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Title: Two Year Durability after Crossover to the Prostatic Urethral Lift from Randomized, Blinded Sham

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Abstract:

Purpose: To evaluate the 2 year 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.

Methods: Fifty-three patients underwent sham procedure as part of the blinded, randomized L.I.F.T. study at 19 centers and elected to enroll 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 sham and then 2 years after crossover PUL with assessments of urinary symptom relief, quality of life, urinary flow rate, sexual function, and adverse events.

Results: At 2 years after crossover PUL, International Prostate Symptom Score (IPSS), quality of life, BPH Impact Index, and peak 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 sham 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 1 patient required additional PUL implants within the two year period. There were no reported instances of de novo, sustained erectile or ejaculatory dysfunction.

Conclusions: PUL procedure is associated with rapid symptom relief, increased urinary flow rate and quality of life improvement that remain stable over two years. Morbidity is low and sexual function is preserved.

Keywords:

Benign Prostatic Hyperplasia (BPH)

Lower urinary tract symptoms (LUTS)

Minimally invasive surgical therapy (MIST)

Sexual function

Introduction

Lower urinary tract symptoms (LUTS) are some of the most common medical complaints experienced by men as they age. It is believed that by the eighth decade of life nearly all men will develop histological evidence of benign prostatic hyperplasia (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 health care 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 6 European countries [2]. Further, these associated expenditures are likely to increase due to the aging 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 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 transurethral resection of the prostate (TURP), tissue vaporisation or thermal heating procedures. TURP, considered the gold standard surgery, offers 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 vapor ablation are associated with fewer serious adverse events than TURP, but are associated with a long period of irritative symptoms and urinary catheterization. [9,10, 11,12]

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 demonstrated 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, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24]. As reported by Roehrborn et al. in 2013, the pivotal study for regulatory clearance enrolled 204 patients in a 2:1 randomized, controlled trial comparing PUL procedure to control sham. For those subjects in the control arm who elected to pursue crossover PUL, the two year durability is presented here. In addition, we report the first detailed analysis of change in individual lower urinary tract symptoms. IPSS element improvements are compared to those seen after blinded, self-controlled sham procedure over a three month period.

Patients and Methods

While enrolled in a randomized, blinded study at 19 centers in the USA, Canada, and Australia, 53 subjects with moderate to severe LUTS underwent a blinded sham procedure that involved rigid cystoscopy and mimicked PUL sounds [15]. After the primary endpoint comparison at 3 months, the patients were unblinded and if eligible, were offered enrollment in a crossover study during which they received PUL treatment and were followed to 2 years.

Patients were eligible for the study if they were aged > 50 years, had an IPSS of ≥ 13, maximum urinary flow rate (Qmax) ≤ 12 mL/s on a voided volume of 125 mL, prostate volume between 30 and 80 mL, and provided informed consent. Exclusion criteria included prior surgical BPH treatment, obstructive median lobe, current urinary retention, post-void residual volume (PVR) ≥ 250 mL, active urinary tract infection, PSA level > 10 ng/mL unless negative biopsy, cystolithiasis within 3 months, bacterial prostatitis within 1 year, and a history of prostate or bladder cancer. Subjects were required to wash out of anticoagulants, 5-alpha-reductase inhibitors, and alpha-blockers prior to the PUL procedure if they were not medication naïve. The study protocol was approved by the regulating authorities (US 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.

Prostatic Urethral Lift 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 (Figure 1). The implants are sized in situ, dependent on the size of the lateral lobe at the deployment location. Typically, 4-6 implants are delivered to create a continuous anterior channel.

Study Endpoints and Statistical Methods

Subjects underwent sham procedure and were assessed at baseline through 3 months via IPSS, Qmax, IPSS quality of life question, BPH Impact Index (BPH II), PVR and sexual function questionnaires by an assessor blinded to enrollment arm. After 3 months, subjects were offered PUL or other intervention if

symptoms persisted. Those subjects who elected PUL treatment were assessed prior to crossover PUL, and at 2 weeks, 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 1 year follow up to assess for implant encrustation.

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) and R (The R Foundation, Vienna, Austria). P value < 0.05 was considered to indicate statistical significance.

Results

During a blinded, randomized study of PUL vs. sham, 66 patients underwent control sham procedure between February and December 2011. After 3 months, all subjects were unblinded. Of the 66 sham patients, 53 subjects (80%) elected to undergo PUL treatment, entering the crossover study. Two subjects were later excluded for protocol deviations associated with data collection methods, leaving 51 patients in the crossover cohort for analysis (Figure 2, Table 1). During the 2 year follow up period, 4 subjects (8%) progressed to TURP and 1 subject (2%) required additional PUL implants. No patients were taking an alpha blocker or 5-alpha-reductase inhibitor for LUTS at the time of 2 year follow up. Three subjects withdrew from the study and 1 subject missed the 2 year visit, leaving 42 subjects available for per protocol evaluation at 2 years.

