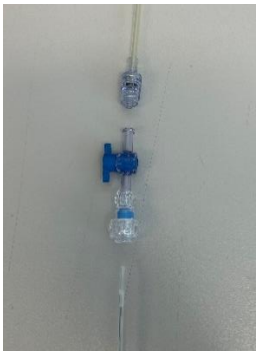
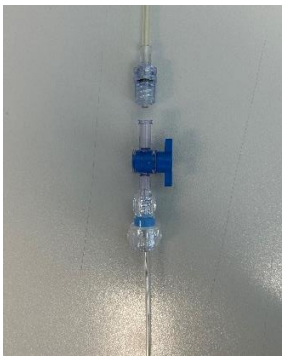
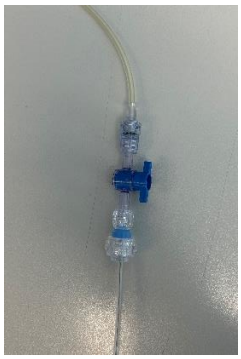
Table 3: Optilume BPH DCB Size Selection

PUL Measurement	PUL 32-37mm	PUL 37-42mm	PUL 42-47mm	PUL >47mm
Catalogue Number (DCB Size)	1189-30030 (90Fr x 30mm)	1189-30035 (90Fr x 35mm)	1189-30040 (90Fr x 40mm)	1189-30045 (90Fr x 45mm)

11.3 Balloon Preparation

Before use, each balloon catheter in the Optilume BPH kit must be prepared for use by evacuating air from the balloon catheter. The balloon lumen of the catheter contains air and the air must be displaced to make certain that only liquid fills the balloon while the catheter is in the urethra. Do not remove the balloon protector sheath during catheter preparation.

1. Open the Optilume BPH Pre-dilation Catheter package and remove the Tuohy-Borst adapter and 1-way stopcock assembly. Ensure the Tuohy-Borst adapter and stopcock are properly threaded to each other.
2. Connect the Tuohy-Borst valve to the proximal catheter shaft. Ensure that the catheter shaft does not interfere with the stopcock operation.

3. Fill the inflation device half-way with sterile saline and attach it to the stopcock. Turn the stopcock so fluid can flow between the inflation device and the balloon catheter.
4. With the inflation device pointing downwards, draw back plunger to full volume of syringe (this creates maximum negative pressure and allows air to evacuate above the fluid level) and hold until no air bubbles can be seen coming out of the saline in the syringe. Repeat as needed to purge the air from the catheter.
5. With catheter preparation complete, disconnect the Tuohy-Borst valve from the catheter shaft.
6. Fill the inflation device with 50cc normal saline and purge air from the line.

11.4 Pre-dilation

Pre-dilation of the prostatic urethra should be completed with the Optilume BPH Pre-dilation Catheter to initiate an anterior commissurotomy prior to treatment with the Optilume BPH DCB Catheter.

1. Prepare the Optilume BPH Pre-dilation Catheter for use per Section 11.3.
2. Assemble and advance the rigid cystoscope (minimum sheath size 19.5Fr) through the urethra and into the bladder. Remove the optics and bridge (if applicable) leaving an open pathway through the rigid sheath into the bladder.
3. Remove the balloon protector sheath from the Optilume BPH Pre-dilation Balloon.
4. Insert the balloon catheter through the rigid cystoscope sheath and into the bladder.
5. Slide the outer rigid cystoscope sheath out of the patient and over the balloon catheter shaft while maintaining the balloon catheter in position.
6. Reassemble the rigid cystoscope sheath with the bridge and optics.

Note: A smaller cystoscope sheath (e.g., 18Fr) may be used to visualize the balloon during placement.

7. Attach the Tuohy-Borst adapter with inflation device to the proximal catheter shaft.
8. Insert the reassembled cystoscope transurethrally up to the external sphincter. The Optilume BPH Catheter is used side-by-side with a cystoscope.
9. Locate the external sphincter with the cystoscope and position the tip of the cystoscope so visualization of the external sphincter can be maintained throughout the procedure.
10. Adjust the position of the balloon by pushing/pulling the catheter shaft until the blue positioning marker is visible at the distal edge of the external urethral sphincter (Figure 4).

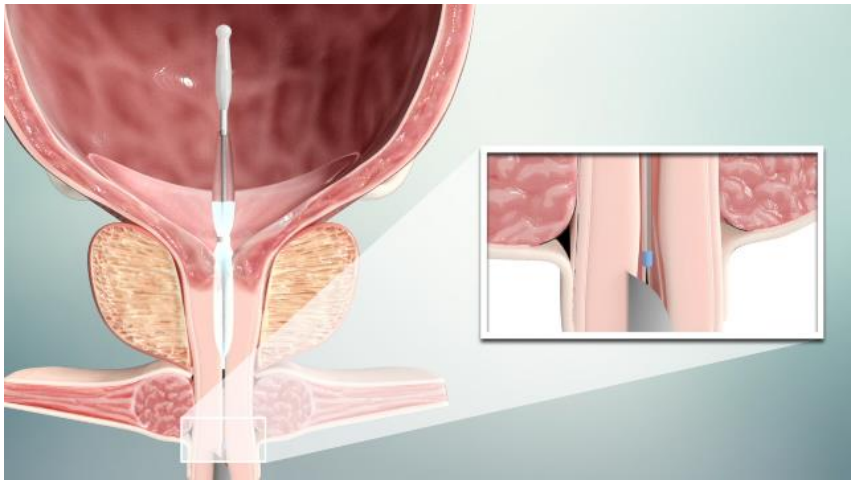


Figure 4. Positioning of the Balloon Within the Prostatic Urethra

11. With the balloon properly positioned, inflate slowly while maintaining traction to seat the balloon at the bladder neck and prevent proximal migration into the bladder. During inflation, monitor the location of the blue positioning marker with the cystoscope. If the marker migrates proximally into the external sphincter (e.g., is no longer visible) or the treatment balloon has slipped into the bladder, deflate, and reposition the balloon as above and repeat the dilation process.

    Warning: If migration of the balloon distally into the external sphincter (toward the user) is observed during inflation, immediately stop, and reposition.

12. Continue slow inflation until the anterior prostatic commissure is separated. Achievement of an anterior commissurotomy is typically accompanied by a sudden drop in pressure on the inflation device pressure gauge as resistance from the tissue is overcome.

    Note: Once the balloon is inflated, check for migration into the bladder by pressing the catheter shaft gently towards the bladder. If the catheter shaft moves freely, the balloon has likely migrated into the bladder. If migration is observed, deflate the balloon, reposition the catheter as above, and repeat the dilation process. Do not repeat this procedure more than 3 times.

    Warning: The balloon catheters should not be inflated to pressures above the rated burst pressure (RBP). Inflation in excess of RBP may cause the balloon to rupture.

13. After complete dilation, deflate the balloon and visually confirm the anterior

commissurotomy by advancing the cystoscope into the prostatic urethra.

Note: If difficulty is encountered visualizing commissurotomy, increase fluid flow/pressure to improve visibility.

14. Do not exceed 3 inflation cycles to rated burst pressure. If a commissurotomy is not achieved after 3 inflation cycles, deflate, and withdraw the Optilume BPH Pre-dilation Balloon per the steps below and proceed to dilation with the DCB.
15. After initiation of the commissurotomy is confirmed, remove the cystoscope.
16. Deflate the balloon by applying negative pressure with the inflation device to aspirate liquid from the balloon. Once the inflation device is filled with fluid, detach from the stopcock, purge fluid into a reservoir, reattach to the catheter, and repeat the aspiration process to ensure complete aspiration of liquid from balloon.

    Warning: If resistance is encountered at any time during insertion or removal, do not force passage. Resistance may cause damage to the device or urethra. Ensure the balloon is fully deflated and under negative pressure during withdrawal.
17. When the balloon is completely deflated, maintain vacuum and gently pull on the catheter shaft to withdraw the catheter from the patient's body.

