BJUI
BJU International

24-month durability after crossover to the prostatic urethral lift from randomised, blinded sham

Daniel Rukstalis*, Prem Rashid†, William K. Bogache‡, Ronald F. Tutrone§, Jack Barkin¶, Peter T. Chin¶¶, Henry H. Woo**, Anthony L. Cantwell††, Barrett E. Cowan‡‡ and Damien M. Bolton§§

*Wake Forest Baptist Health, Winston Salem, NC, USA, †Urology Centre, Port Macquarie, NSW, Australia, ‡Carolina Urologic Research Center, Myrtle Beach, SC , §Chesapeake Urology Research Associates, Baltimore, MD, USA, ¶Toronto Urology Clinical Study Group, Toronto, ON, Canada, ¶¶Illawarra Urology, Figtree , **Sydney Urological Associates, Westmead Public/Private Hospital, Wahroonga, NSW, Australia, ††Advanced Urology Institute, Daytona Beach, FL , ‡‡Urology Associates of Denver, Englewood, CO, USA, and §§Austin Health, Heidelberg, Vic., Australia

Objective

To evaluate the 24-month effectiveness of the prostatic urethral lift (PUL) procedure in men with lower urinary tract symptoms (LUTS) secondary to benign prostatic hyperplasia (BPH) assessed through a crossover study.

Patients and Methods

In all, 53 patients underwent a sham procedure as part of the blinded, randomised L.I.F.T. (Luminal Improvement Following prostatic Tissue approximation for the treatment of LUTS secondary to BPH) study at 19 centres and elected to enrol in this crossover study. The crossover procedure involved placement of permanent implants (UroLift® system) into the prostatic lateral lobes. Patients were followed for 3 months after the sham procedure and then for 24 months after crossover to PUL, with assessments of urinary symptom relief, quality of life (QoL), urinary flow rate, sexual function, and adverse events.

Results

At 24 months after crossover to PUL, the International Prostate Symptom Score (IPSS), QoL, BPH Impact Index, and maximum urinary flow rate improved 36%, 40%, 54%, and 77% from baseline, respectively. Each IPSS parameter on average improved significantly from baseline ($P < 0.005$) and remained stable throughout follow-up. Symptom response after the sham procedure indicated initial improvement at 1 month with significant decay by 3 months. Adverse events were typically mild to moderate and patients returned rapidly to normal activity. Four patients (8%) required intervention with transurethral resection of the prostate and one patient required additional PUL implants within the 24-month period. There were no reported instances of *de novo* sustained erectile or ejaculatory dysfunction.

Conclusions

The PUL procedure is associated with rapid symptom relief, increased urinary flow rate and QoL improvement that remain stable over 24 months. Morbidity is low and sexual function is preserved.

Keywords

benign prostatic hyperplasia, lower urinary tract symptoms, minimally invasive surgical therapy, sexual function

Introduction

LUTS are some of the most common medical complaints experienced by men as they age. It is thought that by the eighth decade of life nearly all men will develop histological evidence of BPH, which often leads to bothersome symptoms such as urgency, frequency, and nocturia [1]. In addition to the personal burdens of this illness, LUTS/BPH imposes an economic burden on the healthcare system. When considering complications, follow-up visits, treatments, and other tests, the estimated cost for the year following initiation of treatment is €858 when averaged across six European countries [2]. Further, these associated expenditures are likely to increase due to the ageing population [3]. For these reasons, a treatment option that has the potential to reduce personal and economic burdens is desirable.

Current treatment options include medications and interventional procedures, each with associated risks and benefits. Medications are used as first-line treatment and are associated with a modest improvement in symptoms as measured by the IPSS. Unfortunately, up to 30% of men

CE: Aisha Begam J | PE: Alex Leo Paul
Dispatch: 15.10.16 | No. of pages: 9
WILEY
BJU | Journal Code | 13666 | Manuscript No.

discontinue their medications due to lack of relief, burden of compliance, or adverse effects such as dizziness and sexual dysfunction [4,5]. Surgical options include TURP, tissue vaporisation or thermal heating procedures. TURP, considered the 'gold standard' surgery, offers a 14.9-point average symptom relief, but is associated with significant morbidity including incontinence (3%), stricture (7%), erectile dysfunction (10%) and ejaculatory dysfunction (65%) [6]. Vaporisation with either laser or electrode reduces bleeding, but is otherwise associated with similar rates of serious adverse events [7,8]. Heating treatments such as microwave, needle ablation, and vapour ablation are associated with fewer serious adverse events than TURP, but are associated with a long period of irritative symptoms and urinary catheterisation [9–12].

The 'prostatic urethral lift' (PUL) is a mechanical approach that does not require cutting, burning, or tissue destruction to achieve LUTS relief. Instead, the PUL procedure transurethrally delivers permanent implants (UroLift ® system, NeoTract, Inc., Pleasanton, CA, USA) to separate the prostate lobes and relieve urethral obstruction. Recent studies have shown that PUL can offer a) rapid and significant relief of symptoms that is faster and more durable than heating treatments, b) lower risk of the serious complications associated with TURP and vaporisation, and c) uniquely preserve sexual function [13–24]. As reported by Roehrborn et al. [15] in 2013, the pivotal study for regulatory clearance enrolled 204 patients in a 2:1 randomised, controlled trial comparing the PUL procedure to a control sham procedure. For those patients in the control arm who elected to pursue crossover to PUL, the 24-month durability is presented here. In addition, we report the first detailed analysis of change in individual LUTS. IPSS element improvements are compared to those seen after blinded self-controlled sham procedure over a 3-month period.

