Received Date : 28-Sep-2016

Revised Date : 27-Oct-2016

Accepted Date : 04-Nov-2016

Article type : Original Article

Article category: Functional Urology

Prostatic Urethral Lift (PUL) vs Transurethral Resection of the Prostate (TURP): 2 Year Results of the BPH6 Prospective, Multi-Center, Randomised Study

Gratzke C*, Barber N, Speakman M, Berges R, Wetterauer U, Greene D, Sievert K-D, Chapple C, Sonksen J

*** Corresponding author**

Christian Gratzke, MD

Department of Urology

Ludwig-Maximilians-University Munich

Germany

christian.gratzke@med.uni-muenchen.de

Tel: +49 89 440072971

Fax: +49 89 440078733

Abstract:

Objectives: To compare Prostatic Urethral Lift (PUL) to Transurethral Resection of the Prostate (TURP) with regard to symptoms, recovery experience, sexual function, continence, safety, quality of life, sleep and overall patient perception.

Subjects/patients and methods: 80 patients with lower urinary tract symptoms due to benign prostatic hyperplasia (BPH) enrolled in a prospective, randomised, controlled, non-blinded study conducted at 10 European centers. The BPH6 responder endpoint assessed symptom relief, quality of recovery, erectile function preservation, ejaculatory function preservation, continence preservation, and safety. Additional evaluations of patient perspective, quality of life, and sleep were prospectively collected, analyzed, and presented here for the first time.

Results: Significant improvements in International prostate symptom score (IPSS), IPSS quality of life (QoL), BPH Impact Index (BPH II), and peak flow rate were observed in both arms through the 2 year follow up. TURP IPSS and peak flow change were superior to PUL. IPSS QoL and BPH II improvements were not statistically different. PUL resulted in superior quality of recovery, ejaculatory function preservation, and performance on the composite BPH6 index. Ejaculatory function bother scores did not demonstrate statistically significant change in either treatment arm. TURP significantly compromised continence function at 2 weeks and 3 months. Only PUL resulted in statistically significant improvement in sleep starting at the 6 month interval and continuing to the end of the study. Over the two year follow up, 6 PUL subjects (13.6%) and 2 TURP subjects (5.7%) underwent secondary treatment for return of LUTS. Most patients perceived LUTS improvement and would recommend their treatment procedure to a friend.

Conclusion: PUL was compared to TURP in a randomised, controlled study which further characterized both modalities so that care providers and patients can better understand the net benefit when selecting a treatment option.

Introduction:

As the population ages, there is a growing need to find ways for people to live longer with satisfactory quality of life, even in the midst of increasing health problems.[1] For the ageing man in particular, quality of life is challenged by two common issues: the onset of bothersome lower urinary tract symptoms (LUTS) due to benign prostatic obstruction (BPO)[2,3] and diminishing ability to maintain normal sexual activity and function.[4] Both issues are important to men, yet often the treatment of the former has adverse effects on the latter.[3,5,6]

BPO, caused by histologic benign prostatic hyperplasia (BPH), is a common condition that increases in prevalence with age and causes LUTS that take a substantial toll on quality of life, often leading to social isolation, depression, decreased productivity and poor sleep.[3] At the same time, many men desire to remain sexually active later in life. In a global survey of 13,618 middle-aged to older men across 29 countries, the percentage of men who rated sex as being very or extremely important was over 70% in several countries.[4]

Treatments for BPO offer symptomatic improvement to LUTS but their overall impact on other factors that affect quality of life must be considered.[6,7] For instance, when evaluating treatment options for BPH, issues of sexual function are an important measure of patient satisfaction with the outcome of

treatment.[7] Treatments that improve LUTS but adversely affect a patient's sexual function, may negatively affect a patient's quality of life overall with the patient viewing this as a treatment failure.[6] Iatrogenic incontinence carries a particularly negative impact on quality of life.[8] Similarly, perioperative complications and recovery time are important considerations in patient satisfaction with surgical treatment.[9]

It is with this more comprehensive view of patient satisfaction and overall improved health outcome that a new endpoint for evaluating BPH treatments was developed and previously described.[10] The BPH6 is a composite of validated instruments to assess: 1) adequate relief from LUTS, 2) high quality recovery experience, 3) maintenance of erectile function, 4) maintenance of ejaculatory function, 5) maintenance of continence, and 6) avoidance of high grade complications.