11.5 Drug Coated Balloon Dilation

1. Prepare the Optilume BPH DCB for use per Section 11.3.
2. Advance the rigid cystoscope through the urethra and into the bladder. Remove the optics and bridge (if applicable) leaving an open pathway through the rigid sheath into the bladder.
3. Remove the balloon protector sheath from the Optilume BPH DCB.
4. Insert the Optilume BPH DCB through the rigid cystoscope and into the bladder.
5. Slide the outer rigid cystoscope sheath out of the patient and over the balloon catheter shaft while maintaining the balloon catheter in position.
6. Reassemble the rigid cystoscope sheath with the bridge and optics.
7. Attach the Tuohy-Borst adapter with inflation device to the proximal catheter shaft of the Optilume BPH DCB.
8. Insert the reassembled cystoscope transurethrally up to the external sphincter. The Optilume BPH Catheter is used side-by-side with a rigid cystoscope.
9. Locate the external sphincter with the cystoscope and position the tip of the cystoscope so visualization of the external sphincter can be maintained through the procedure.
10. Adjust the position of the balloon by pushing/pulling the catheter shaft until the blue positioning marker is visible at the distal edge of the external urethral sphincter (Figure 4). This step should be completed in approximately 1 minute while the drug coating is hydrating, such that the balloon can be inflated after hydration is complete.
11. With the balloon properly positioned, inflate slowly while maintaining traction to seat the balloon at the bladder neck and prevent proximal migration into the bladder. During inflation, monitor the location of the blue positioning marker with the cystoscope. If the marker migrates proximally into the external urethral sphincter (e.g., is no longer visible) or the treatment balloon has slipped into the bladder, deflate and reposition the balloon as above and repeat the dilation process.

Warning*:* If migration of the balloon distally into the external sphincter (toward the user) is observed during inflation, immediately stop and reposition.

12. With the balloon properly positioned, inflate the balloon using the inflation device. Maintain inflation for a minimum of 5 minutes to assure complete propagation of the anterior commissurotomy and appropriate drug delivery. To optimize the anterior commissurotomy and drug delivery, inflation times > 5 minutes may be utilized at the discretion of the operator.

    Warning: The balloon catheters should not be inflated to pressures above the rated burst pressure (RBP). Inflation in excess of RBP may cause the balloon to rupture.

13. Once the balloon is inflated, check for migration into the bladder by pressing the catheter shaft gently towards the bladder. If the catheter shaft moves freely, the balloon has likely migrated into the bladder. If migration is observed, deflate the balloon, reposition the catheter as above, and repeat the dilation process.

14. After completion of the commissurotomy, remove the cystoscope.

    Note: Avoid visualizing the prostatic urethra with the cystoscope after dilation with the Optilume BPH DCB, as the irrigation fluid from the scope may disturb the drug coating delivered to the prostatic urethra.

15. Deflate the balloon by applying negative pressure with the inflation device to aspirate liquid from the balloon. Once the inflation device is filled with fluid, detach from the stopcock, purge fluid into a reservoir, reattach to the catheter, and repeat the aspiration process to ensure complete aspiration of liquid from the balloon.

    Warning: If resistance is encountered at any time during insertion or removal, do not force passage. Resistance may cause damage to device or urethra. Ensure the balloon is fully deflated and under negative pressure during withdrawal.

16. When the balloon is completely deflated, maintain vacuum and gently pull on the catheter shaft to withdraw the catheter from the patient's body.

11.6 Post Procedure Care

1. Upon completion of the dilation procedure, insert a Foley catheter and flush the bladder with sterile saline until the effluent returns clear.

    Note: If difficulty is encountered during placement of the Foley catheter, it is recommended to place a guidewire and advance a council tip Foley over the guidewire to aid in placement. Rigid catheter guides are not recommended.

2. It is recommended to place the Foley catheter on mild-to-moderate traction during the recovery period post-procedure to provide tamponade of any bleeding prostatic vessels.

    Note: Use of traction for approximately 30 minutes post-procedure with at least a 30cc Foley balloon was found to reduce the rate of hematuria complications during clinical trials.

3. The Foley catheter should remain in place for a minimum of 2 days to allow adequate healing and absorption of the drug into the prostatic adenoma.

12 SUMMARY OF CLINICAL STUDIES

12.1 Primary Study

The PINNACLE study was a prospective, multicenter, double blind, 2:1 randomized controlled

trial comparing the Optilume BPH Catheter System to a sham control procedure. In addition, a single arm of 15 non-randomized subjects were enrolled and treated with the Optilume BPH Catheter System to gather paclitaxel pharmacokinetic data. Subjects randomized to the Sham arm were allowed to cross over to receive the Optilume BPH Catheter System prior to the close of their 12-month visit window.

Study enrollment began in January 2020 and was completed in September 2021. A total of 148 subjects were randomized in the study, 100 to the Optilume BPH arm and 48 to the Sham arm at 18 investigational sites. Treatment with the Optilume BPH Catheter System included use of the Optilume BPH Pre-dilation Balloon to initiate an anterior commissurotomy followed by dilation with the Optilume BPH DCB to further dilate and deliver drug to the prostatic urethra. The sham procedure utilized rigid cystoscopy followed by insertion of a sheathed (21Fr) Optilume BPH Pre-dilation Balloon that was modified to prevent inflation. Follow-up was completed at Foley removal, 14 days, 30 days, 3 months, 6 months, and 12 months and will be performed annually through 5 years for subjects treated with the Optilume BPH Catheter System.

12.1.1 Subject Accountability

At the time of database lock, of 477 patients enrolled in the PMA clinical study, 148 were randomized, and 14 included in the PK sub-study. Subject disposition and visit compliance for the randomized cohort through 12 months is summarized in Table 4 and Figure 5.

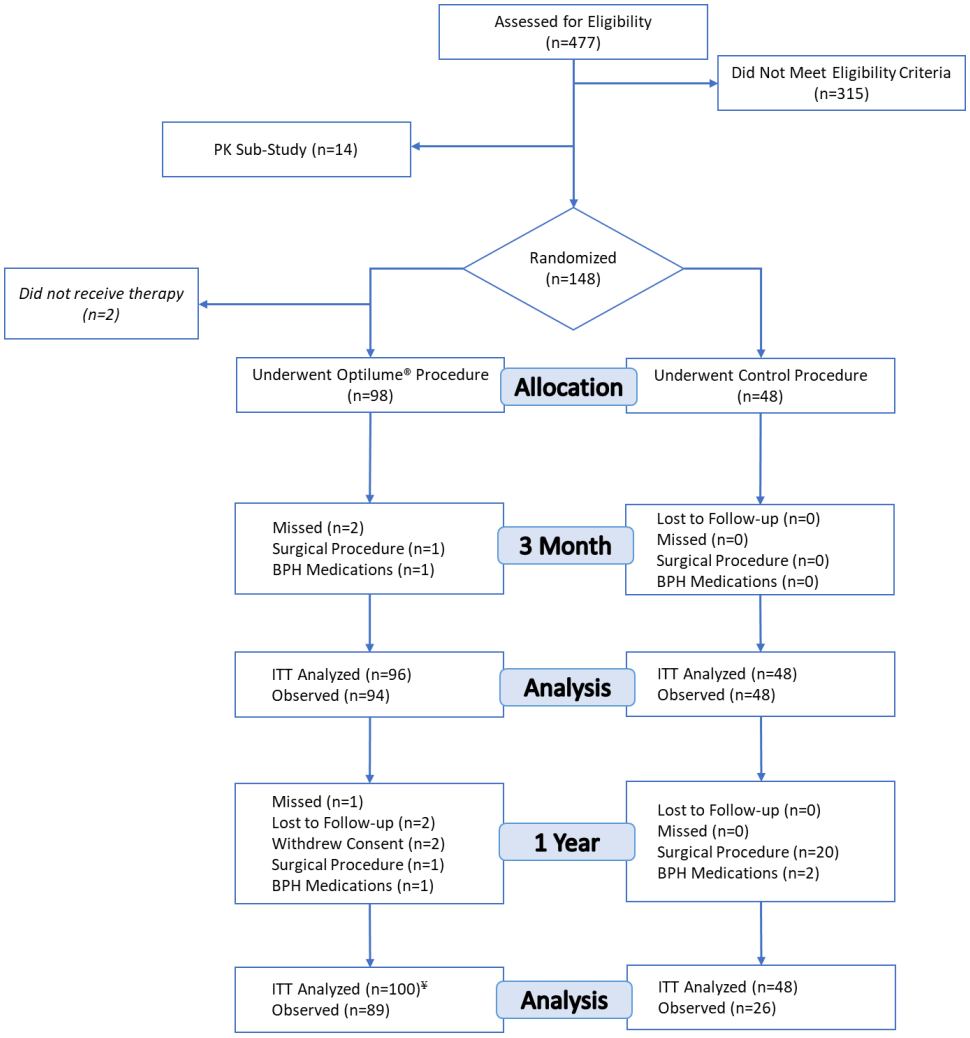
Withdrawals prior to the 12-month visit included 10 subjects randomized to the Optilume BPH arm (2 withdrew prior to receiving the study treatment, 2 lost to follow-up, 2 withdrew consent, 2 underwent a BPH surgical procedure, 2 initiated BPH medications) and 2 subjects randomized to the Sham arm (2 initiated BPH medications). Twenty subjects in the Sham arm crossed over to receive Optilume BPH prior to the 12-month visit.