Patients and Methods

While enrolled in a randomised, blinded study at 19 centres in the USA, Canada, and Australia, 53 patients with moderate-to-severe LUTS who had undergone a blinded sham procedure that involved rigid cystoscopy and mimicked PUL sounds were included [15]. After the primary endpoint comparison at 3 months, the patients were unblinded and if eligible, were offered enrolment in a crossover study during which they received PUL treatment and were followed to 24 months.

Patients were eligible for the study if they were aged >50 years, had an IPSS of ≥13, maximum urinary flow rate (Q_{max}) of ≤12 mL/s on a voided volume of 125 mL, prostate volume of 30–80 mL, and provided informed consent. Exclusion criteria included: prior surgical BPH treatment, obstructive median lobe, current urinary retention, post-void residual volume (PVR) of ≥250 mL, active UTI, PSA level of >10 ng/mL unless negative biopsy, cystolithiasis within 3 months, bacterial prostatitis within 1 year, and a history of prostate or bladder cancer. Patients were required to wash out of anticoagulants, 5α-reductase inhibitors, and α-blockers before the PUL procedure if they were not medication naïve. The study protocol was approved by the regulating authorities (USA Food and Drug Administration, Health Canada, and Therapeutic Goods Administration of Australia), as well as the Institutional Review Boards at each of the investigational sites (Clinicaltrials.gov: NCT01294150).

Control (sham) Procedure

The rigid cystoscopy control (sham) procedure was performed in a manner that simulated active PUL treatment. A visual obstruction kept the patient from seeing the operator or the monitoring screen. During the procedure, the operator would ask for the active treatment devices and support personnel would open the associated packaging materials. At appropriate times during the procedure, the operator would simulate UroLift delivery device sounds by activating a standard disposable biopsy device that was not inserted into the patient.

PUL Procedure

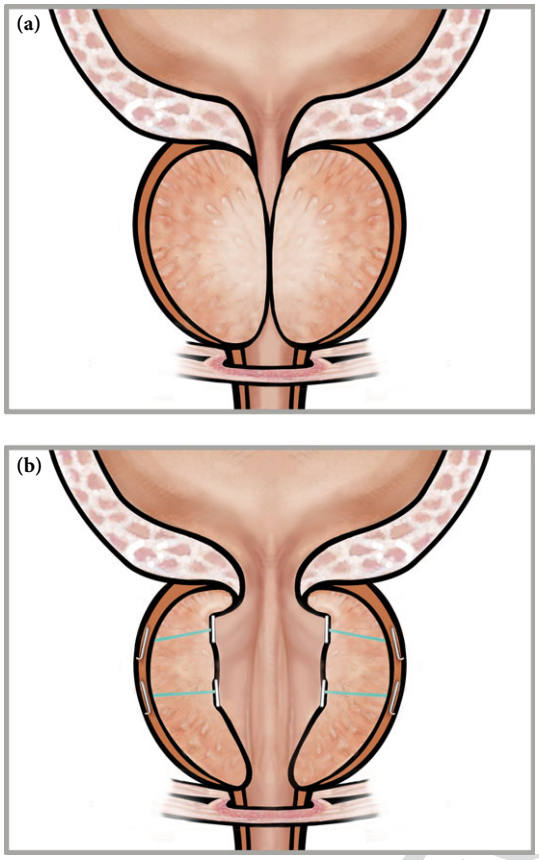
The PUL procedure requires the use of the UroLift delivery system to transurethrally deploy implants into the lateral lobes of the prostate. Before deployment, the urethra is assessed using standard cystoscopy equipment and target locations are identified. Next, the delivery tool is inserted into the 20-F sheath and used to compress the lateral lobe in an anterolateral direction. Implants are then deployed through a 19-G needle and affix the lateral lobes in a retracted position (Fig. 1). The implants are sized *in situ*, dependent on the size of the lateral lobe at the deployment location. Typically, four to six implants are delivered to create a continuous anterior channel.

Study Endpoints and Statistical Methods

Patients underwent a sham procedure and were assessed at baseline through to 3 months via IPSS, Q_{max}, IPSS quality of life (QoL) question, BPH Impact Index (BPHII), PVR, and sexual function questionnaires by an assessor blinded to the enrolment arm. After 3 months, patients were offered PUL or another intervention if symptoms persisted. Those patients who elected PUL treatment were assessed before crossover to PUL, and at 0.5, 1, 3, 6, 12, and 24 months after PUL. Adverse events were adjudicated by an independent clinical events committee for severity and for relationship to device and procedure. Flexible cystoscopy with retroflexion of the scope was conducted at the 24-month follow-up to assess for implant encrustation.

COLOR

Fig. 1 PUL procedure (**a**) before and (**b**) after installation of implants that retract prostatic tissue toward the prostate capsule, thus opening the prostatic fossa. Images courtesy of NeoTract, Inc.