Figure 3 shows overall mean IPSS and peak urinary flow improvement over time, indicating that maximum sham symptom improvement occurred by 1 month and then diminished over time. By 3 to 6 months after sham, IPSS returned to near pre-sham baseline, while Qmax diminished but remained elevated over baseline. After crossover PUL treatment, IPSS improved significantly within 2 weeks, and both IPSS and Qmax achieved peak improvement by 3 months. Both IPSS and Qmax showed significant and durable improvement through 2 years with IPSS reduced 9.6 points and Qmax increased 4.2 mL/s compared to pre-sham baseline (Table 2). Quality of life and BPH Impact Index were significantly improved by 1 month after PUL procedure and at 2 years remained improved with 40% and 54% respective change from baseline ($p < 0.001$). Peak flow rate showed stepwise improvement, increasing

from 8.1 ± 2.5 to 10.0 ± 4.6 at 3 months after sham. The flow rate further increased to 12.0 ± 5.8 at 3 months, 12.1 ± 5.3 at 1 year and 12.2 ± 5.8 at 2 years.

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

Adverse events were in general mild to moderate and typically resolved by 2 weeks. At the time of the procedure, 241 devices were successfully implanted into the 53 crossover subjects. 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 visualization is needed, in order to remove any implant that protrudes into the bladder vesicle. Over the 2 year follow up period, **b** 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 demonstrated significant average improvement over baseline from 1 month through 2 years ($p<0.005$). 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 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 Prostatic Urethral Lift 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 modalities. Patients in this study returned to pre-operative activity on average in 3 days and experienced relatively little post-operative 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 likely a result of the placebo effect, dilation from rigid cystoscopy, and regression to the mean. As noted by Welliver et al., studies of sham controlled interventions demonstrate considerable improvement in symptom scores (29%) and peak urinary flow rate (1.3 ml/s) after sham procedure [26]. This crossover study provides the unique opportunity to analyze the response to sham 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 demonstrates that irritative and obstructive domains initially improve after sham from dilation 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 2 years. 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 dilation and placebo are severely diminished by that time. These 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 demonstrate [27].

In this 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 likely 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 quality of life of men of all ages and should be considered when counseling patients [29]. For those subjects 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 this study corroborate the results of previously published studies in that the Urolift is consistently shown to rapidly and durably improve symptoms in subjects suffering from lower urinary tract symptoms secondary to BPH [13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24]. In the Roehrborn et al. randomized pivotal study of 140 subjects and in the Chin et al. first-in-man study of 64 subjects, the 2

year IPSS improvement was 9.2 points, similar to the 9.6 point change reported here [14, 15]. Despite differences in study design and other factors, the results after the PUL procedure appear repeatable, consistent, and durable. Limitations of this study include modest enrollment and duration to two years. The inability to blind the crossover PUL procedure may also be a limitation, though crossover results closely mimic those of the blinded group comparisons [15, 16].

Conclusions

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

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Table 1: Baseline characteristics and procedure details of treated patients

Characteristics	Crossover (N=51) [1]
Age (years) [1]	64, 7.8 [50 - 79], (51)
Prostate volume (cc)	40.53, 9.92 [30.0 – 67.8], (51)
Prostate length (mm)	45.71, 5.50 [33.0 – 56.2], (51)
PSA	2.16, 1.75 [0.3- 7.1], (51)
IPSS	25.41, 5.48 [13 - 33], (51)
Qmax (mL/s) [† 2]	8.04, 2.39 [3.0 - 12.0], (51)

Characteristics	Crossover (N=51) [1]
Post void residual (mL)	88.08, 70.40 [0 - 244], (51)
SHIM[3]	15.38, 7.86 [1 - 25], (42)
MSHQ-EjD function[3]	8.79, 3.01 [1 - 15], (42)
MSHQ-EjD bother[3]	2.17, 1.71 [0 - 5], (42)
Anesthesia time (min)	51.25, 15.65 [29 - 110], (51)
Number of Implants	4.5, 1.5 [2 - 8], (53)
Time to discharge (days)	0.12, 0.38 [0 - 2], (51)
Return to pre-operative activity level (days)	2.59, 4.40 [0 - 28], (51)

[1] Two subjects have been excluded for protocol deviations.

[2] If voided volume < 125 ml, Qmax data is excluded.

[3] SHIM, MSHQ-EjD function, MSHQ-EjD bother, exclude data if "sexual activity" response is "no."