In this study, the Prostatic Urethral Lift (PUL) treatment was compared in a prospective, randomised study to transurethral resection of the prostate (TURP) using the BPH6 endpoint, its individual validated instruments, and additional health outcome measures. PUL is a minimally invasive procedure that uses small implants to compress the prostatic lobes, reducing urethral lumen obstruction without resection, ablation or other thermal injury to the prostate. PUL has been shown in numerous studies to achieve significant symptom relief with low morbidity, including uniquely reproducible preservation of sexual function.[11-15] TURP has long been considered the "gold standard" surgical treatment for maximal relief of LUTS associated with BPO and is considered standard of care. While TURP is the gold standard in maximal LUTS relief, it may not be the gold standard in overall patient satisfaction for those patients who value other aspects of their health. TURP is associated with a 20% rate of perioperative morbidity and long-term complications that include urinary incontinence (1-3%), urethral stricture (7%),transurethral resection syndrome (1.4%), bleeding requiring transfusions (2.9%), erectile dysfunction (10%) and ejaculatory dysfunction (65%).[16-19] We previously published on the 1 year primary endpoint results of this study demonstrating that PUL is superior to TURP when using this new BPH6 endpoint.[10] We now present the 2 year results of this study looking not only at the BPH6 concept, but also at the results of prospectively measured overall quality of life indicators including the Patient Global Impression of Improvement, the Short Form Health Survey utility score, and the Jenkins Sleep Score. These additional measures allow for a more complete characterization of patient experience after BPH LUTS treatment. Our goal is to provide a comprehensive comparison that allows a patient and physician to weigh important net health outcomes when choosing the best treatment option for the individual.

Subjects/patients and methods:

Study Protocol and Procedure

A prospective, randomised, controlled, non-blinded study was conducted at 10 European centers across three countries. Ethics committee approval was obtained at each site (Clinicaltrials.gov: NCT 01533038). A subject was eligible for enrollment if he was at least 50 years old and a candidate for TURP with IPSS > 12, Qmax ≤ 15 ml/s, and prostate volume ≤ 60 cc per ultrasound. Parallel 1:1 randomization was performed using permuted blocks of random sizes, stratified by study site, concealed through a password protected computer system and revealed at the time of the procedure.

The PUL procedure involves transurethrally placing small permanent implants (UroLift® System) to compress tissue, enlarge the urethral lumen and reduce obstruction.[20] Investigator experience ranged from 0 to 20 PUL procedures prior to study commencement. Each investigator had extensive prior experience with TURP and conducted TURP procedures in accordance with their own standards and practices. Subjects were followed with visits at 2 weeks, 1 month, 3 months, 6 months, 1 year and 2 years.

Endpoints & Analyses

The BPH6 primary study endpoint is a composite of 6 validated instruments that assess a subject's net health outcome at one year: International Prostate Symptom Score (IPSS), Sexual Health Inventory for Men (SHIM), Male Sexual Health Questionnaire for Ejaculatory Dysfunction (MSHQ-EjD), Incontinence Severity Index (ISI), Quality of Recovery Visual Analog Score (QoR VAS), and the Clavien-Dindo classification of adverse events. Changes from baseline in these measures were compared across treatment groups at each follow up visit using a t-test. The chi-square test or Fisher's exact test was used to test for significant differences in the BPH-6 composite and for elements of the composite. The effect of multiple testing was evaluated using the Hochberg method which controlled the family-wise error rate at 0.05 for the three families of hypotheses: tests for significant change within the TURP group, within the PUL group, and for significant difference between the TURP and PUL groups. All statistical analyses were performed using SAS version 9.3 or StatXact© (Cytel Corporation).

Several measures of quality of life and patient satisfaction were assessed throughout follow up including the Patient Global Impression of Improvement (PGI-I), the 12-item Short Form Health Survey (SF-12), and the derivative single index SF-6D utility score.[21,22] The PGI-I is a 1-item questionnaire that asks an individual subject to rate his perceived change in condition after treatment ("very much better," "much better," "a little better," "no change," "a little worse," "much worse," and "very much worse"). This measure has been used in several clinical studies worldwide and evidence of the construct validity for BPH-LUTS has been presented.[22,23,24] The SF-12 Health Survey is a widely used tool for measuring the function health and well-being of subjects that has been demonstrated to be reliable and valid in clinical applications in several countries.[21,25] It consists of 12 questions that assess for physical and emotional health. The SF-6D is a single index measure derived from the SF-12 responses and is anchored at 1 for full health and 0 for dead. The health domains captured by the SF-6D utility values are physical functioning, mental health, role limitations due to physical health and mental problems, pain, vitality, and social functioning. The calculation of SF-12 score and SF-6D utility values were performed using Health Outcomes ™ Scoring Software 4.5 (QualityMetric Incorporated).

Calculation of a Minimal Clinically Important Difference (MCID) has been established as a method of giving clinical relevance to changes in standardized measures. It is the smallest difference in a Health-Related Quality of Life (HRQOL) score that patients perceive as beneficial

in the management of their condition. The MCID is dependent on the patient's disease category and post-operative expectations. Halme et al. determined that a change of 0.0126 in SF-6D represents the MCID in this HRQOL when studying urinary incontinence, and we have further applied this MCID to LUTS.[26]

The proportion of subjects achieving the SF-6D MCID at each visit was compared between PUL and TURP using the chi-square test. The association between achieving the BPH-6 primary composite endpoint and achieving this MCID was evaluated using a logistic general estimating equation (GEE) model to account for the multiple responses recorded for subjects over time, with the BPH-6 primary endpoint as the independent variable and SF-6D MCID as the binary dependent variable. This model was used to estimate the ratio in the odds of achieving the SF-6D MCID for subjects that met the primary BPH-6 endpoint as compared to those that that did not.