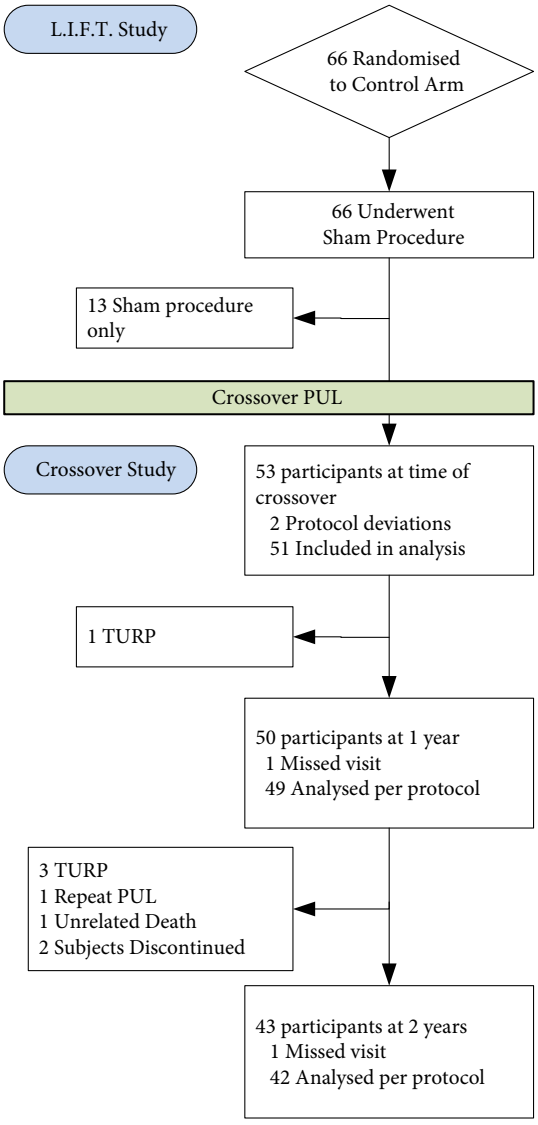


To evaluate per protocol change from pre-sham baseline, a general estimating equation model was fit to each output parameter. Change from baseline was the dependent variable; visit and baseline score were used as the dependent variable. An exchangeable correlation structure and identity link were used. This model was used to calculate *P* values for each follow-up interval compared to baseline using SAS (SAS Institute, Inc. Cary, NC, USA) and R (The R Foundation, Vienna, Austria). A $P < 0.05$ was considered to indicate statistical significance.

Results

During a blinded, randomised study of PUL vs sham, 66 patients underwent the control sham procedure between February and December 2011. After 3 months, all patients were unblinded. Of the 66 sham patients, 53 (80%) elected to undergo PUL treatment, entering the crossover study. Two patients were later excluded for protocol deviations associated with data collection methods, leaving 51 patients in the crossover cohort for analysis (Fig. 2, Table 1). During the 24-month follow-up period, four patients (8%) progressed to TURP and one (2%) required additional PUL implants. No

Fig. 2 Consolidated Standards of Reporting Trials (CONSORT) diagram.



COLOR

patients were taking an α-blocker or 5α-reductase inhibitor for LUTS at the time of the 24-month follow-up. Three patients withdrew from the study and one missed the 24-month follow-up visit, leaving 42 subjects available for per protocol evaluation at 24 months.

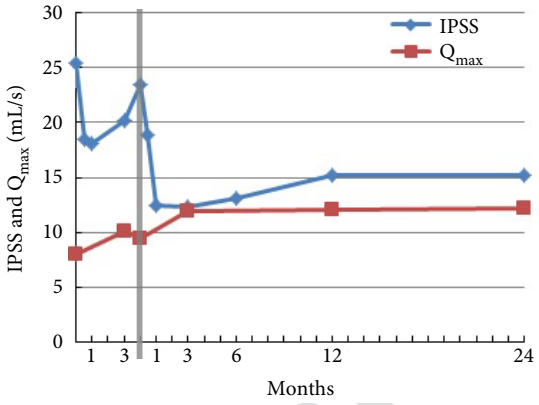
Figure 3 shows the overall mean IPSS and Q_{max} improvement over time, indicating that maximum sham symptom improvement occurred by 1 month and then diminished over time. By 3–6 months after the sham procedure, the IPSS returned to near pre-sham baseline, while Q_{max} diminished but remained elevated over baseline. After crossover PUL treatment, the IPSS improved significantly within 0.5 month, and both IPSS and Q_{max} achieved peak improvement by 3 months. Both the IPSS and Q_{max} showed significant and durable improvement through 24 months, with the IPSS

Table 1 Baseline characteristics and procedure details of treated patients.

Characteristics of crossover patients*	Value, mean (SD, range)
Age, years (n = 51)	64 (7.8, 50–79)
Prostate volume, mL (n = 51)	40.53 (9.92, 30.0–67.8)
Prostate length, mm (n = 51)	45.71 (5.50, 33.0–56.2)
PSA level, ng/mL (n = 51)	2.16 (1.75, 0.3–7.1)
IPSS (n = 51)	25.41 (5.48, 13–33)
Q_{max}, mL/s† (n = 51)	8.04 (2.39, 3.0–12.0)
PVR, mL (n = 51)	88.08 (70.40, 0–244)
SHIM‡ (n = 42)	15.38 (7.86, 1–25)
MSHQ-EjD function‡ (n = 42)	8.79 (3.01, 1–15)
MSHQ-EjD bother‡ (n = 42)	2.17 (1.71, 0–5)
Anaesthesia time, min (n = 51)	51.25 (15.65, 29–110)
Number of implants(n = 51)	4.5 (1.5, 2–8)
Time to discharge, days (n = 51)	0.12 (0.38, 0–2)
Return to preoperative activity level, days (n = 51)	2.59 (4.40, 0–28)

**Two subjects have been excluded for protocol deviations. †If voided volume <125 mL, Q_{max} data is excluded. ‡SHIM, MSHQ-EjD function, MSHQ-EjD bother, data is excluded if 'sexual activity' response was 'no'.*

Fig. 3 Mean IPSS and Q_{max} from baseline through the blinded sham period and 24-month period after crossover PUL treatment.



reduced by 9.6 points and Q_{max} increased by 4.2 mL/s compared to pre-sham baseline (Table 2). QoL and BPHII were significantly improved by 1 month after the PUL procedure and at 24 months remained improved with a 40% and 54% respective change from baseline ($P < 0.001$). The Q_{max} showed a stepwise improvement, increasing from a mean (SD) of 8.1 (2.5) to 10.0 (4.6) mL/s at 3 months after the sham procedure. The Q_{max} further increased to a mean (SD) of 12.0 (5.8) mL/s at 3 months, 12.1 (5.3) mL/s at 12 months, and 12.2 (5.8) mL/s at 24 months after PUL.