Primary efficacy and secondary endpoint analyses were performed using the intent-to-treat (ITT) data set which included all randomized subjects. Safety analyses were performed using the as-treated (AT) data set based on the treatment received. The AT data set excludes two subjects who were randomized to the Optilume BPH arm but did not receive the study treatment.

Table 4. Visit Compliance for Randomized Cohort

Study Visit	Visit Compliance[1]	
	Optilume BPH (n=100)	**Sham (n=48)**
Participants who received study treatment	98.0% (98/100)	100.0% (48/48)
Participants who completed Foley Removal	100.0% (98/98)	100.0% (48/48)
Participants who completed 14 Day visit	98.0% (96/98)	97.9% (47/48)
Participants who completed 30 Day visit	99.0% (97/98)	100.0% (48/48)
Participants who completed 3 Month visit	97.9% (94/96)	100.0% (48/48)
Participants who completed 6 Month visit	97.9% (91/94)	97.2% (35/36)
Participants who completed 12 Month visit	98.9% (89/90)	100.0% (26/26)

[1]Denominator represents the number of subjects eligible for a visit, while the numerator represents the number of visits completed. Subjects that are withdrawn from the study prior to the visit window opening are excluded from the denominator.



¥ For the primary endpoint intent-to-treat (ITT) analysis, subjects receiving alternative BPH therapy were imputed as having no improvement, while endpoint status for subjects with missing data were imputed via multiple imputation.

Figure 5. Subject Accountability Diagram for Randomized Cohort

12.1.2 Study Population Demographics and Baseline Parameters

The demographics of the study population are typical for a BPH study performed in the US. Demographics, baseline genitourinary medical history, and baseline prostate characteristics were well matched between groups.

Table 5. Demographics and Genitourinary Medical History

Characteristic	Optilume BPH (N=100)	Sham (N=48)	P-Value[1]
Demographics			
Age	64.5 ± 6.4 (98)	65.5 ± 5.6 (47)	0.3769
Race			
American Indian or Alaska Native	0.0% (0/100)	0.0% (0/48)	0.1877
Asian	2.0% (2/100)	0.0% (0/48)	
Black or African American	3.0% (3/100)	10.4% (5/48)	
Hawaiian or Pacific Islander	0.0% (0/100)	0.0% (0/48)	
White	94.0% (94/100)	89.6% (43/48)	
Multi-Racial	1.0% (1/100)	0.0% (0/48)	
Ethnicity			
Hispanic or Latino	13.0% (13/100)	6.3% (3/48)	0.2157
Not Hispanic or Latino	87.0% (87/100)	93.8% (45/48)	
BMI	29.32 ± 4.45 (100)	29.06 ± 4.72 (48)	0.7420
Medical History			
Urinary Incontinence			
No	100.0% (100/100)	100.0% (48/48)	N/A
Yes	0.0% (0/100)	0.0% (0/48)	
LUTS			
Dysuria	16.0% (16/100)	16.7% (8/48)	0.9180
Frequency	91.0% (91/100)	100.0% (48/48)	0.0586
Hesitancy	73.0% (73/100)	79.2% (38/48)	0.4173
Incomplete Voiding	85.0% (85/100)	91.7% (44/48)	0.2564
Nocturia	91.0% (91/100)	95.8% (46/48)	0.3445
Poor Stream	89.0% (89/100)	91.7% (44/48)	0.7745
Terminal Dribbling	49.0% (49/100)	52.1% (25/48)	0.7254
Urgency	80.0% (80/100)	91.7% (44/48)	0.0715
Hematuria	6.0% (6/100)	2.1% (1/48)	0.4284
Retention	13.0% (13/100)	18.8% (9/48)	0.3573
Other Genitourinary History			
Kidney Stone	13.0% (13/100)	20.8% (10/48)	0.2182
Erectile Dysfunction	56.0% (56/100)	54.2% (26/48)	0.8336
Bladder Stone	3.0% (3/100)	0.0% (0/48)	0.5512
Urinary Tract Infection	6.0% (6/100)	4.2% (2/48)	0.7235
Bacterial Prostatitis	5.0% (5/100)	4.2% (2/48)	1.0000
Cystitis	2.0% (2/100)	0.0% (0/48)	0.5587
Other	34.0% (34/100)	29.2% (14/48)	0.5565
Prostate Specific Antigen (ng/mL)	2.42 ± 1.98 (100)	2.20 ± 1.82 (48)	0.5135
IPSS Score	23.4 ± 5.5 (100)	24.3 ± 5.8 (48)	0.3916
Qmax (mL/sec)	8.85 ± 2.17 (100)	8.95 ± 1.80 (48)	0.7888
Post-Void Residual Volume (mL)	84.1 ± 70.2 (99)	89.4 ± 73.9 (48)	0.6750

[1]Continuous variables tested with two-sample t-test and categorical variables tested with chi square test. When expected cell counts were < 5, then an Exact Chi-Square test was used.

Table 6. Baseline Prostate Characteristics

Prostate Characteristics	Optilume BPH (N=100)	Sham (N=48)	P-Value[1]
Prostate Width (mm)	48.90 ± 6.72 (100)	49.99 ± 5.05 (48)	0.2754
Prostate Height (mm)	37.07 ± 7.52 (100)	36.18 ± 7.14 (48)	0.4976
Prostate Length (mm)	46.62 ± 6.33 (100)	46.46 ± 5.39 (48)	0.8791
Prostate Volume (mL)	44.88 ± 14.53 (100)	45.00 ± 13.16 (48)	0.9633
Intravesical Prostatic Protrusion	28.0% (28/100)	33.3% (16/48)	0.5064
IPP Size (mm)	5.07 ± 2.19 (28)	5.31 ± 1.54 (15)	0.7059
[1]Continuous variables tested with two-sample t-test and categorical variables tested with chi-square test.			

12.1.3 Efficacy Outcomes

12.1.3.1 Primary Efficacy Endpoint

The primary efficacy endpoint was a comparison of the change in International Prostate Symptom Score (IPSS) at 3 months for the Control group and at 12 months for the Optilume BPH group. The endpoint incorporated a super-superiority margin of 25% for the sham effect at 3 months. The analysis was based on the ITT cohort which included 148 evaluable subjects (48 sham subjects at 3 months and 100 Optilume BPH subjects at 12 months). Subjects undergoing alternative therapy for ongoing/recurrent LUTS prior to the scheduled timepoint were imputed as having no change from baseline. Missing data were accounted for using multiple imputation. Incorporating the 25% super superiority margin, the imputed difference between arms was +1.4 (p=0.178). The improvement in IPSS for the Optilume BPH arm at 12 months did not reach statistical significance with a 25% super-superiority margin when compared to the improvement in the Sham arm at 3 months (Table 7).

Table 7. Primary Efficacy Endpoint – Improvement in IPSS (ITT, Multiple Imputation)

Variable	Sham (3 Months, N=48)	Optilume BPH (12 Months, N=100)	Difference [95%CI]
Improvement in IPSS Mean [95%CI]	8.0 [5.8, 10.3]	11.5 [9.7, 13.2]	3.4 [0.6, 6.2]
Improvement in IPSS (*w/ 25% Margin)* Mean [95%CI]	10.0 [7.5, 12.5]		1.4 [-1.6, 4.5]
P-value is based on a two-sample, independent t-test.			