The proportion of subjects perceiving improvement after treatment was assessed using the PGI-I. Majority response was tested using a chi-square test with a null hypothesis of a 50% proportion. Statistical significance in all tests was defined as p-value of 0.05 or less.

Continence was defined as having an Incontinence Severity Index (ISI) of 4 or less; a subject was considered to be incontinent whenever he reported an ISI score greater than 4.[27] As controlled by eligibility criteria (ISI≤4), all subjects were considered continent at the time of enrollment. As an assessment of how important continence preservation is to subjects, a logistic GEE regression model was used to determine whether having loss of continence was associated with statistically significant increase in the odds of have decreased quality of life. Decreased quality of life was defined as a drop in SF-6D equal to or greater than the MCID value.

The Jenkins Sleep Questionnaire was administered throughout follow up to assess for sleep disturbances.[28] This questionnaire consists of 4 items that cover 1) trouble falling asleep, 2) awakening several times per night, 3) trouble staying asleep, and 4) waking up feeling tired and worn out. Responses are rated on a 6 step Likert scale of 0 (no sleep disturbance) to 5 (sleep disturbance) with a total possible score of 0 to 20. Changes from baseline in Jenkins score for each time point were assessed for both arms of the study. The statistical significance of change from baseline within each group was assessed using a Wilcoxon Signed Rank test due to significant departure from normality and ordinal nature of the change scores.

The relationship between improvements in sleep and improvements in HRQOL were evaluated by comparing change in the Jenkins Sleep Questionnaire score from baseline with the probability of achieving the MCID for SF-6D. The change score for the Jenkins Sleep Questionnaire was used as a linear predictor of the probability of achieving SF-6D MCID using a logistic GEE model. The results are expressed as the change in odds (odds ratio) of obtaining SF-

6D MCID with each unit increase in sleep improvement. Additionally, a receiver operating characteristic (ROC) analysis was performed to identify the minimum change in sleep improvement that would best predict the achievement of SF-6D MCID. This was done by picking the sleep change score point along the ROC curve that maximizes sensitivity and specificity simultaneously, each weighted equally.

Results:

Eighty subjects were enrolled in a prospective, randomised, controlled study between February 2012 and October 2013. Significant improvements in IPSS, IPSS QoL, BPH Impact Index and peak flow rate (Qmax) were observed in both arms through 2 year follow up (Table 1). TURP IPSS change was superior to PUL at 1 and 2 years, and TURP Qmax was superior at all time points (Table 1). Quality of Life and BPH II improvements were not statistically different. Quality of recovery, as defined by at least a score of 70 on the Quality of Recovery Visual Analog Score (QoR VAS 0 to 100 scale), was superior for PUL over TURP, with 82% of PUL subjects achieving the recovery endpoint by 1 month compared to 53% for TURP ($p=0.008$). The proportion of subjects who met the BPH6 primary endpoint was found to favor PUL vs TURP (non-inferiority $p=0.0002$, superiority $p=0.006$).

Over the two year follow up, 6 PUL subjects (13.6%) and 2 TURP subjects (5.7%) underwent secondary treatment for return of LUTS. Secondary treatments included an additional PUL, intradetrusor botox, laser or TURP procedure. One PUL subject underwent removal of an implant that had been deployed too proximally such that part of the implant was exposed to the bladder and caused intermittent hematuria. Two other subjects were not included in the analysis: one TURP subject discontinued study participation after extended hospital stay for epididymitis and one PUL subject was censored from analysis for protocol deviation.

Erectile function was preserved in both arms as assessed by SHIM (Table 1), with the vast majority of patients achieving the erectile function category of the BPH6 endpoint at 2 years (98% for PUL, 94% for TURP). Ejaculatory function was superior for PUL over TURP ($p<0.001$), with TURP patients suffering from significant decline ($p<0.001$) in MSHQ-EjD function score from 1 month post procedure and onwards. This difference was further demonstrated in the BPH6 ejaculatory function category, as 100% of PUL subjects had preserved function, while 34% TURP subjects reported they “could not ejaculate” at 2 years.

The number of subjects who achieved the minimal clinically important difference (MCID) in the SF-6D utility (general health) index was compared between groups (Table 2). Both treatments achieved a clinically important improvement in HRQOL. PUL consistently delivered a higher proportion of patients achieving HRQOL improvement, but the difference was not statistically

significant. Subjects who met the BPH6 primary endpoint were significantly more likely to achieve an MCID in HRQOL with odds ratio 2.0 (p=0.02).

The majority of subjects in both treatment arms indicated perceived improvement via the Patient Global Impression of Improvement (PGI-I) question (p value for improvement <0.0001 at all visits, Figure 1), with the distribution skewed towards the "very much better" and "much better" responses. Of further interest, the number of patients in each category who achieved an MCID in HRQOL is displayed in darkest color with crosshatching at the bottom of each column, indicating those who perceived an improvement in LUTS condition often also reported a significant improvement in health related quality of life. The patients whose quality of life did not significantly change are presented with the dotted medium color. A small proportion of patients indicated by the lightest color in Figure 1 didn't complete the SF-12 questionnaire and the impacts on their quality of life are unknown. The percentage of patients who would recommend their index procedure to a friend at 2 years is 81% for the PUL arm and 82% for the TURP arm.