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

Assessment		Sham			Post Crossover					
		2 Weeks	1 Month	3 Months	2 Weeks	1 Month	3 Months	6 Months	1 Year	2 Years
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	<.0001	<.0001	<.0001	<.0001	<.0001	<.0001	<.0001	<.0001	<.0001
Qmax	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			0.0051			<.0001		<.0001	0.0003
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

	Assessment	Sham			Post Crossover					
		2 Weeks	1 Month	3 Months	2 Weeks	1 Month	3 Months	6 Months	1 Year	2 Years
	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	<.0001	<.0001	<.0001	0.1775	<.0001	<.0001	<.0001	<.0001	<.0001
QOL	N (paired)	**50**[1]	**51**	**51**	**51**	**51**	**50**	**51**	**49**	**42**
QOL	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
QOL	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
QOL	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
QOL	% 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%
QOL	P-Value	<.0001	<.0001	<.0001	<.0001	<.0001	<.0001	<.0001	<.0001	<.0001
PVR	N (paired)			**50**			**50**		**48**	**42**
PVR	Baseline			85.34 +/-68.32			89.26 +/-70.61		87.98 +/-71.80	86.55 +/-72.71
PVR	Follow-Up			66.24 +/-65.01			52.95 +/-74.41		56.74 +/-58.66	79.23 +/-69.11
PVR	Change			-19.10 +/-66.32			-36.31 +/-87.24		-31.24 +/-81.03	-7.32 +/-74.56
PVR	% Change			-8.4% +/-83.5%			20.0% +/-257.2%		16.6% +/-176.3%	28.4% +/-142.8%
PVR	P-Value			0.0237			0.0032		0.0041	0.3159
SH IM	N (paired)		**39**	**38**		**34**	**37**	**38**	**34**	**31**

Assessment		Sham			Post Crossover					
		2 Weeks	1 Month	3 Months	2 Weeks	1 Month	3 Months	6 Months	1 Year	2 Years
	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		0.3459	0.1717		0.9903	0.9403	0.5248	0.3857	0.6803
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		<.0001	<.0001		<.0001	<.0001	<.0001	<.0001	0.0007
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%

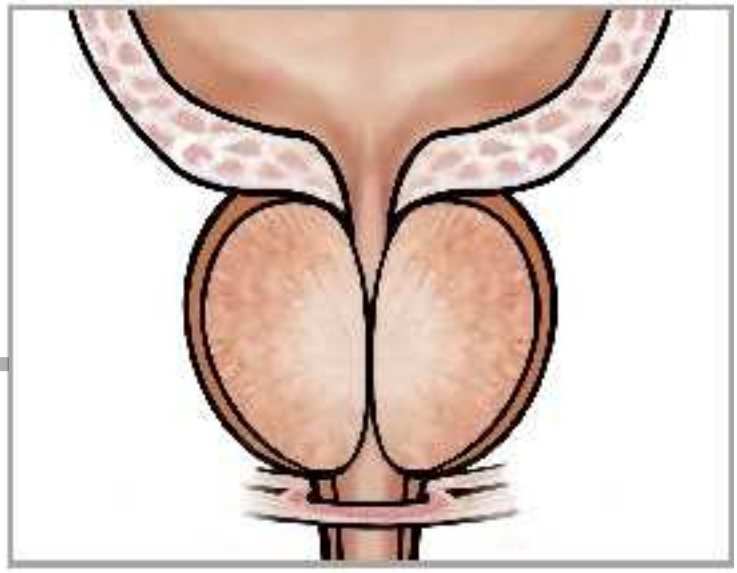
Table 3: Crossover vs. sham procedure response of paired subjects to individual IPSS questions.

		2 Weeks		1 Month		3 Months	
Test/ Procedure	**Measure**	**SHAM**	**Cross-over**	**SHAM**	**Cross-over**	**SHAM**	**Cross-over**
IPSS Q1- emptying	N (paired)	50	50	51	51	50	50
	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- mean (SD)	-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	0.5299		<.0001		<.0001	
IPSS Q2- frequency	N (paired)	50	50	51	51	50	50
	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- mean (SD)	-0.8 (1.4)	-0.8 (1.6)	-0.8 (1.5)	-1.8 (1.4)	-0.6 (1.5)	-1.8 (1.5)
	Change (SHAM - Crossover)	-0.0		1.1		1.1	
	P-value	0.8668		<.0001		<.0001	
IPSS Q3- intermittency	N (paired)	50	50	51	51	50	50
	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- mean	-1.2 (1.6)	-1.2 (1.7)	-1.3 (1.5)	-2.2 (1.6)	-0.9 (1.5)	-2.1 (1.5)

