Editorial Commentary

A critical evaluation of Optilume® BPH as a novel minimally invasive surgical treatment for the management of lower urinary tract symptoms in men

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Expert summary

The prospective, double-blind, randomised, sham-controlled PINNACLE study assessed the safety and efficacy of Optilume® BPH (Urotonic, Inc., Minneapolis, MN, USA) compared to a sham procedure in 148 men with symptomatic benign prostatic hyperplasia (BPH) as characterised by International Prostate Symptom Score (IPSS) of ≥13 and maximum urinary flow rate (Qmax) between 5–12 mL/s (1). Full inclusion and exclusion criteria are listed in *Table 1*.

Patients were randomised in a 2:1 ratio to receive Optilume BPH (n=100) or the sham therapy (n=48), stratified by centre and IPSS severity (≤19 or >19). Baseline characteristics were comparable across both groups. A maximum follow-up of 12 months was planned but was discontinued in patients who received additional BPH treatment if lower urinary tract symptoms (LUTS) continued. Patients randomised to the sham arm were permitted to cross over to receive treatment with Optilume BPH after the 3-month follow-up. The primary outcome was improvement in IPSS from baseline to 3 months in the sham arm against improvement from baseline to 1 year in the Optilume BPH arm.

Optilume BPH combines anterior commissurotomy and simultaneous delivery of paclitaxel to prostatic adenoma in aim to create long-lasting channel patency in an ambulatory surgical setting. Prior to the procedure, prostatic urethral lengths are measured by transrectal ultrasound, with the intention to precisely select 1 of 4 drug-coated balloons (DCB) for each individual. Patients can receive general or local anaesthesia, in conjunction with oral sedation and local lubrication. Once the patient is draped and placed in a lithotomy position, cystoscopy is performed with a 20-Fr rigid cystoscope. First, a pre-dilatation balloon with a diameter of up to 90 Fr is inserted under direct vision

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Table 1 Abbreviated inclusion and exclusion criteria for PINNACLE study

Eligibility criteria	Specific criteria
Inclusion criteria	Men
	50–80 years
	IPSS score ≥13
	Qmax 5–12 mL/s
	Prostate volume 20–80 g
	Prostatic urethral length 32–55 mm
Exclusion criteria	Previous minimally invasive or surgical intervention on the prostate
	PSA >10 ng/mL without negative biopsy
	Diagnosis or suspicion of prostate or bladder cancer
	Active UTI
	Post void residual of >300 mL
	Confounding urinary or bladder tract diagnoses that could impact bladder function (e.g., urethral stricture, neurogenic bladder, etc.)

IPSS, International Prostate Symptoms Score; Qmax, maximum urinary flow rate; PSA, prostate-specific antigen; UTI, urinary tract infection.

and inflated for 5 minutes, and then removed. Then, a DCB catheter is inserted and inflated for 10 minutes, to deliver paclitaxel to the prostatic adenoma via the anterior commissurotomy. A 22–24-Fr 3 way in-dwelling catheter is placed, and continuous bladder irrigation is run for 30 minutes. The in-dwelling catheter remained *in situ* for 2 days postoperatively for both treatment arms.

The trial reported positive efficacy results, meeting the primary outcome. Patients receiving Optilume BPH had a significantly greater IPSS improvement at 12 months (–11.5±7.8) compared to patients in the sham arm at 3 months (–8.0±8.3), however appeared insignificant when a 25% super-superiority margin (P=0.18) was assessed. Significantly more patients received an IPSS improvement ≥30% in the Optilume BPH arm compared to the sham arm [66/96 (68.8%) *vs.* 25/48 (52.1%), P=0.003]. Qmax improvement at 12 months compared to baseline was significantly more evident in patients receiving Optilume BPH over sham at 3 months (+9.7±10.1 *vs.* +5.5±7.4 mL/s, P=0.009).

Between 3 and 6 months, one patient in the Optilume arm received BPH medication and one was lost to follow-up. In the control arm, 11 patients underwent a surgical procedure and one commenced BPH medication. Four patients from the Optilume BPH arm went on to have medical or surgical management of BPH, whereas 22—or almost half—of patients in the sham arm had either medical or surgical management of BPH during the follow-up window.

Four patients (4%) had haematuria directly resulting from Optilume BPH that required further cystoscopic management. A false passage requiring extended catheterisation occurred in one patient (1%). Regardless if attributable to Optilume BPH, 39 (40%) and 14 (14%) patients experienced haematuria and urinary tract infections respectively. While no treatment-related *de novo* erectile dysfunction was noted, four patients in Optilume BPH experienced ejaculatory dysfunction compared to one in the sham arm. On average, sexual function was not significantly impacted in either arm.