Continence function as assessed by average ISI score was maintained throughout follow up for the PUL group and did not demonstrate significant change from baseline at any time point (Figure 2). For the TURP group, subjects experienced a significant worsening at both 2 weeks and 3 months (Table 1, Figure 2). Loss of continence was significantly associated with a clinically important drop in HRQOL (p = 0.007). When continence was preserved, 47% of responses to the SF-12 questionnaire indicated that a positive MCID in HRQOL could be achieved. When subjects experienced a loss of continence, they were far less likely to achieve an improvement in HRQOL (9%) and were likely to experience a significant decrease in HRQOL (65%). GEE regression model indicated that subjects who became incontinent had an odds ratio of 3.25 (triple the chance) of experiencing a significant decline in HRQOL.

Although both treatment arms experienced average improvements in Jenkins sleep scores by the earliest follow up visit, only PUL provided statistically significant improvement (at 6, 12, and 24 months, Table 3). Both treatment arms showed statistically significant improvement in nocturia as measured by the IPSS question (Table 4), though TURP nocturia was worsened until 1 month. GEE regression model indicated that the odds ratio is 1.12 of achieving a significant change in HRQOL with improvement in sleep (p value <0.0001). Receiver operating characteristic curves indicate a threshold of 2 point improvement in Jenkins sleep score maximizes the specificity and sensitivity for MCID improvement in HRQOL.

Discussion:

The BPH6 study provides a prospective head-to-head comparison of PUL against TURP for outcomes that are important to patients and influence their health related quality of life. It has been long established that TURP offers maximal improvement in IPSS and Qmax, but the BPH6 study results indicate that an exclusive focus on these two goals may not result the greatest improvement in health related quality of life for patients who value other important health outcomes. Often when evaluating LUTS treatment options, quality of life improvement is assessed only by the IPSS question 8, which asks specifically and exclusively about the patient's LUTS. If a man is likely satisfied with the 43% mean IPSS improvement PUL offers at 2 years and highly values avoiding sexual dysfunction or episodic incontinence, PUL is perhaps the better choice. If on the other hand, sexual function and high quality, rapid recovery are not important concerns, TURP may be the better choice to maximize impact on LUTS.

The BPH6 composite endpoint is as yet not validated though it is composed of individually validated instruments. Achieving the BPH6 endpoint, regardless of treatment option, strongly predicts improved health related quality of life. This finding supports moving forward with a BPH6 validation study across BPO LUTS therapies. In the meantime, we have offered in depth separate analyses of BPH6 elements, so that the study offers the ability to compare these two disparate therapies with regard to several important health outcome measures. Unfortunately, a larger scale randomization between these two treatments is problematic, since they are clearly different in nature and both generally available; it is unlikely that many men would allow for random selection between these disparate treatment options. This fact is testimony to the need for offering both options and tailoring treatment to individual patient needs.

Durability of effect is another important characteristic of treatment options. This study demonstrates PUL durability through 2 years with 11% requiring additional procedure for LUTS compared to 6% for TURP. Recently, Roehrborn reported PUL durability in a larger randomised study, showing 13.6% additional LUTS procedures through 4 years.[12] This durability appears to be of a greater magnitude than that reported for minimally invasive procedures that rely on heat ablation (20% to 40% by 3 years).[11,12] Additional context with regard to durability is provided by Strope, showing that in a study of over 6,000 men after TURP or laser vaporization, 22% remain on LUTS medication at 3 years.[29]

The importance of preserving continence when treating LUTS was demonstrated in this study by the strong tendency for loss of continence to cause a drop in HRQOL. PUL patients were found to have stable average Incontinence Severity Index scores, whereas TURP patients demonstrated a significant drop in continence at 2 weeks and 3 months. The probability of experiencing weeks to months of incontinence, though not permanent, would appear to

represent another important issue to discuss in patient consult and to consider in treatment choice.

Poor sleep and its deleterious effects on quality of life represent a common chief complaint in male LUTS. The ability to achieve high quality sleep (as assessed with the Jenkins questionnaire) improves after LUTS treatment, as demonstrated in both arms of this study. Improvement in sleep is correlated with MCID in HRQOL ($p<0.0001$). Of note, an individual who experiences at least a 2 point change in Jenkins sleep score maximizes the chance of improving his HRQOL. Results from this study indicate that an exclusive focus on nocturia may not fully address sleep disorder. Clearly, reducing nocturia is a primary objective for a LUTS treatment, but iatrogenic negative effects on sleep should also be considered. While both TURP and PUL showed significant improvement in reducing nocturia through two years, only PUL showed significant improvement in overall Jenkins sleep quality. The origins of this difference are unknown, but represent an interesting area for further study in larger cohorts.