A post-hoc analysis was performed comparing the improvement in IPSS at 12 months for the Optilume BPH group to the improvement of a historical sham control at 3 months based on a systematic review of the literature of sham endoscopic procedures in randomized trials for BPH. A total of 8 studies were included in the analysis and used to generate the pooled sham effect (weighted average) across studies.[1-10] Four studies reported a paired change in IPSS from baseline to 3 months.[5,6,8,9] Comparing the improvement in IPSS against the pooled sham effect from the literature as a performance goal shows a benefit for Optilume BPH both with and without a 25% super-superiority margin (Table 8). A similar outcome is seen when utilizing only

[1] Albala DM, Fulmer BR, Turk TM, Koleski F, Andriole G, Davis BE, et al. J Endourol. 2002;16(1):57-61.
[4] Barbalias GA, Liatsikos EN. Int J Urol. 1998;5(2):157-62.
[5] Blute ML, Patterson DE, Segura JW, Tomera KM, Hellerstein DK. J Endourol. 1996;10(6):565-73.
[6] Chughtai B, Elterman D, Shore N, Gittleman M, Motola J, Pike S, et al. Urology. 2021;153:270-6.
[7] Larson TR, Blute ML, Bruskewitz RC, Mayer RD, Ugarte RR, Utz WJ. Urology. 1998;51(5):731-42.
[8] McVary KT, Gange SN, Gittelman MC, Goldberg KA, Patel K, Shore ND, et al. J Urol. 2016;195(5):1529-38.
[9] Roehrborn CG, Gange SN, Shore ND, Giddens JL, Bolton DM, Cowan BE, et al. J Urol. 2013;190(6):2161-7.
[10] Roehrborn CG, Preminger G, Newhall P, Denstedt J, Razvi H, Chin LJ, et al. Urology. 1998;51(1):19-28.

those publications reporting paired change scores.

Table 8. Comparison of Literature Sham Improvement in IPSS at 3 Months to Optilume BPH at 12 Months

Variable	Literature Sham (3 Months)	Optilume BPH (12 Months)
Composite Literature Outcomes	5.9 (n=401)	11.5 ± 7.8 (n=94)
Composite Literature Outcomes (w/ 25% Super Superiority Margin)	7.4 (n=401)	
Composite Literature Outcomes (paired)	5.6 ± 8.0 (n=215)	
Composite Literature Outcomes (paired, w/ 25% Super Superiority Margin)	7.0 ± 10.0 (n=215)	
Optilume BPH mean improvement utilizing 'Retreatments Imputed' methodology, where those receiving alternative treatment are imputed as having no improvement.		

12.1.3.2 Secondary Endpoints

Hypotheses for the secondary endpoints were not formally tested because the study failed to meet its primary effectiveness endpoint and supplemented by post-hoc analysis.

Secondary Endpoint 1 – Average IPSS Improvement in Test Arm at 12 Months

The average percent improvement in IPSS from baseline to 12 months was compared against a performance goal of 30%. Subjects undergoing alternative therapy for ongoing/recurrent LUTS prior to the scheduled timepoint were considered as having no improvement, while subjects considered missing at random were imputed utilizing multiple imputation as per the primary efficacy endpoint analysis. The average improvement from baseline to 12 months for the Optilume BPH arm was 49%, which is greater than the target 30% threshold.

Table 9. Secondary Endpoint 1 – Average IPSS Improvement at 12 Months

Endpoint	Optilume BPH (n=100)
% Improvement in IPSS	
Mean ± SE	49.1% ± 3.2%
[95% CI]	[42.7%, 55.4%]

Secondary Endpoint 2 – Responder Rate at 3 Months (Optilume BPH) vs 3 Months (Sham)

The rate of responders at 3 months in the Optilume BPH arm was compared to the rate of responders at 3 months in the Sham arm. A responder is defined as a subject who has an IPSS improvement of ≥30% at the listed timepoint compared to baseline. Subjects undergoing alternative therapy for ongoing/recurrent LUTS prior to the scheduled timepoint were considered as having no improvement in the analysis. The responder rate at 3 months was numerically higher in the Optilume BPH arm compared to the Sham arm.

Table 10. Secondary Endpoint 2 – Responder Rate at 3 Months

Endpoint	Sham	Optilume BPH
Responder Rate (≥30%)		
Proportion (n/N)	52.1% (25/48)	68.8% (66/96)
[95% CI]	[37.2%, 66.7%]	[58.5%, 77.8%]
N=4 patients excluded from analysis due to missing values.		

Secondary Endpoint 3 – Responder Rate at 12 Months (Optilume BPH) vs 3 Months (Sham)

The rate of responders at 12 months in the Optilume BPH arm was compared to the rate of responders at 3 months in the Sham arm. A responder is defined as a subject who has an IPSS improvement of ≥30% at the listed timepoint compared to baseline. Subjects undergoing alternative therapy for ongoing/recurrent LUTS prior to the scheduled timepoint were considered as having no improvement in the analysis. The responder rate at 12 months in the Optilume BPH arm was higher than the responder rate at 3 months in the Sham arm (76.6% vs 52.1%).

Table 11. Secondary Endpoint 3 – Responder Rate at 12 Months

Endpoint	Sham (3 months)	Optilume BPH (12 months)
Responder Rate (≥30%) Proportion (n/N) [95% CI]	 52.1% (25/48) [37.2%, 66.7%]	 76.6% (72/94) [66.7%, 84.7%]
N=6 patients excluded from analysis due to missing values.		

Secondary Endpoint 4 – Change in Qmax

The change in Qmax at 12 months in the Optilume BPH arm was compared to the change in Qmax at 3 months in the Sham arm. Subjects opting to receive alternative therapy or withdrawing due to perceived lack of effectiveness were considered as having no improvement. The Optilume BPH arm showed a higher increase in Qmax at 12 months when compared to the increase in Qmax seen in the Sham arm at 3 months.

Table 12. Secondary Endpoint 4 Change in Qmax from Baseline

Variable	Optilume BPH – 12 Months (n=87)	Sham – 3 Months (n=43)	Point Estimate of Difference [95%CI]
Change in Qmax (Mean ± SD, [95% CI])	+9.7 ± 10.14 [7.5, 11.8]	+5.5 ± 7.44 [3.2, 7.8]	-4.2 [-7.6, -0.8]
Uroflows with a voided volume <150mL were excluded from this analysis.			

12.1.3.3 Ancillary Endpoints

Analysis of the following ancillary endpoints demonstrated improvement through 12 months follow-up.

Ancillary Endpoint 1 – Additional Responder Analyses with a Responder Defined as IPSS Improvement of 35%, 40% and 50%

The change in IPSS for both arms is presented using a Retreatments Imputed analysis which carries forward baseline values for subjects considered treatment failures (Table 9). The proportion of subjects with at least 35%, 40% and 50% improvement in IPSS is higher in the Optilume BPH arm compared to the Sham arm at all timepoints evaluated (Table 10).