Sexual function was preserved with no reported incidences of new onset, sustained erectile dysfunction or anejaculation. The sexual function questionnaire-based average measures showed an improvement trend after PUL, as assessed by the Sexual Health in Men (SHIM) score and Male Sexual Health Questionnaire for Ejaculatory Dysfunction (MSHQ-EjD) function and bother scores; ejaculatory bother showed a significant improvement over the 24-month follow-up ($P <$ 0.005, Table 2).

Adverse events were in general mild to moderate and typically resolved by 0.5 month. At the time of the procedure, 241 devices were successfully implanted into the 53 crossover patients. Of these, 10 devices (4%) were later found to have been inadvertently deployed such that part of the implant was exposed to urine within the bladder and developed surface encrustation. The possibility of misplaced implants has been described. At the end of each procedure, it is important to interrogate the bladder neck cystoscopically with a rigid cystoscope or with a flexible cystoscope, if better visualisation is needed, in order to remove any implant that protrudes into the bladder vesicle. Over the 24-month follow-up period, three patents had their encrusted devices removed, and one additional patient underwent removal of a non-encrusted device prophylactically. In each case LUTS either remained stable or improved after removal.

A secondary analysis was conducted in which each IPSS element and subgroup was evaluated individually (Table 3). Each element showed a significant average improvement over baseline from 1 month through to 24 months ($P < 0.005$). Further, when compared directly to the sham response, each element of the voiding domain (incomplete emptying, intermittency, weak stream, and hesitancy) was significantly better after PUL compared to the sham procedure, with significant differences evidenced in each parameter by 1 month. Storage symptoms (frequency, urgency, and nocturia) followed, with each parameter achieving statistical significance over sham response by 3 months.

Discussion

The PUL procedure is a minimally invasive approach to treating LUTS secondary to BPH that relieves obstruction without cutting, heating or removing prostate tissue. The therapy has been found to offer rapid, sustained results without the negative consequences of more invasive methods. Patients in the present study returned to preoperative activity on average in 3 days and experienced relatively little postoperative morbidity. The efficiencies offered by this minimally invasive approach to LUTS/BPH have been shown to lower healthcare costs when compared to standard surgical treatment, an important concern due to the ageing population [25].

The sham effect in this and other studies is substantial. It is probably a result of the placebo effect, dilatation from rigid cystoscopy, and regression to the mean. As noted by Welliver et al. [26], studies of sham-controlled interventions show considerable improvement in symptom scores (29%) and Q_{max} (1.3 mL/s) after sham procedures. The present

Table 2 Outcome measures in patients after the sham procedure and after crossover to PUL. All follow-up parameters are presented as paired data with pre-sham baseline values.