Subjects in both treatment arms felt that their condition improved after therapy (per PGI-I) with the majority in both arms indicating their post-operative condition to be “much better” or “very much better” through 2 years. Both procedures also translated into improvements in health related quality of life with a high proportion of subjects achieving the MCID in HRQOL after their procedure. Further, the vast majority of patients were satisfied with their treatment enough to recommend the procedure to a friend. In both patient satisfaction and HRQOL improvement, PUL showed a trend of greater improvement up to 1 year, where the two treatments leveled out to 2 years. This may be reflective of PUL superiority of Quality of Recovery in the early post-operative period.[10]

Study limitations include modest patient number that may not have provided sufficient statistical power to detect differences in some of the secondary outcome variables. For instance, the trend in PUL’s greater percent improvement in MCID HRQOL is interesting and warrants further investigation. It was not possible to blind the randomised comparison because episode of care and outcomes of these two treatment options are so different. The MSHQ-EjD bother score did not reflect significant changes in function score, suggesting either a lack of subject concern with ejaculatory function or a non-linear relationship between assessments. As prior studies had shown that PUL preserves ejaculatory function, it may also be that those particularly concerned with preserving ejaculation might not have been willing to be randomised to TURP and thus did not elect to enroll in this study. Analysis of the SF-6D threshold for minimal clinically important difference is relatively new to urology and also warrants further study with respect to treatment options specifically for male LUTS.

In conclusion, both PUL and TURP procedures offered significant improvement in symptoms, flow rate, and quality of life. Erectile function was preserved in both arms, whereas ejaculatory function was superior for PUL compared to TURP. TURP has been found to significantly compromise continence function at 2 weeks and 3 months whereas average continence scores in PUL patients were stable. For both treatment modalities, most patients perceive LUTS improvement after their procedure and are likely to recommend the procedure to a friend. Unlike TURP, the PUL procedure has been found to offer significant improvement in overall quality of sleep. Finally, the results of this study indicate that the BPH6 endpoint is predictive of clinically significant improvement in health related quality of life.

Acknowledgements:

The authors would like to express their appreciation of the contributions of the research coordinators who facilitated the collection of data. Special thanks to Drs. Rodney Anderson, Kyle Anderson, and Rajesh Shinghal for their participation on the independent clinical events committee. The authors would also like to thank Jacqueline Nerney Welch, M.D., Ph.D. and Theodore Lamson, Ph.D. for their support in the preparation of this manuscript.

References:

1) Low G, Molzahn A, Schopflocher D. Attitudes to Aging Mediate the Relationship Between Older People's Subjective Health and Quality of Life in 20 Countries. Health and Quality of Life Outcomes 2013; 11: 146
2) Berry S, Coffey D, Walsh P and Ewing L. The Development of Human Benign Prostatic Hyperplasia with Age. J Urol 1984; 132: 474-479.
3) Rosenberg M, Staskin D, Kaplan S, MacDiarmid S, Newman K, and Ohl D. A Practical Guide to the Evaluation of Treatment of Male Lower Urinary Tract Symptoms in the Primary Care Setting. Int J Clin Pract 2007; 61 (9): 1535-1546.
4) Laumann E, Paik A, Glasser D, et al. A Cross-National Study of Subjective Sexual Well-Being Among Older Women and Men: Findings From the Global Study of Sexual Attitudes and Behaviors. Arch Sexual Behavior 2006; 35(2): 145-161.
5) Rosen R, Altwein J, Boyle P, et al. Lower Urinary Tract Symptoms and Male Sexual Dysfunction: The Multinational Survey of the Aging Male (MSAM-7) Eur Urol 2003; 44: 637-649.
6) Martin D and Mulhall J. Enlarging the Scope of Managing Benign Prostatic Hyperplasia: Addressing Sexual Function and Quality of Life. Int J Clin Pract 2005; 59(5): 579-590.
7) Carbone D and Hodges S. Medical Therapy for Benign Prostatic Hyperplasia: Sexual Dysfunction and Impact on Quality of Life. Int J Impotence Res 2003; 15: 299-306.
8) Haltbakk J, Hanestad B, and Hunskaar S. How Important Are Men's Lower Urinary Tract Symptoms (LUTS) and Their Impact on the Quality of Life (QOL)? Quality of Life Research 2005; 14(7): 1733-1741.
9) Patel V, Sivaraman A, Coelho R, et al. Pentafecta: a new concert for reporting outcomes of robot-assisted laparoscopic radical prostatectomy. Eur Urol 2011; 59:702–7.
10) Sonksen J, Barber N, Speakman M, et al. Prospective, Randomized, Multinational Study of Prostatic Urethral Lift Versus Transurethral Resection of the Prostate: 12-month Results from the BPH6 Study. Eur Urol 2015; 68: 643-652.
11) 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(3): 7772-7782.