Table 9. Change in IPSS Over Time (Retreatments Imputed)

Group	Baseline	14 Day	30 Day	3 Month	6 Month	12 Month
Optilume BPH (N=100)						
n	100	87	97	96	94	94
Mean ± SD	23.4 ± 5.5	15.7 ± 8.9	13.4 ± 7.0	13.0 ± 7.6	12.8 ± 7.8	11.8 ± 7.6
Median	23.0	14.0	13.0	12.0	12.5	10.0
Min, Max	13, 34	1, 35	1, 35	0, 32	1, 33	0, 32
Sham (N=48)						
n	48	47	48	48	47	48
Mean ± SD	24.3 ± 5.8	15.1 ± 7.6	15.0 ± 8.0	16.2 ± 8.9	18.1 ± 7.8	19.5 ± 9.2
Median	25.5	13.0	13.0	15.0	18.0	21.0
Min, Max	12, 34	3, 33	2, 33	4, 34	5, 32	4, 34

Table 10. Responder Rate Based on IPSS Improvement of 35%, 40% and 50%

Visit	Improvement of percentage in IPSS (%)					
	≥35%		≥40%		≥50%	
	Optilume BPH	Sham	Optilume BPH	Sham	Optilume BPH	Sham
30 Day						
% (n/N)	63.9% (62/97)	54.2% (26/48)	59.8% (58/97)	52.1% (25/48)	43.3% (42/97)	37.5% (18/48)
95% CI[1]	53.5%, 73.4%	39.2%, 68.6%	49.3%, 69.6%	37.2%, 66.7%	33.3%, 53.7%	24.0%, 52.6%
3 Month						
% (n/N)	66.7% (64/96)	50.0% (24/48)	61.5% (59/96)	45.8% (22/48)	47.9% (46/96)	39.6% (19/48)
95% CI[1]	56.3%, 76.0%	35.2%, 64.8%	51.0%, 71.2%	31.4%, 60.8%	37.6%, 58.4%	25.8%, 54.7%
6 Month						
% (n/N)	68.1% (64/94)	36.2% (17/47)	60.6% (57/94)	31.9% (15/47)	45.7% (43/94)	25.5% (12/47)
95% CI[1]	57.7%, 77.3%	22.7%, 51.5%	50.0%, 70.6%	19.1%, 47.1%	35.4%, 56.3%	13.9%, 40.3%
12 Month						
% (n/N)	71.3% (67/94)	31.3% (15/48)	69.1% (65/94)	27.1% (13/48)	59.6% (56/94)	22.9% (11/48)
95% CI[1]	61.0%, 80.1%	18.7%, 46.3%	58.8%, 78.3%	15.3%, 41.8%	49.0%, 69.6%	12.0%, 37.3%

Note: Timepoints after study exit due to treatment failure or crossover to treatment are imputed as failures
[1]Confidence intervals (CI) are estimated using the Clopper-Pearson (exact) approach.

Ancillary Endpoints 2 and 8 – Change in Post-void Residual (PVR) Urine Volume and Peak Flow Rate (Qmax)

Table 11. Change in Qmax and PVR Over Time (Retreatments Imputed)

Measure	Group	Baseline	30 Day	3 Month	6 Month	12 Month
QMax (mL/sec)	Optilume BPH (N=100)					
	n	98	79	81	86	87
	Mean ± SD	8.9 ± 2.2	17.6 ± 9.0	18.6 ± 9.7	16.9 ± 8.9	18.5 ± 10.2
	Median	8.9	16.8	17.2	14.7	17.0
	Min, Max	5, 12	4, 49	4, 66	5, 59	5, 60
	Sham (N=48)					
	n	48	43	43	43	48
	Mean ± SD	8.9 ± 1.8	13.2 ± 6.3	14.5 ± 7.8	13.2 ± 6.8	12.1 ± 6.5
	Median	9.0	11.5	13.0	10.9	10.0
	Min, Max	6, 12	5, 32	5, 42	6, 38	6, 38

Measure	Group	Baseline	30 Day	3 Month	6 Month	12 Month
PVR (mL)	Optilume BPH (N=100)					
	n	99	92	91	90	90
	Mean ± SD	84.1 ± 70.2	60.5 ± 54.4	69.5 ± 68.6	61.4 ± 58.8	59.5 ± 52.6
	Median	69.0	47.5	55.0	45.0	42.5
	Min, Max	0, 298	0, 248	0, 435	0, 313	0, 202
	Sham (N=48)					
	n	48	46	48	47	47
	Mean ± SD	89.4 ± 73.9	91.8 ± 81.6	98.4 ± 102.4	96.9 ± 103.8	93.4 ± 98.0
	Median	66.0	76.5	57.0	56.0	69.0
	Min, Max	0, 284	0, 348	0, 385	10, 534	0, 500
Voided volumes < 150 mL are excluded from the Qmax analysis.						

Ancillary Endpoint 3 – Change in Sexual Function (International Index of Erectile Function (IIEF), Male Sexual Health Questionnaire - Ejaculatory Dysfunction (MSHQ-EjD))

Table 12. IIEF Over Time (As Observed)

Measure	Group	Baseline	3 Month	6 Month	12 Month
Erectile Function	Optilume BPH (N=98)				
	n	97	92	91	87
	Mean ± SD	15.6 ± 10.3	16.5 ± 10.8	17.3 ± 11.0	17.1 ± 11.1
	Median	15.0	16.5	19.0	16.0
	Min, Max	1, 30	1, 30	1, 30	1, 30
	Sham (N=48)				
	n	48	47	35	26
	Mean ± SD	16.8 ± 9.3	17.6 ± 9.8	19.8 ± 8.7	20.1 ± 8.4
	Median	19.0	18.0	22.0	22.5
	Min, Max	1, 30	1, 30	1, 30	4, 30
Intercourse Satisfaction	Optilume BPH (N=98)				
	n	98	92	91	88
	Mean ± SD	5.7 ± 5.0	5.8 ± 5.2	6.5 ± 5.4	6.4 ± 5.4
	Median	7.0	7.0	8.0	8.0
	Min, Max	0, 15	0, 14	0, 15	0, 15
	Sham (N=48)				
	n	48	47	35	26
	Mean ± SD	6.3 ± 4.9	6.9 ± 5.0	7.5 ± 4.5	8.3 ± 4.4
	Median	8.0	7.0	9.0	9.5
	Min, Max	0, 15	0, 15	0, 13	0, 14
Orgasmic Function	Optilume BPH (N=98)				
	n	98	92	91	88
	Mean ± SD	5.8 ± 3.8	5.6 ± 3.9	6.7 ± 3.9	6.3 ± 3.8
	Median	6.5	6.0	8.0	8.0
	Min, Max	0, 10	0, 10	0, 10	0, 10
	Sham (N=48)				
	n	48	47	35	26
	Mean ± SD	6.1 ± 3.5	6.3 ± 3.5	6.6 ± 2.9	7.3 ± 2.9
	Median	6.5	7.0	6.0	8.0
	Min, Max	0, 10	0, 10	0, 10	0, 10

Measure	Group	Baseline	3 Month	6 Month	12 Month
Sexual Desire	Optilume BPH (N=98)				
	n	97	92	91	89
	Mean ± SD	6.3 ± 2.2	6.5 ± 2.1	6.6 ± 2.2	6.5 ± 2.2
	Median	6.0	7.0	7.0	7.0
	Min, Max	2, 10	2, 10	2, 10	2, 10
	Sham (N=48)				
	n	48	47	35	26
	Mean ± SD	6.4 ± 1.9	6.1 ± 1.8	6.3 ± 1.7	6.4 ± 2.0
	Median	7.0	6.0	6.0	6.5
	Min, Max	2, 10	2, 9	3, 10	2, 10
Overall Satisfaction	Optilume BPH (N=98)				
	n	96	92	91	86
	Mean ± SD	5.6 ± 2.7	6.2 ± 2.8	6.3 ± 2.9	6.3 ± 2.9
	Median	6.0	6.0	6.0	6.0
	Min, Max	2, 10	2, 10	2, 10	2, 10
	Sham (N=48)				
	n	47	45	35	26
	Mean ± SD	5.4 ± 2.7	5.9 ± 2.8	6.4 ± 2.8	6.5 ± 2.8
	Median	5.0	6.0	6.0	6.5
	Min, Max	2, 10	2, 10	2, 10	2, 10
Note: A higher score indicates higher sexual function.					