Assessment	Sham follow-up, mean (SD)			Follow-up after crossover, mean (SD)					
	0.5 month	1 month	3 months	0.5 month	1 month	3 months	6 months	12 months	24 months
IPSS									
N (paired)	50[1]	51	51	51	51	50	51	49	42
Baseline	25.34 (5.51)	25.41 (5.48)	25.41 (5.48)	25.41 (5.48)	25.41 (5.48)	25.44 (5.53)	25.41 (5.48)	25.49 (5.58)	24.76 (5.69)
Follow-up	18.48 (8.15)	18.14 (8.83)	20.20 (8.40)	18.92 (8.28)	12.43 (7.09)	12.32 (8.01)	13.06 (7.71)	15.22 (8.14)	15.17 (7.20)
Change	−6.86 (8.20)	−7.27 (8.01)	−5.22 (7.66)	−6.49 (7.88)	−12.98 (7.39)	−13.12 (7.34)	−12.35 (7.91)	−10.27 (7.82)	−9.60 (8.48)
% change	−25.6 (32.7)	−29.1 (32.9)	−19.8 (32.6)	−24.6 (33.0)	−50.9 (27.1)	−52.7 (27.9)	−48.2 (30.5)	−40.2 (31.6)	−35.5 (38.2)
P value	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
$Q_{max,\ mL/s}$									
N (paired)			43			42		43	36
Baseline			8.09 (2.46)			7.95 (2.45)		8.09 (2.50)	8.00 (2.55)
Follow-up			10.02 (4.61)			11.95 (5.79)		12.07 (5.28)	12.18 (5.76)
Change			1.93 (5.16)			4.00 (6.53)		3.98 (5.57)	4.18 (6.50)
% change			42.9 (141.0)			76.0 (162.1)		69.0 (134.6)	77.2 (146.6)
P value			0.005			<0.001		<0.001	<0.001
BPHII									
N (paired)	51	51	51	51	51	50	51	49	42
Baseline	7.33 (3.10)	7.33 (3.10)	7.33 (3.10)	7.33 (3.10)	7.33 (3.10)	7.32 (3.13	7.33 (3.10)	7.43 (3.06)	7.12 (3.04
Follow-up	5.20 (3.05)	4.37 (2.92)	5.33 (3.24)	6.63 (3.25)	3.24 (3.09)	2.94 (2.94	2.84 (2.51)	3.43 (2.84)	3.19 (2.76
Change	−2.14 (2.92)	−2.96 (3.55)	−2.00 (3.36)	−0.71 (3.78)	−4.10 (3.61)	−4.38 (3.31	−4.49 (3.23)	−4.00 (3.37)	−3.93 (3.13
% change	−23.2 (50.0)	−31.8 (52.8)	−16.7 (59.5)	4.1 (70.3)	−50.9 (55.7)	−58.2 (40.9)	−59.6 (38.0)	−51.9 (40.2)	−53.8 (36.9)
P value	<0.001	<0.001	<0.001	0.178	<0.001	<0.001	<0.001	<0.001	<0.001
QoL									
N (paired)	50[1]	51	51	51	51	50	51	49	42
Baseline	4.80 (1.09)	4.80 (1.08)	4.80 (1.08)	4.80 (1.08)	4.80 (1.08)	4.78 (1.07)	4.80 (1.08)	4.78 (1.09)	4.64 (1.10
Follow-up	3.60 (1.63)	3.63 (1.66)	3.92 (1.59)	3.43 (1.63)	2.35 (1.49)	2.18 (1.53)	2.45 (1.43)	2.73 (1.68)	2.64 (1.50
Change	−1.20 (1.55)	−1.18 (1.53)	−0.88 (1.44)	−1.37 (1.67)	−2.45 (1.63)	−2.60 (1.63)	−2.35 (1.60)	−2.04 (1.79)	−2.00 (1.77
% change	−24.6 (34.4)	−24.2 (33.1)	−17.5 (30.5)	−26.5 (35.7)	−49.6 (30.7)	−53.4 (34.0)	−47.4 (32.5)	−40.3 (44.9)	−40.0 (36.7)
P value	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
PVR, mL									
N (paired)			50			50		48	42
Baseline			85.34 (68.32)			89.26 (70.61)		87.98 (71.80)	86.55 (72.71)
Follow-up			66.24 (65.01)			52.95 (74.41)		56.74 (58.66)	79.23 (69.11)
Change			−19.10 (66.32)			−36.31 (87.24)		−31.24 (81.03)	−7.32 (74.56)
% change			−8.4 (83.5)			20.0 (257.2)		16.6 (176.3)	28.4 (142.8)
P value			0.024			0.003		0.004	0.316
SHIM									
N (paired)		39	38		34	37	38	34	31
Baseline		15.74 (7.72)	16.03 (7.40)		15.65 (7.85)	16.46 (7.26)	16.05 (7.56)	17.12 (6.79)	16.29 (7.93)
Follow-up		16.21 (8.02)	16.97 (7.19)		16.15 (8.08)	16.51 (8.17)	16.55 (7.68)	17.79 (6.68)	17.06 (8.43)
Change		0.46 (3.09)	0.95 (4.31)		0.50 (6.27)	0.05 (6.29)	0.50 (5.68)	0.68 (4.73)	0.77 (6.36)
% change		12.0 (42.9)	22.5 (62.0)		23.2 (67.8)	11.4 (48.6)	20.2 (77.3)	17.4 (79.7)	17.0 (63.7)
P value		0.346	0.172		0.990	0.940	0.525	0.386	0.680
MSHQ-EjD Function									
N (paired)		39	39		34	37	38	34	31
Baseline		8.82 (3.07)	8.72 (2.92)		8.71 (3.16)	8.86 (3.16)	8.82 (3.12)	8.88 (3.26)	8.94 (3.12)
Follow-up		10.69 (2.97)	10.77 (3.26)		11.56 (3.16)	11.19 (3.37)	11.11 (2.88)	10.94 (2.91)	10.65 (3.01)
Change		1.87 (2.62)	2.05 (2.75)		2.85 (2.55)	2.32 (3.14)	2.29 (2.63)	2.06 (2.85)	1.71 (2.78)
% change		41.2 (113.5)	42.5 (114.6)		52.8 (103.2)	48.1 (119.3)	47.7 (114.8)	49.7 (137.3)	40.6 (110.4)
P value		<0.001	<0.001		<0.001	<0.001	<0.001	<0.001	<0.001

Table 2 (continued)

Assessment	Sham follow-up, mean (SD)			Follow-up after crossover, mean (SD)					
	0.5 month	1 month	3 months	0.5 month	1 month	3 months	6 months	12 months	24 months
MSHQ-EjD Bother									
N (paired)	39	39		34	36	38	34	31	
Baseline	2.23 (1.72)	2.23 (1.72)		2.24 (1.76)	2.14 (1.76)	2.13 (1.73)	2.09 (1.78	2.13 (1.73	
Follow-up	1.38 (1.55)	1.36 (1.65		1.12 (1.59)	1.11 (1.56)	1.05 (1.27	1.06 (1.39	1.13 (1.52	
Change	−0.85 (1.37)	−0.87 (1.63		−1.12 (1.47)	−1.03 (1.42)	−1.08 (1.76	−1.03 (1.53	−1.00 (1.65	
% change	−30.9 (61.3)	−41.7 (66.0)		−52.1 (45.2)	−51.1% (53.8)	−55.7 (50.0)	−40.1 (66.6)	−50.0 (50.2)	
P value	<0.001	0.002		<0.001	<0.001	<0.001	<0.001	0.001	

crossover study provides the unique opportunity to analyse the response to the sham procedure of individual and combined domains of the IPSS; we are not aware of another BPH surgery study in which men were allowed to crossover and serve as their own control. Specifically, it shows that irritative and obstructive domains initially improve after sham from dilatation with a rigid cystoscope, but the obstructive response diminishes rapidly. This stands in contrast to the response after de-obstruction with the PUL procedure, where obstructive symptoms improve through 3 months and then remain stable out to 24 months. Considered further, when individual aspects of the IPSS are evaluated, each symptom is significantly better after PUL compared to sham by 3 months, as the effect of dilatation and placebo are severely diminished by that time. The present results highlight the ability of PUL to sustainably de-obstruct the urethra and achieve long-term therapeutic results, an achievement that minimally invasive injectable therapies have struggled to achieve [27].