12) Roehrborn C. Prostatic Urethral Lift: A Unique Minimally Invasive Surgical Treatment of Male Lower Urinary Tract Symptoms Secondary to Benign Prostatic Hyperplasia. Urol Clin N Am 2016; 43: 357-369.
13) Shore N, Freedman S, Gange S, et al. Prospective Multi-center Study Elucidating Patient Experience after Prostatic Urethral Lift. Can J Urol 2014; 21(1): 7094-7101.
14) Cantwell A, Bogache W, Richardson S, et al. Multicentre Prospective Crossover Study of the 'Prostatic Urethral Lift' for the Treatment of Lower Urinary Tract Symptoms Secondary to Benign Prostatic Hyperplasia. BJU Int 2014; 113: 615-622.
15) Chin P, Boton D, Jack G, 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.
16) Gravas S, Bach T, Bachmann A, et al. Management of Non-Neurogenic Male Lower Urinary Tract Symptoms (LUTS), incl. Benign Prostatic Obstruction (BPO). European Association of Urology; 2015.
17) Roehrborn C, McConnell J, Barry M, et al. American Urological Association Guideline: Management of Benign Prostatic Hyperplasia (BPH). American Urological Association; 2003.
18) Miano R, De Nunzio C, Asimakopoulos A, Germani S, Tubaro A. Treatment Options for Benign Prostatic Hyperplasia in Older Men. Med Sci Monit 2008; 14: RA94-102.
19) Reich O, Gratzke C, Bachmann A, et al. Morbidity, Mortality and Early Outcome of Transurethral Resection of the Prostate: A Prospective Multicenter Evaluation of 10,654 Patients. J Urol 2008; 180 (1):246-249.
20) McNicholas T, Woo H, Chin P, et al. Minimally Invasive Prostatic Urethral Lift: Surgical Technique and Multinational Experience.. Eur Urol 2013; 64: 292-299.
21) Ware JE, Jr, Kosinski M, Keller SD. A 12-Item Short-Form Health Survey: Construction of Scales and Preliminary Tests of Reliability and Validity. Medical Care. 1996; 34(3):220–233.
22) Viktrup L, Hayes R, Wang P, and Shen W. Construct validation of patient global impression of severity (PGI-S) and improvement (PGI-I) questionnaires in the treatment of men with lower urinary tract symptoms secondary to benign prostatic hyperplasia. BMC Urology 2012; 12:30.
23) Hossack T, Woo H. Validation of a patient reported outcome questionnaire for assessing success of endoscopic prostatectomy. Prostate Int. 2014; 2(4): 182-187.
24) Sacco E, Bientinesi R, Marangi F, et al. Patient-reported outcomes in men with lower urinary tract symptoms (LUTS) due to benign prostatic hyperplasia (BPH) treated with intraprostatic OnabotulinumtoxinA: 3-month results of a prospective single-armed cohort study. BJU International 2012; 110:e837-844.
25) Gandek B, Ware JE, Aaronson NK, Apolone G, Bjorner JB, Brazier JE, Bullinger M, Kaasa S, Leplege A, Prieto L, Sullivan M. Cross-validation of Item Selection and Scoring for the SF-12 Health Survey in Nine Countries: Results from the IQOLA Project. Journal of Clinical Epidemiology. 1998; 51(11):1171–8.
26) Halme A, Fritel X, Benedetti A, Eng K, and Tannenbaum C. Implications of the Minimal Clinically Important Difference for Health-Related Quality-of-Life Outcomes: A Comparison of Sample Size Requirements for an Incontinence Treatment Trial. Value in Health 2015; 18: 292-298.
27) Casanova N, Jackson R, Dunn Ro, Faerber G, and Wei J. Incontinence-related Outcomes Following Photoselective Vaporization of. J Urol 2010; 183(4): e741.
28) Jenkins C, Stanton B, Niemcryk S, et al. A Scale for the Estimation of Sleep Problems in Clinical Research. J Clin Epidemiol. 1988; 41(4):313-321.
29) Strope S, Vetter J, Elliott S, Andriole G and Olsen M. Use of Medical Therapy and Success of Laser Surgery and Transurethral Resection of the Prostate for Benign Prostatic Hyperplasia. Urology 2015; 86: 1115-1122.

Conflicts of Interest:

Dr. Gratzke reports honoraria from Astellas, Lilly, Janssen, and Amgen. Dr. Barber reports support from NeoTract, Inc., Olympus, Boston Scientific, and Intuitive Surgical for proctoring and lecturing. Dr. Speakman reports grants from NeoTract, Inc. during the conduct of the study. Dr. Berges reports grants from NeoTract, Inc. during the conduct of the study. Dr. Wetterauer has nothing to disclose. Dr. Greene has nothing to disclose. Dr. Sievert reports grants from NeoTract, Inc. during the conduct of the study.

Dr. Chapple reports personal fees and non-financial support from Allergan, grants, personal fees and non-financial support from Astellas, personal fees and non-financial support from Boston, personal fees and non-financial support from Medtronic, personal fees from Pfizer, personal fees and non-financial support from Recordati, and grants from NeoTract, Inc. during the conduct of the study. Dr. Sonksen reports grants from NeoTract, Inc. during the conduct of the study and support from NeoTract, Inc. for proctoring and lecturing.