	(SD)						
	Change (SHAM - Crossover)	0.0		1.0		1.2	
	P-value	1.000		<.0001		<.0001	
IPSS Q4-urgency	N (paired)	50	50	51	51	50	50
	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- mean (SD)	-0.9 (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		0.4056		0.0001	
IPSS Q5-weak stream	N (paired)	50	50	51	51	50	50
	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- mean (SD)	-1.1 (1.6)	-1.6 (1.7)	-1.3 (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	0.0752		<.0001		<.0001	
IPSS Q6-hesitancy	N (paired)	50	50	51	51	50	50
	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- mean (SD)	-1.0 (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	0.5325		<.0001		<.0001	
IPSS Q7-nocturia	N (paired)	50	50	51	51	50	50
	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- mean (SD)	-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	0.9106		0.164		0.0008	
Storage/irritative	N (paired)	50	50	51	51	50	50
	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- mean (SD)	-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	0.1805		0.0032		<.0001	
Voiding/obstructive	N (paired)	50	50	51	51	50	50
	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- mean (SD)	-4.6 (5.4)	-5.2 (5.3)	-4.9 (5.1)	-9.0 (5.1)	-3.4 (5.1)	-8.8 (4.9)
	Change (SHAM -	0.5		4.1		5.4	

	Crossover)			



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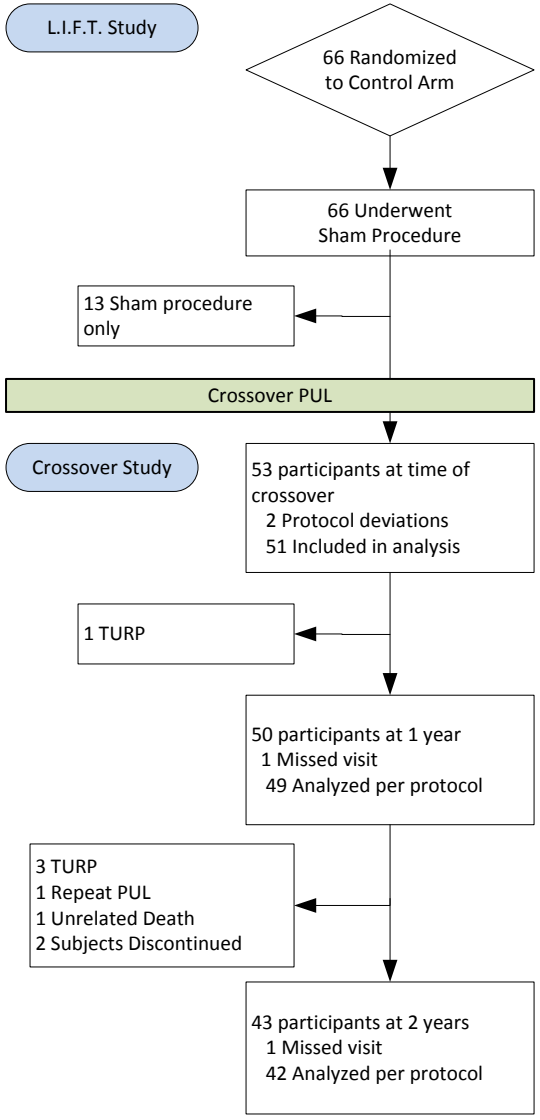

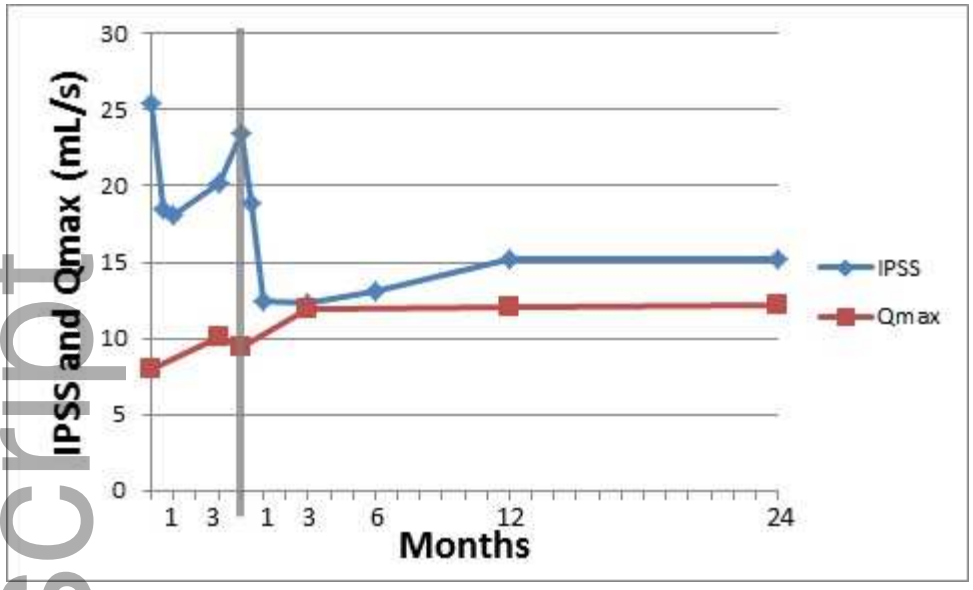

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