Table 13. MSHQ-EjD Over Time (As Observed)

Measure	Group	Baseline	3 Month	6 Month	12 Month
Ejaculatory Function[1]	Optilume BPH (N=98)				
	n	98	86	87	87
	Mean ± SD	7.5 ± 3.9	8.5 ± 4.8	8.3 ± 4.5	8.4 ± 4.6
	Median	7.0	9.0	9.0	9.0
	Min, Max	1, 15	1, 15	1, 15	1, 15
	Sham (N=48)				
	n	47	47	35	26
	Mean ± SD	8.0 ± 3.4	8.8 ± 3.9	9.1 ± 3.4	9.9 ± 3.5
	Median	8.0	9.0	10.0	10.0
	Min, Max	1, 15	1, 15	1, 15	4, 15
Ejaculation Bother[2]	Optilume BPH (N=98)				
	n	98	86	87	87
	Mean ± SD	2.5 ± 1.7	1.9 ± 1.6	2.1 ± 1.7	2.0 ± 1.7
	Median	3.0	2.0	2.0	2.0
	Min, Max	0, 5	0, 5	0, 5	0, 5
	Sham (N=48)				
	n	47	47	35	26
	Mean ± SD	2.2 ± 1.7	2.0 ± 1.5	2.1 ± 1.6	2.0 ± 1.8
	Median	2.0	2.0	2.0	1.5
	Min, Max	0, 5	0, 5	0, 5	0, 5
[1]Higher score = Less ejaculation dysfunction (Possible Range 1 - 15) [2]Higher score = Greater bother with ejaculation difficulties (Possible Range 0 - 5)					

Ancillary Endpoint 4 – Change in BPH Impact Index (BPH-II)

Table 14. BPH Impact Index Over Time (As Observed)

Group	Baseline	30 Day	3 Month	6 Month	12 Month
Optilume BPH (N=98)					
n	98	96	93	91	89
Mean ± SD	7.0 ± 2.9	5.3 ± 3.2	4.5 ± 3.2	2.9 ± 2.8	2.3 ± 2.5
Median	7.0	5.0	4.0	2.0	2.0
Min, Max	1, 12	0, 13	0, 12	0, 12	0, 11
Sham (N=48)					
n	48	48	48	35	26
Mean ± SD	7.0 ± 3.0	3.8 ± 3.1	3.9 ± 3.5	3.6 ± 2.7	3.4 ± 3.1
Median	7.0	3.0	3.0	4.0	3.0
Min, Max	0, 12	0, 13	0, 12	0, 9	0, 12

Ancillary Endpoint 5 – Change in Quality of Life (EQ-5D)

Table 15. EQ-5D Composite Over Time (As Observed)

Measure	Baseline	30 Day	3 Month	6 Month	12 Month
Optilume BPH (N=98)					
n	98	96	93	90	88
Mean ± SD	0.865 ± 0.123	0.866 ± 0.116	0.875 ± 0.120	0.888 ± 0.132	0.878 ± 0.132
Median	0.861	0.861	0.861	0.876	0.876
Min, Max	0.49, 1.00	0.39, 1.00	0.38, 1.00	0.46, 1.00	0.46, 1.00
Sham (N=48)					
n	48	47	47	35	26
Mean ± SD	0.854 ± 0.108	0.900 ± 0.106	0.893 ± 0.101	0.886 ± 0.096	0.887 ± 0.099
Median	0.854	0.876	0.876	0.861	0.861
Min, Max	0.51, 1.00	0.49, 1.00	0.62, 1.00	0.72, 1.00	0.72, 1.00

Table 16. EQ-5D VAS Over Time (As Observed)

Measure	Baseline	30 Day	3 Month	6 Month	12 Month
Optilume BPH (N=98)					
n	98	96	93	90	88
Mean ± SD	81.6 ± 14.4	82.6 ± 13.9	85.8 ± 11.4	84.6 ± 14.0	86.5 ± 10.0
Median	85.0	87.5	90.0	89.0	89.0
Min, Max	25, 100	40, 100	40, 100	10, 100	45, 100
Sham (N=48)					
n	48	47	47	35	26
Mean ± SD	78.9 ± 13.7	83.5 ± 11.0	83.1 ± 10.4	82.8 ± 7.9	84.3 ± 8.9
Median	80.0	85.0	85.0	85.0	85.0
Min, Max	30, 100	50, 100	50, 100	70, 95	57, 100

Ancillary Endpoint 6 – Change in Pain Score

Table 17. Peri-operative VAS Pain Scores (As Observed)

Group	Baseline	Procedure	Foley Removal	14 Day	30 Day	3 Month
Optilume BPH (N=98)						
n	98	97	96	95	97	94
Mean ± SD	1.2 ± 2.0	4.1 ± 2.3	2.4 ± 2.2	1.6 ± 1.9	1.4 ± 1.8	1.1 ± 1.6
Median	0.0	4.0	2.0	1.0	1.0	0.0
Min, Max	0, 8	0, 10	0, 10	0, 9	0, 8	0, 6
Sham (N=48)						
n	48	48	48	47	48	48
Mean ± SD	1.3 ± 2.0	2.6 ± 1.9	2.8 ± 2.5	0.9 ± 1.6	0.6 ± 1.3	0.9 ± 1.6
Median	0.0	3.0	2.0	0.0	0.0	0.0
Min, Max	0, 7	0, 7	0, 8	0, 8	0, 6	0, 8

Ancillary Endpoint 7 – Procedure Parameters

Procedures were performed in an ambulatory surgical center (81.5%) or office-based location (18.5%). The average (SD) time for the Optilume BPH procedure from cystoscope insertion to removal of the treatment device was 26.0 (8.2) minutes (n=98).

Ancillary Endpoint 9 – Proportion of Subjects Experiencing a Return to 'Normal' Symptom Severity (IPSS<8)

Approximately one-third of subjects (30.9%, 29/94) treated with the Optilume BPH Catheter System returned to 'normal' symptom levels by 12 months post-treatment compared to 14.6% (7/48) in the Control group.

Table 18. Proportion of Subjects with IPSS<8

Visit	Proportion of Subjects with IPSS <8	
	Optilume BPH	Sham
3 Month		
% (n/N)	25.0% (24/96)	20.8% (10/48)
95% CI[1]	16.7%, 34.9%	10.5%, 35.0%
6 Month		
% (n/N)	29.8% (28/94)	8.5% (4/47)
95% CI[1]	20.8%, 40.1%	2.4%, 20.4%
12 Month		
% (n/N)	30.9% (29/94)	14.6% (7/48)
95% CI[1]	21.7%, 41.2%	6.1%, 27.8%

Note: Timepoints after study exit due to treatment failure or crossover to treatment are imputed as failures
[1]Confidence intervals (CI) are estimated using the Clopper-Pearson (exact) approach.

12.1.4 Safety Outcomes

The primary safety endpoint of the PINNACLE study was defined as the proportion of subjects experiencing a composite of major device-related serious complications through 12 months post-procedure: rectal or gastrointestinal fistula, fistula between the rectum and urethra, new onset severe urinary retention lasting >14 consecutive days post-healing, unresolved de novo stress urinary incontinence by 90 days, bleeding requiring transfusion, and urethra or prostatic capsule rupture requiring surgical intervention. No subjects experienced an event qualifying for the pre-defined composite of serious device-related complications through 12 months as adjudicated by the Clinical Events Committee (CEC).

Table 14. Primary Safety Endpoint – Freedom from Major Device Related Complications

Endpoint	Sham (n=48)	Optilume BPH (n=100)	Difference (95% CI)
Major device-related complications at 12 months	0.0% (0/48)	0.0% (0/100)	0.0% (0.0%, 0.0%)

Adverse event summaries are based on the As-Treated cohort which included 98 subjects in the Optilume BPH arm treated with the device (Table 19). A summary of events adjudicated by the CEC as related to the study device or procedure is shown in Table 20.

Table 19. Summary of Adverse Events by Arm (As Treated)

	Optilume BPH (N=98)		Sham (N=48)	
Event Types	**Events**	**Participant % (n/N)**	**Events**	**Participant % (n/N)**
Adverse Events	241	82.7% (81/98)	58	62.5% (30/48)
Serious Adverse Events	15	14.3% (14/98)	3	6.3% (3/48)
Treatment Related Adverse Events	143	71.4% (70/98)	15	25.0% (12/48)
Device Related AE	*121*	*67.3% (66/98)*	*11*	*16.7% (8/48)*
Procedure Related AE	*22*	*18.4% (18/98)*	*4*	*8.3% (4/48)*
Treatment Related Serious Adverse Events	6	6.1% (6/98)	0	0.0% (0/48)
Device Related SAE	*5*	*5.1% (5/98)*	*0*	*0.0% (0/48)*
Procedure Related SAE	*1*	*1.0% (1/98)*	*0*	*0.0% (0/48)*

Treatment-related serious adverse events were reported in 6 (6.1%) subjects, most commonly post-procedure hematuria (4 events) which resolved without sequelae. The most frequently reported treatment-related adverse events included hematuria (39.8%), urinary tract infection (11.2%), dysuria (8.2%), and mild stress urinary incontinence (7.1%). Treatment-related adverse events were mostly mild or moderate in severity (138/143, 97%). There were no life threatening (Grade 4) or fatal (Grade 5) events related to either the study device or procedure.