Table 1: Paired outcomes after PUL and TURP treatment

	2 Weeks		1 Month		3 Months		6 Months		12 Months		24 Months	
IPSS	**PUL**	**TURP**	**PUL**	**TURP**	**PUL**	**TURP**	**PUL**	**TURP**	**PUL**	**TURP**	**PUL**	**TURP**
N (paired)	42	34	44	33	42	34	40	33	40	32	37	32
Baseline (SD)	21.9 (5.7)	22.6 (6.0)	22.1 (5.7)	22.8 (5.8)	22.3 (5.8)	22.6 (6.0)	22.2 (5.7)	22.6 (6.0)	21.8 (5.5)	22.8 (5.9)	21.4 (5.5)	22.8 (5.9)
Follow Up (SD)	14.6 (7.7)	15.7 (7.3)	10.5 (7.6)	12.9 (5.9)	10.5 (7.4)	10.8 (8.4)	9.2 (7.5)	8.0 (7.2)	10.9 (8.0)	7.3 (6.3)	12.2 (8.9)	7.4 (6.7)
Change (SD)	-7.3 (9.4)	-6.8 (8.8)	-11.6 (9.3)	-10.0 (7.9)	-11.7 (8.5)	-11.8 (9.5)	-13.0 (8.1)	-14.6 (8.5)	-10.9 (7.9)	-15.4 (6.8)	-9.2 (9.2)	-15.3 (7.5)
Change P-Value	<.0001	<.0001	<.0001	<.0001	<.0001	<.0001	<.0001	<.0001	<.0001	<.0001	<.0001	<.0001
Comparison P-Value	0.8272		0.4169		0.9784		0.4212		0.0128*		0.0037*	

IPSS-QOL	PUL	TURP	PUL	TURP	PUL	TURP	PUL	TURP	PUL	TURP	PUL	TURP
N (paired)	43	34	44	33	43	34	40	33	40	32	37	32
Baseline (SD)	4.7 (1.1)	4.8 (1.2)	4.6 (1.1)	4.8 (1.2)	4.7 (1.1)	4.8 (1.2)	4.7 (1.1)	4.7 (1.2)	4.7 (1.0)	4.6 (1.2)	4.6 (1.1)	4.6 (1.2)
Follow Up (SD)	3.0 (1.9)	3.7 (1.7)	2.2 (1.8)	3.0 (1.9)	2.1 (1.5)	2.4 (2.0)	1.9 (1.6)	1.8 (1.7)	1.9 (1.6)	1.5 (1.5)	2.1 (1.6)	1.3 (1.5)
Change (SD)	-1.7 (2.3)	-1.0 (1.5)	-2.5 (2.0)	-1.8 (1.9)	-2.6 (1.7)	-2.4 (2.0)	-2.8 (1.6)	-2.9 (1.9)	-2.8 (1.8)	-3.1 (1.6)	-2.5 (1.8)	-3.3 (1.6)
Change P-Value	<.0001	0.0004	<.0001	<.0001	<.0001	<.0001	<.0001	<.0001	<.0001	<.0001	<.0001	<.0001
Comparison P-Value	0.1429		0.1377		0.5499		0.7906		0.4357		0.0658	
BPHII	**PUL**	**TURP**	**PUL**	**TURP**	**PUL**	**TURP**	**PUL**	**TURP**	**PUL**	**TURP**	**PUL**	**TURP**
N (paired)	43	32	43	32	42	33	40	32	40	30	36	31
Baseline (SD)	7.3 (2.5)	7.2 (3.0)	7.3 (2.5)	7.3 (3.1)	7.4 (2.4)	7.3 (3.1)	7.5 (2.4)	7.2 (3.1)	7.3 (2.4)	7.0 (3.1)	7.1 (2.4)	7.0 (3.1)
Follow Up (SD)	6.3 (3.3)	7.0 (3.1)	4.0 (3.1)	5.3 (3.0)	2.6 (2.8)	3.8 (3.4)	2.3 (2.5)	2.2 (2.5)	2.3 (2.8)	1.8 (2.6)	3.0 (2.9)	1.5 (2.7)
Change (SD)	-1.0 (4.3)	-0.2 (3.7)	-3.4 (4.3)	-2.0 (3.6)	-4.8 (3.6)	-3.4 (3.5)	-5.2 (2.9)	-5.0 (3.3)	-5.0 (3.7)	-5.2 (3.2)	-4.1 (3.7)	-5.4 (3.3)
Change P-Value	0.1312	0.7748	<.0001	0.0033*	<.0001	<.0001	<.0001	<.0001	<.0001	<.0001	<.0001	<.0001
Comparison P-Value	0.3897		0.1382		0.1008		0.7946		0.8359		0.1308	