Expert opinion

The contemporary nexus of urology and bioengineering has led to an increase in the urologist's armamentarium to combat BPH on the backdrop of an ageing population. Novel minimally invasive surgical therapies (MIST) aim to bridge the gap between medical therapy and surgical resection of prostatic tissue. It is estimated that 2.1–10.1% of men receive some form of surgical intervention for LUTS (2,3). With such rapid innovation, it has become increasingly complex to select the most suitable intervention for patients with significant LUTS. Optilume has previously demonstrated efficacy in the treatment of anterior urethral

strictures (4). Now, applicability is extended to BPH. The open label EVEREST-I trial previously reported the favourable 2-year outcome results of the Optilume BPH in management of LUTS (5). Similar to its predecessor in balloon dilatation which yielded mixed long-term efficacy, the future of Optilume BPH remains to be ascertained.

Optilume BPH must be considered with reference to other MIST. The study found that Optilume BPH achieves comparable IPSS improvement with superior Qmax and post-void residual volume (PVR) improvement with other MIST. In respect to transurethral resection of the prostate (TURP), MIST boasts significant reduction in sexual dysfunction post-procedurally (6). Optilume BPH likewise preserves sexual function with no significant impact on erectile or ejaculatory function. Recent advancements in MIST technologies include Aquablation achieving a –16.475 IPSS at 3 months with sustained results (7). Similarly, robotically assisted simple prostatectomy has also been demonstrated as an emerging modality in comparison with other simple prostatectomies or endoscopic enucleation techniques (8).

Most patients in PINNACLE received deep sedation or general anaesthesia in both treatment arms (84.7% *vs.* 87.5%, P=0.9). This brings into question the true applicability of Optilume BPH in patients who may be unfit for general anaesthesia or deep sedation. Most MIST modalities utilise a mixture of anaesthetic techniques.

While no theoretical limit has been described, PINNACLE and EVEREST-I only demonstrate results in men with 20–80 mL prostate volumes (PVs). While BPH is often seen as a homogenous disease, PVs may assist in dictating suitable therapy. Additional subgroup analysis is necessary to understand durability of Optilume on small PVs which may have significant urinary bother. The trial's inclusion criteria are aligned with other MIST therapies, however, limit the broader applicability of results. No heterogeneity in baseline characteristics were noted. In turn, MIST trials urge urologists to consider often neglected patient populations, with the need to include difficult or abnormal anatomy within future studies.

A limitation common to all MIST trials has been the comparison to sham treatments. The recent findings from PINNACLE shed light on the need for clinical equipoise in trial design. While PINNACLE innovates upon previous studies by including blinding and follow-up to 12 months in the interventional arm, extended follow-up is essential to assess long-term retreatment rates.

Additionally, assessment of reoperative TURP on failed Optilume® BPH or other MISTs have not been extensively documented, with data only possible on long-term assessments. Given the chemotoxic effects of paclitaxel, uncertainty remains on surgical difficulty of consequent BPH operations. Taxane-based chemotherapy, such as docetaxel and cabazitaxel, are well established in castration-resistant prostate cancer (9,10). While previous experience of Optilume in urethral strictures have proved safe, uncertainty remains if there are implications of early taxane exposure for consequent prostate cancer treatment. Paclitaxel is theorised to reduce smooth muscle proliferation however direct mechanisms are yet to be established (11). On the other hand, patients receiving MIST may not require the durable benefits of TURP perhaps due to life expectancy, but require immediate and safe alleviation of LUTS.

While IPSS improvement as measured by percentage change was recorded in this study, further insight may be provided with IPSS category change to better account for patient perspective. There are also concerns about the impact of placebo effect as patients in the sham arm, receiving no active treatment, reported a clinically meaningful benefit at 3 months as measured by IPSS and Qmax. However, despite the potential placebo, the benefits of Optilume BPH remained consistent across the entirety of follow-up, whereas the sham arm saw a reduction in IPSS monotonically across follow-up time points.

Given the proprietary technology involved with MIST, procedural related costs for the patient and wider healthcare system must be considered. As Optilume BPH enters clinical practice, cost-benefit comparison to other BPH related treatments should be assessed. For the treatment of anterior urethral strictures in the United Kingdom, Optilume is quoted to cost £1,350 per unit (12). Evidence shows the potential for MIST to be a first-line alternative to pharmacotherapy given its cost-effectiveness, immediate symptomatic improvement, and no lifelong commitment to daily medications (13).

Optilume BPH is another potential tool for urologists to tackle the treatment of BPH, however it is currently unclear how Optilume BPH will measure up to other MIST in the long term. The current trial provides encouraging data for Optilume BPH in improving IPSS whilst preserving sexual function on Sexual Health Inventory for Men (SHIM).

While we eagerly await the long-term outcomes of Optilume BPH, the authors believe that younger patients wanting to improve bothersome LUTS and avoid impacts to sexual function should be considered for this novel technology. There may also be a role for Optilume BPH

in comorbid patients wishing to avoid general anaesthesia. Given the abundance of treatment options, urologists must carefully consider patient factors and select the most appropriate treatment for the individual.

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