A total of 41 hematuria and post-procedural hematuria events occurred in 39 subjects (39.8%) with most events being mild or moderate in severity (37/41, 90.2%) with a median time to resolution of 34 days. The rate and severity of hematuria events was decreased after implementation of post-operative care guidelines as described in section 11.6.

Table 20. Device/Procedure Related Adverse Events (As Treated)

System Organ Class/ CTC Term	Optilume BPH (N=98)				Sham (N=48)			
	Grade 1-2		Grade 3		Grade 1-2		Grade 3	
	Events	Participant % (n/N)	Events	Participant % (n/N)	Events	Participant % (n/N)	Events	Participant % (n/N)
Gastrointestinal Disorders	**0**	**0.0% (0/98)**	**0**	**0.0% (0/98)**	**1**	**2.1% (1/48)**	**0**	**0.0% (0/48)**
Abdominal pain	0	0.0% (0/98)	0	0.0% (0/98)	1	2.1% (1/48)	0	0.0% (0/48)
General Disorders And Administration Site Conditions	**0**	**0.0% (0/98)**	**0**	**0.0% (0/98)**	**1**	**2.1% (1/48)**	**0**	**0.0% (0/48)**
Fever	0	0.0% (0/98)	0	0.0% (0/98)	1	2.1% (1/48)	0	0.0% (0/48)
Infections And Infestations	**12**	**11.2% (11/98)**	**0**	**0.0% (0/98)**	**4**	**6.3% (3/48)**	**0**	**0.0% (0/48)**
Bladder infection	0	0.0% (0/98)	0	0.0% (0/98)	1	2.1% (1/48)	0	0.0% (0/48)
Urinary tract infection	12	11.2% (11/98)	0	0.0% (0/98)	3	4.2% (2/48)	0	0.0% (0/48)

System Organ Class/ CTC Term	Optilume BPH (N=98)				Sham (N=48)			
	Grade 1-2		Grade 3		Grade 1-2		Grade 3	
	Events	Participant % (n/N)	Events	Participant % (n/N)	Events	Participant % (n/N)	Events	Participant % (n/N)
Injury, Poisoning And Procedural Complications	**0**	**0.0% (0/98)**	**0**	**0.0% (0/98)**	**0**	**0.0% (0/48)**	**0**	**0.0% (0/48)**
Investigations	**2**	**2.0% (2/98)**	**0**	**0.0% (0/98)**	**0**	**0.0% (0/48)**	**0**	**0.0% (0/48)**
Elevated prostate specific antigen [PSA]	2	2.0% (2/98)	0	0.0% (0/98)	0	0.0% (0/48)	0	0.0% (0/48)
Musculoskeletal And Connective Tissue Disorders	**2**	**1.0% (1/98)**	**0**	**0.0% (0/98)**	**0**	**0.0% (0/48)**	**0**	**0.0% (0/48)**
Groin pain	1	1.0% (1/98)	0	0.0% (0/98)	0	0.0% (0/48)	0	0.0% (0/48)
Low back pain	1	1.0% (1/98)	0	0.0% (0/98)	0	0.0% (0/48)	0	0.0% (0/48)
Product Issues	**1**	**1.0% (1/98)**	**0**	**0.0% (0/98)**	**0**	**0.0% (0/48)**	**0**	**0.0% (0/48)**
Catheter blockage	1	1.0% (1/98)	0	0.0% (0/98)	0	0.0% (0/48)	0	0.0% (0/48)
Renal And Urinary Disorders	**99**	**65.3% (64/98)**	**5**	**5.1% (5/98)**	**7**	**12.5% (6/48)**	**0**	**0.0% (0/48)**
Bladder cancer	0	0.0% (0/98)	0	0.0% (0/98)	1	2.1% (1/48)	0	0.0% (0/48)
Bladder perforation	0	0.0% (0/98)	1	1.0% (1/98)	0	0.0% (0/48)	0	0.0% (0/48)
Bladder spasm	6	6.1% (6/98)	0	0.0% (0/98)	0	0.0% (0/48)	0	0.0% (0/48)
Dysuria	8	8.2% (8/98)	0	0.0% (0/98)	1	2.1% (1/48)	0	0.0% (0/48)
Frequency of micturition	3	3.1% (3/98)	0	0.0% (0/98)	1	2.1% (1/48)	0	0.0% (0/48)
Hematuria	11	10.2% (10/98)	0	0.0% (0/98)	1	2.1% (1/48)	0	0.0% (0/48)
Leukocyturia	1	1.0% (1/98)	0	0.0% (0/98)	0	0.0% (0/48)	0	0.0% (0/48)
Lower urinary tract symptoms	5	4.1% (4/98)	0	0.0% (0/98)	0	0.0% (0/48)	0	0.0% (0/48)
Meatal stenosis	1	1.0% (1/98)	0	0.0% (0/98)	1	2.1% (1/48)	0	0.0% (0/48)
Nocturia	3	3.1% (3/98)	0	0.0% (0/98)	0	0.0% (0/48)	0	0.0% (0/48)
Overactive bladder	2	2.0% (2/98)	0	0.0% (0/98)	0	0.0% (0/48)	0	0.0% (0/48)
Post micturition dribble	1	1.0% (1/98)	0	0.0% (0/98)	0	0.0% (0/48)	0	0.0% (0/48)
Post procedural hematuria	26	25.5% (25/98)	4	4.1% (4/98)	0	0.0% (0/48)	0	0.0% (0/48)
Stress urinary incontinence	7	7.1% (7/98)	0	0.0% (0/98)	0	0.0% (0/48)	0	0.0% (0/48)
Urethral false passage	1	1.0% (1/98)	0	0.0% (0/98)	0	0.0% (0/48)	0	0.0% (0/48)
Urethral pain	2	2.0% (2/98)	0	0.0% (0/98)	0	0.0% (0/48)	0	0.0% (0/48)
Urethral stricture	4	4.1% (4/98)	0	0.0% (0/98)	1	2.1% (1/48)	0	0.0% (0/48)
Urethritis	1	1.0% (1/98)	0	0.0% (0/98)	0	0.0% (0/48)	0	0.0% (0/48)
Urinary incontinence (U*rge/Mixed)*	5	5.1% (5/98)	0	0.0% (0/98)	1	2.1% (1/48)	0	0.0% (0/48)
Urinary retention	3	3.1% (3/98)	0	0.0% (0/98)	0	0.0% (0/48)	0	0.0% (0/48)
Urinary urgency	6	6.1% (6/98)	0	0.0% (0/98)	0	0.0% (0/48)	0	0.0% (0/48)
Voiding difficulty	3	2.0% (2/98)	0	0.0% (0/98)	0	0.0% (0/48)	0	0.0% (0/48)
Reproductive System And Breast Disorders	**21**	**15.3% (15/98)**	**0**	**0.0% (0/98)**	**2**	**4.2% (2/48)**	**0**	**0.0% (0/48)**
Anejaculation	1	1.0% (1/98)	0	0.0% (0/98)	0	0.0% (0/48)	0	0.0% (0/48)
Ejaculation decreased	1	1.0% (1/98)	0	0.0% (0/98)	1	2.1% (1/48)	0	0.0% (0/48)
Epididymitis	0	0.0% (0/98)	0	0.0% (0/98)	1	2.1% (1/48)	0	0.0% (0/48)
Hematospermia	4	4.1% (4/98)	0	0.0% (0/98)	0	0.0% (0/48)	0	0.0% (0/48)
Painful ejaculation	1	1.0% (1/98)	0	0.0% (0/98)	0	0.0% (0/48)	0	0.0% (0/48)
Painful orgasm	1	1.0% (1/98)	0	0.0% (0/98)	0	0.0% (0/48)	0	0.0% (0/48)
Pelvic pain	6	5.1% (5/98)	0	0.0% (0/98)	0	0.0% (0/48)	0	0.0% (0/48)
Penile pain	1	1.0% (1/98)	0	0.0% (0/98)	0	0.0% (0/48)	0	0.0% (0/48)
Perineal pain	3	3.1% (3/98)	0	0.0% (0/98)	0	0.0% (0/48)	0	0.0% (0/48)
Prostatitis	1	1.0% (1/98)	0	0.0% (0/98)	0	0.0% (0/48)	0	0.0% (0/48)
Retrograde ejaculation	2	2.0% (2/98)	0	0.0% (0/98)	0	0.0% (0/48)	0	0.0% (0/48)