In the present crossover study, there were no reported incidences of new onset, sustained erectile or ejaculatory dysfunction. Erectile function, as assessed by the SHIM score, remained stable throughout follow-up. Ejaculatory function as assessed by the MSHQ-EjD was also maintained, with a significant improvement noted at every follow-up interval. Similarly, the bother associated with ejaculation was significantly improved throughout follow-up (Table 2). The potential for iatrogenic sexual dysfunction probably influences a patient's decision making concerning surgical intervention and may be underappreciated by treating urologists [28]. In addition to the consideration of erectile function, the preservation of ejaculatory function is an aspect of LUTS/BPH therapy that affects the QoL of men of all ages and should be considered when counselling patients [29]. For those patients who are concerned with their sexual function, the PUL procedure appears to be associated with minimal morbidity in terms of both erection and ejaculation.

The results of the present study corroborate the results of previously published studies, in that the UroLift system has been consistently shown to rapidly and durably improve symptoms in patients with LUTS secondary to BPH [13–24]. In the Roehrborn et al. [15] randomised pivotal study of 140 patients and in the Chin et al. [14] first-in-man study of 64 patients, the 24-months IPSS improvement was 9.2 points, similar to the 9.6 point change reported in the present study. Despite differences in study design and other factors, the results after the PUL procedure appear repeatable, consistent, and durable. Limitations of the present study include modest enrolment and follow-up duration of 24 months. The inability to blind the crossover PUL procedure may also be a limitation, although crossover results closely mimic those of the blinded group comparisons [15,16].

Table 3 Crossover vs sham procedure response of paired subjects to individual IPSS questions.

Test/procedure	Measure	0.5 month		1 month		3 months	
		Sham	Crossover	Sham	Crossover	Sham	Crossover
IPSS Q1 – emptying	*N* (paired)	50	50	51	51	50	50
	Mean (SD)						
	Baseline	4.1 (1.1)	4.1 (1.1)	4.1 (1.0)	4.1 (1.0)	4.1 (1.0)	4.1 (1.0)
	Follow-up	2.7 (1.5)	2.8 (1.7)	2.7 (1.6)	1.7 (1.4)	3.2 (1.6)	1.8 (1.7)
	Change-	−1.4 (1.5)	−1.2 (1.8)	−1.4 (1.6)	−2.4 (1.7)	−0.9 (1.8)	−2.3 (1.9)
	Change (sham–crossover)	−0.2		1.0		1.4	
	P value	0.530		<0.001		<0.001	
IPSS Q2 – frequency	*N* (paired)	50	50	51	51	50	50
	Mean (SD)						
	Baseline	4.0 (1.1)	4.0 (1.1)	4.0 (1.1)	4.0 (1.1)	4.0 (1.1)	4.0 (1.1)
	Follow-up	3.2 (1.4)	3.2 (1.5)	3.2 (1.5)	2.1 (1.1)	3.4 (1.5)	2.2 (1.4)
	Change	−0.8 (1.4)	−0.8 (1.6)	−0.8 (1.5)	−1.9 (1.4)	−0.6 (1.5)	−1.8 (1.5)
	Change (sham–crossover)	−0.0		1.1		1.1	
	P value	0.867		<0.001		<0.001	
IPSS Q3 – intermittency	*N* (paired)	50	50	51	51	50	50
	Mean (SD)						
	Baseline	3.9 (1.3)	3.9 (1.3)	3.9 (1.3)	3.9 (1.3)	3.9 (1.3)	3.9 (1.3)
	Follow-up	2.6 (1.5)	2.6 (1.7)	2.6 (1.6)	1.6 (1.5)	3.0 (1.6)	1.8 (1.5)
	Change	−1.2 (1.6)	−1.2 (1.7)	−1.3 (1.5)	−2.3 (1.6)	−0.9 (1.5)	−2.1 (1.5)
	Change (sham–crossover)	0.0		1.0		1.2	
	P value	1.000		<0.001		<0.001	
IPSS Q4 – urgency	*N* (paired)	50	50	51	51	50	50
	Mean (SD)						
	Baseline	3.3 (1.5)	3.3 (1.5)	3.3 (1.5)	3.3 (1.5)	3.3 (1.6)	3.3 (1.6)
	Follow-up	2.5 (1.6)	3.1 (1.5)	2.4 (1.6)	2.2 (1.6)	2.8 (1.6)	1.9 (1.6)
	Change	−0.8 (1.7)	−0.2 (2.0)	−0.9 (1.7)	−1.1 (1.8)	−0.5 (1.6)	−1.4 (1.6)
	Change (sham–crossover)	−0.6		0.2		0.9	
	P value	0.011		0.406		<0.001	
IPSS Q5 – weak stream	*N* (paired)	50	50	51	51	50	50
	Mean (SD):						
	Baseline	4.2 (0.9)	4.2 (0.9)	4.2 (0.9)	4.2 (0.9)	4.2 (0.9)	4.2 (0.9)
	Follow-up	3.1 (1.6)	2.6 (1.8)	3.0 (1.6)	1.7 (1.4)	3.3 (1.6)	1.7 (1.4)
	Change	−1.1 (1.6)	−1.6 (1.7)	−1.2 (1.5)	−2.5 (1.5)	−1.0 (1.6)	−2.5 (1.4)
	Change (sham–crossover)	0.5		1.3		1.5	
	P value	0.075		<0.001		<0.001	
IPSS Q6 – hesitancy	*N* (paired)	50	50	51	51	50	50
	Mean (SD):						
	Baseline	2.8 (1.6)	2.8 (1.6)	2.9 (1.6)	2.9 (1.6)	2.9 (1.6)	2.9 (1.6)
	Follow-up	1.9 (1.7)	1.7 (1.7)	1.9 (1.6)	1.0 (1.2)	2.2 (1.7)	0.9 (1.3)
	Change	−0.9 (1.9)	−1.1 (1.8)	−1.0 (1.9)	−1.9 (1.8)	−0.6 (1.9)	−1.9 (1.7)
	Change (sham–crossover)	0.2		0.9		1.3	
	P value	0.533		<0.001		<0.001	
IPSS Q7 – octuria	*N* (paired)	50	50	51	51	50	50
	Mean (SD)						
	Baseline	3.1 (1.4)	3.1 (1.4)	3.1 (1.3)	3.1 (1.3)	3.1 (1.3)	3.1 (1.3)
	Follow-up	2.5 (1.5)	2.6 (1.3)	2.4 (1.5)	2.1 (1.3)	2.6 (1.4)	2.0 (1.3)
	Change	−0.5 (1.3)	−0.5 (1.1)	−0.7 (1.3)	−1.0 (1.1)	−0.5 (1.1)	−1.1 (1.2)
	Change (sham–crossover)	−0.0		0.3		0.6	
	P value	0.911		0.164		<0.001	
Storage/irritative	*N* (paired)	50	50	51	51	50	50
	Mean (SD)						
	Baseline	10.4 (2.9)	10.4 (2.9)	10.4 (2.9)	10.4 (2.9)	10.4 (2.9)	10.4 (2.9)
	Follow-up	8.2 (3.6)	8.9 (3.2)	8.0 (3.9)	6.4 (3.0)	8.7 (3.7)	6.1 (3.5)
	Change	−2.2 (3.5)	−1.5 (3.6)	−2.4 (3.5)	−4.0 (3.1)	−1.6 (3.2)	−4.3 (3.2)
	Change (sham–crossover)	−0.7		1.6		2.7	
	P value	0.181		0.003		<0.001	
Voiding/obstructive	*N* (paired)	50	50	51	51	50	50
	Mean (SD)						
	Baseline	15.0 (3.4)	15.0 (3.4)	15.0 (3.5)	15.0 (3.5)	15.1 (3.5)	15.1 (3.5)
	Follow-up	10.3 (5.4)	9.8 (5.7)	10.1 (5.6)	6.0 (4.9)	11.6 (5.4)	6.2 (5.0)
	Change	−4.7 (5.4)	−5.2 (5.3)	−4.9 (5.1)	−9.0 (5.1)	−3.4 (5.1)	−8.8 (4.9)
	Change (sham–crossover)	0.5		4.1		5.4	
	P value	0.532		<0.001		<0.001	

Conclusions

The PUL procedure is associated with rapid symptom relief, increased urinary flow rate and QoL improvement in a sham procedure crossover study. These improvements remain stable over 24 months. Patients can quickly return to normal activity and experience minimal adverse effects. Furthermore, PUL is associated with preservation of sexual function, an attribute uncommon among BPH LUTS therapies.

Acknowledgements

We would like to thank our staff and research coordinators for their help in collecting this data. Further, we would like to acknowledge the contributions of the clinical events committee members Rodney Anderson, Kyle Anderson and Rajesh Shingal. We would also like to thank Theodore Lamson, PhD, Jacqueline Nerney Welch, MD PhD, and the team at NeoTract, Inc. for their organisation and support in the preparation of this manuscript.

Conflicts of Interest

Funding: unrestricted research grant from NeoTract Inc. Pleasanton, CA, USA.

References

1 **Lepor H.** Pathophysiology of benign prostatic hyperplasia in the aging male population. *Rev Urol* 2005; 7(Suppl. 4): S3–12

2 **van Exel N, Koopmanschap M, McDonnell J et al.** Medical consumption and costs during a one-year follow-up of patients with LUTS suggestive of BPH in six European countries: report of the TRIUMPH study. *Eur Urol* 2006; 49: 92–102

3 **Speakman M, Kirby R, Doyle S, Ioannou C.** Burden of male lower urinary tract symptoms (LUTS) suggestive of benign prostatic hyperplasia (BPH) – focus on the UK. *BJU Int* 2015; 115: 508–19

4 **Roehrborn C.** Current medical therapies for men with lower urinary tract symptoms and benign prostatic hyperplasia: achievements and limitations. *Rev Urol* 2008; 10: 14–25

5 **Verhamme K, Dieleman J, Bleumink G, Bosch J, Stricker B, Sturkenboom M.** Treatment strategies, patterns of drug use and treatment discontinuation in men with LUTS suggestive of benign prostatic hyperplasia: the Triumph project. *Eur Urol* 2003; 44: 539–45

6 **Roehrborn C, McConnell J, Barry M et al.** *American Urological Association Guideline: Management of Benign Prostatic Hyperplasia (BPH).* American Urological Association Education and Research, Inc., 2003. Available at: https://www.auanet.org/education/guidelines/benign-prostatic-hyperplasia.cfm. Accessed October 2016

7 **Bachmann A, Tubaro A, Barber N et al.** 180-W XPS GreenLight laser vaporization versus transurethral resection of the prostate for the treatment of benign prostatic obstruction: 6-month safety and efficacy results of a European multicentre randomised trial—the GOLIATH study. *Eur Urol* 2014; 65: 931–42