System Organ Class/ CTC Term	Optilume BPH (N=98)				Sham (N=48)			
	Grade 1-2		Grade 3		Grade 1-2		Grade 3	
	Events	Participant % (n/N)	Events	Participant % (n/N)	Events	Participant % (n/N)	Events	Participant % (n/N)
Respiratory, Thoracic And Mediastinal Disorders	**1**	**1.0% (1/98)**	**0**	**0.0% (0/98)**	**0**	**0.0% (0/48)**	**0**	**0.0% (0/48)**
Aspiration pneumonia	1	1.0% (1/98)	0	0.0% (0/98)	0	0.0% (0/48)	0	0.0% (0/48)

12.1.5 Pharmacokinetic Profile

A sub-study including 15 non-randomized subjects was conducted to determine the pharmacokinetic profile of paclitaxel in blood (plasma), urine, and semen after treatment with the Optilume BPH DCB. Determination of plasma paclitaxel concentration was evaluated immediately after completion of the procedure, at 1, 3, and 5 hours, and at Foley removal, 30 days, 3 months, and 6 months post-procedure. Urine paclitaxel concentration was evaluated immediately post-procedure, at Foley removal, and at 30 days, 3 months, and 6 months. Semen paclitaxel concentration was evaluated at 30 days, 3 months, and 6 months post-procedure.

A summary of pharmacokinetic parameters, including maximum concentration (C_{max}) and time to maximum concentration (T_{max}) for plasma is in Table 21. Paclitaxel concentration over time in urine and semen can be found in Table 22 and Table 23, respectively. On average, paclitaxel concentration in plasma fell below the limit of quantitation of the method (0.10 ng/mL or 0.1 part per billion) by the time of Foley removal, while average paclitaxel concentration in urine approached the limit of quantitation by 6 months. Analysis of paclitaxel concentration in semen showed low but persistent levels of paclitaxel in semen through 6 months post-treatment. Of the three subjects who had evaluable data at 12 months post-treatment, one had detectable paclitaxel concentration in semen (0.16 ng/mL).

Table 21. Summary of Plasma Pharmacokinetic Parameters

Parameter	Plasma
C_{max} (ng/mL)	
n	15
Mean	0.40 ± 0.54
Min, Max	<0.10, 2.24
T_{max} (hr)	
n	15
Median	1.0 ± 1.71
Min, Max	0.25, 5

Table 22. Urine Paclitaxel Concentration Over Time

Measure	Urine Paclitaxel Concentration (ng/mL)					
	Baseline	0hr	Foley Removal	30 Days	3 Months	6 Months
Mean ± SD	<0.1 ± 0.0	1,892.8 ± 4,530.6	134.6 ± 221.9	1.3 ± 1.5	0.4 ± 0.7	0.1 ± 0.2
Median	<0.1	536.5	65.1	0.7	0.2	<0.1
Max, Min	<0.1	17,500, 64.4	841, 3.6	5.5, <0.1	2.8, <0.1	0.6, <0.1
Subjects with Measurable Amt	0/13 (0.0%)	14/14 (100.0%)	13/13 (100.0%)	12/14 (85.7%)	9/14 (64.3%)	3/15 (20.0%)

Table 23. Semen Paclitaxel Concentration Over Time

Measure	Semen Concentration (ng/mL)				
	Baseline	30 Days	3 Months	6 Months	12 Months
Mean ± SD	<0.10 ± 0.0	2.34 ± 3.69	1.30 ± 2.76	0.29 ± 0.53	0.09 ± 0.06
Median	<0.10	0.86	0.27	<0.10	<0.10
Max, Min	<0.10	8.89, <0.10	7.54, <0.10	1.75, <0.10	0.16, <0.10
Subjects with Measurable Amt	0/6 (0.0%)	4/5 (80.0%)	5/7 (71.4%)	4/10 (40.0%)	1/3[α] (33.3%)
[α]Only subjects with confirmed or suspected paclitaxel present in their semen at 6 months were required to provide 12-month semen samples.					

12.2 Supplemental Clinical Study

EVEREST-I was a prospective, non-randomized, open label, multicenter study to evaluate the safety and efficacy of the Optilume BPH Catheter system for the treatment of LUTS secondary to BPH. Eligible subjects were men >50 years of age with LUTS secondary to BPH, IPSS ≥13, peak urinary flow rate 5-15 mL/sec, post-void residual ≤250 mL, prostate volume 20-80 grams, and prostatic urethral length 35-55 mm. Key exclusions included prior minimally invasive or surgical intervention of the prostate, intravesical prostatic protrusion >1 cm, and confounding urologic conditions (e.g., neurogenic bladder, stricture). Subjects had to undergo drug washouts prior to treatment including alpha blockers for 3 weeks and 5-alpha reductase inhibitors for 6 months. Subjects were followed at Foley removal, 2 weeks, 30 days, 3 months, 6 months, and 1-year post-treatment, and annually thereafter through 3 years. Follow-up is planned through 5 years.

A total of 80 subjects were enrolled and treated at 6 clinical sites in Panama and the Dominican Republic. Subjects were 65 years old on average with a prostate volume of 35.9 grams. The primary efficacy endpoint was the responder rate at 3 months based on an improvement in IPSS ≥40% from baseline without requiring additional therapy. At 3 months, 81.3% (65/80) were considered responders with a lower 90% confidence limit of 72.6% which met the performance goal of 50%.

Table 24. EVEREST-I Results Summary

Measure	Baseline	3 months	6 months	1 year	2 years	3 years
IPSS n Mean ± SD	 80 22.3 ± 4.9	 79 8.1 ± 6.1	 77 8.0 ± 7.2	 75 7.9 ± 7.6	 68 8.2 ± 7.3	 63 9.8 ± 8.0
IPSS QoL n Mean ± SD	 80 4.6 ± 0.86	 79 1.5 ± 1.33	 77 1.6 ± 1.62	 75 1.3 ± 1.38	 68 1.6 ± 1.58	 63 1.8 ± 1.74
Qmax (mL/sec) n Mean ± SD	 80 10.9 ± 2.92	 77 20.5 ± 9.54	 74 19.6 ± 8.67	 74 18.4 ± 8.21	 56 17.2 ± 8.98	 58 16.7 ± 10.63
PVR (mL) n Mean ± SD	 80 63.1 ± 55.01	 77 34.3 ± 33.08	 74 28.8 ± 29.53	 74 34.4 ± 35.25	 56 45.0 ± 50.94	 58 49.1 ± 79.29

The primary safety endpoint was a composite of device and procedure related serious complications at 3 months including new onset severe urinary retention lasting >14 consecutive days post-healing, unresolved new onset stress urinary incontinence by 90 days, and bleeding requiring transfusion. Two subjects experienced stress urinary incontinence meeting the

endpoint criteria for a rate of 2.5%. Both subjects were treated with a larger diameter balloon that is no longer included in the matrix of available device sizes.

13 WARRANTY

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Urotronic, Inc.
2495 Xenium Lane North
Minneapolis, MN 55441 USA
www.urotronic.com

14 SYMBOLS USED IN THE DEVICE LABELS

	Quantity of 1 per box
	Caution: Federal law restricts this device to sale by or on the order of a physician
	Catalogue number
	Lot number
	Date of manufacture
	Do not resterilize
	Do not re-use
	Do not use if package is damaged
	Fragile
	Use-by date
	Keep away from sunlight
	Keep dry
	Manufacturer
	Does not contain latex
	Temperature limit 15°C - 30°C (59°F - 86°F)
	Caution: Consult instructions for use
	Sterilized using ethylene oxide
	Single sterile barrier system
	Single sterile barrier system with protective packaging outside
	Medical device
	Unique device identifier
	Contains a medicinal substance