8 **Wroclawski ML, Carneiro A, Amarante RD et al.** 'Button type' bipolar plasma vaporisation of the prostate compared with standard transurethral resection: a systematic review and meta-analysis of short-term outcome studies. *BJU Int* 2016; 117: 662–8

9 **Wagrell L, Schelin S, Nordling J et al.** Feedback microwave thermotherapy versus TURP for clinical BPH – a randomized controlled multicenter study. *Urology* 2002; 60: 292–9

10 **Hill B, Belvill W, Bruskewitz R et al.** Transurethral needle ablation versus transurethral resection of the prostate for the treatment of symptomatic benign prostatic hyperplasia: 5-year results of a prospective, randomized, multicenter clinical trial. *J Urol* 2004; 171: 2336–40

11 **Bouza C, Lopez T, Magro A, Navalpotro L, Amate J.** Systematic review and meta-analysis of transurethral needle ablation in symptomatic benign prostatic hyperplasia. *BMC Urology* 2006; 6: 14

12 **Dixon CM, Rijo CE, Mynderse LA, Larson TR.** Transurethral convective water vapor as a treatment for lower urinary tract symptomatology due to benign prostatic hyperplasia using the Rezum system: evaluation of acute ablation capabilities in the human prostate. *Res Rep Urol* 2015; 7: 13–18

13 **Woo HH, Chin PT, McNicholas TA et al.** Safety and feasibility of the prostatic urethral lift: A novel, minimally invasive treatment for lower urinary tract symptoms (LUTS) secondary to benign prostatic hyperplasia (BPH). *BJU Int* 2011; 108: 82–8

14 **Chin P, Bolton D, Jack D et al.** Prostatic urethral lift: two-year results after treatment for lower urinary tract symptoms secondary to benign prostatic hyperplasia. *Urology* 2012; 79: 5–11

15 **Roehrborn C, Gange S, Shore N et al.** Multi-center randomized controlled blinded study of the Prostatic Urethral Lift for the treatment of LUTS associated with prostate enlargement due to BPH: the LIFT study. *J Urol* 2013; 190: 2161–7

16 **Cantwell A, Bogache W, Richardson S et al.** Multi-center prospective crossover study of the Prostatic Urethral Lift for the treatment of LUTS secondary to BPH. *BJU Int* 2014; 113: 615–22

17 **Barkin J, Giddens J, Incze P et al.** UroLift system for relief of prostate obstruction under local anesthesia. *Can J Urol* 2012; 19: 6217–22

18 **Shore N, Freedman S, Gange S et al.** Prospective multi-center study elucidating patient experience after prostatic urethral lift. *Can J Urol* 2014; 21: 7094–101

19 **McNicholas T, Woo H, Chin P et al.** Minimally invasive Prostatic Urethral Lift: surgical technique and multinational experience. *Eur Urol* 2013; 64: 292–9

20 **Roehrborn C, Rukstalis D, Barkin J et al.** Three year results of the prostatic urethral L.I.F.T. study. *Can J Urol* 2015; 22: 7772–82

21 **Roehrborn C, Gange S, Shore N et al.** Durability of the Prostatic Urethral Lift: 2-year results of the L.I.F.T. study. *Urol Pract* 2015; 2: 26–32

22 **Sonksen J, Barber N, Speakman M et al.** Prospective, randomized, multinational study of the prostatic urethral lift versus transurethral resection of the prostate: 12-month results of the BPH6 Study. *Eur Urol* 2015; 68: 643–52

23 **McVary K, Gange S, Shore N et al.** Treatment of LUTS secondary to BPH while preserving sexual function: randomized controlled study of Prostatic Urethral Lift. *J Sex Med* 2014; 11: 279–87

24 **Woo H, Bolton D, Laborde E et al.** Preservation of sexual function with the Prostatic Urethral Lift: a novel treatment for lower urinary tract symptoms secondary to benign prostatic hyperplasia. *J Sex Med* 2012; 9: 568–75

25 **National Institute for Health and Care Excellence (NICE).** *UroLift for Treating Lower Urinary Tract Symptoms of Benign Prostatic Hyperplasia. Medical Technologies Guidance (MTG26).* London: NICE, 2015. Available at: https://www.nice.org.uk/guidance/mtg26?unlid. Accessed October 2016

26 **Welliver C, Kottwitz M, Feustel P, McVary K.** Clinically and statistically significant changes seen in sham surgery arms of randomized, controlled benign prostatic hyperplasia surgery trials. *J Urol* 2015; 193(4S): e93

27 **Magistro G, Stief C, Gratzke C.** New intraprostatic injectables and prostatic urethral life for male LUTS. *Nat. Rev. Urol* 2015; 12: 461–71

28 **Becher E, McVary K.** Surgical procedures for BPH/LUTS: Impact on Male Sexual Health. *Sex Med Rev* 2014; 2: 47–55

29 **Marra G, Sturch P, Oderda M, Tabatabaei S, Muir G, Gontero P.** Systematic review of lower urinary tract symptoms/benign prostatic hyperplasia surgical treatments on men's ejaculatory function: Time for a bespoke approach? *Int J Urol* 2016; 23: 22–35

Correspondence: Damien M. Bolton, Department of Surgery, Austin and Repatriation Hospitals Medical Centre, University of Melbourne, 5/210 Burgundy Street, Heidelberg, Vic. 3084, Australia.

e-mail: damienbolton@gmail.com

Abbreviations: BPHII, BPH Impact Index; MSHQ-EjD, Male Sexual Health Questionnaire for Ejaculatory Dysfunction; PUL, prostatic urethral lift; PVR, post-void residual volume; Q_{max}, maximum urinary flow rate; QoL, quality of life; SHIM, Sexual Health in Men.