Qmax	PUL	TURP	PUL	TURP	PUL	TURP	PUL	TURP	PUL	TURP	PUL	TURP
N (paired)					33	25	34	27	32	29	27	27
Baseline (SD)					9.4 (3.5)	9.0 (3.1)	9.6 (3.4)	9.4 (3.2)	9.6 (3.5)	9.5 (3.3)	9.3 (3.4)	9.6 (3.4)
Follow Up (SD)					13.6 (5.3)	21.7 (9.1)	13.5 (5.4)	19.0 (8.8)	13.6 (5.5)	23.2 (10.5)	14.3 (5.3)	25.5 (17.2)
Change (SD)					4.2 (5.0)	12.7 (9.8)	3.9 (5.2)	9.6 (9.2)	4.0 (4.8)	13.7 (10.4)	5.0 (5.5)	15.8 (16.5)
Change P-Value					<.0001	0.0034	<.0001	0.0021	<.0001	0.0034	<.0001	0.0021
Comparison P-Value					<.0001		0.0034*		<.0001		0.0021*	
PVR	**PUL**	**TURP**	**PUL**	**TURP**	**PUL**	**TURP**	**PUL**	**TURP**	**PUL**	**TURP**	**PUL**	**TURP**
N (paired)					39	32	40	31	41	32	35	31
Baseline (SD)					87.6 (74.1)	98.6 (84.9)	85.5 (73.4)	100.5 (85.7)	86.3 (73.2)	103.5 (89.7)	80.5 (61.0)	98.8 (87.1)
Follow Up (SD)					77.3 (74.4)	47.6 (48.7)	80.7 (91.0)	46.2 (49.1)	93.7 (156.5)	33.6 (38.6)	69.9 (62.5)	56.4 (63.0)
Change (SD)					-10.3 (56.2)	-51.0 (78.7)	-4.8 (70.7)	-54.2 (84.6)	7.4 (115.2)	-70.0 (79.0)	-10.6 (56.7)	-42.5 (91.7)
Change P-Value					0.2576	0.0009	0.6701	0.0012	0.6837	<.0001	0.2772	0.0151*
Comparison P-Value					0.0136*		0.0092*		0.0018*		0.0904	

SHIM	PUL	TURP	PUL	TURP	PUL	TURP	PUL	TURP	PUL	TURP	PUL	TURP
N (paired)			36	20	38	27	34	30	32	27	29	28
Baseline (SD)			20.3 (4.3)	17.6 (6.2)	20.4 (4.0)	19.2 (5.0)	20.6 (4.1)	18.4 (5.4)	20.8 (4.0)	18.6 (5.4)	20.4 (4.5)	18.5 (5.3)
Follow Up (SD)			20.9 (4.3)	17.2 (7.3)	19.7 (5.6)	18.2 (6.5)	20.0 (5.4)	17.6 (6.5)	20.7 (5.2)	17.7 (6.3)	20.3 (5.6)	16.7 (7.3)
Change (SD)			0.6 (2.5)	-0.4 (4.9)	-0.7 (5.2)	-1.0 (5.0)	-0.5 (4.4)	-0.8 (4.6)	-0.1 (4.7)	-0.9 (4.3)	-0.2 (4.3)	-1.8 (4.9)
Change P-Value			0.1321	0.7514	0.3863	0.3287	0.4836	0.3672	0.9404	0.2896	0.8320	0.0673
Comparison P-Value			0.3175		0.8612		0.8327		0.4855		0.2008	
MSHQ-EjD Function	**PUL**	**TURP**	**PUL**	**TURP**	**PUL**	**TURP**	**PUL**	**TURP**	**PUL**	**TURP**	**PUL**	**TURP**
N (paired)			36	18	38	27	35	29	32	27	29	27
Baseline (SD)			10.6 (2.6)	8.6 (2.5)	10.8 (2.7)	9.3 (2.4)	10.8 (2.7)	8.9 (2.4)	10.6 (2.7)	9.3 (2.1)	10.6 (2.8)	8.9 (2.3)
Follow Up (SD)			12.3 (3.4)	7.7 (5.0)	11.5 (3.5)	6.3 (4.5)	11.9 (2.5)	5.7 (4.2)	11.9 (3.0)	5.6 (4.0)	10.9 (3.3)	4.9 (4.6)
Change (SD)			1.7 (4.3)	-0.9 (5.0)	0.7 (3.9)	-3.0 (4.1)	1.1 (2.4)	-3.2 (4.5)	1.3 (3.3)	-3.7 (4.1)	0.3 (3.4)	-4.0 (4.6)
Change P-Value			0.0232*	0.4350	0.2510	0.0008	0.0085*	0.0006	0.0297*	<.0001	0.6656	0.0001

Comparison P-Value			0.0489*		0.0004		<.0001		<.0001		0.0002	
MSHQ-EjD Bother	**PUL**	**TURP**	**PUL**	**TURP**	**PUL**	**TURP**	**PUL**	**TURP**	**PUL**	**TURP**	**PUL**	**TURP**
N (paired)			36	18	38	28	35	29	32	27	29	27
Baseline (SD)			1.8 (1.8)	1.9 (1.7)	1.7 (1.8)	1.9 (1.5)	1.6 (1.8)	2.0 (1.6)	1.7 (1.8)	2.0 (1.5)	1.5 (1.8)	2.0 (1.6)
Follow Up (SD)			1.0 (1.3)	1.7 (1.3)	1.1 (1.4)	2.1 (1.4)	1.5 (1.5)	1.9 (1.5)	1.2 (1.1)	2.0 (1.3)	1.3 (1.4)	1.7 (1.4)
Change (SD)			-0.8 (1.9)	-0.2 (2.3)	-0.7 (2.1)	0.2 (1.5)	-0.1 (1.9)	-0.1 (1.7)	-0.5 (2.2)	-0.0 (1.5)	-0.1 (2.2)	-0.3 (1.9)
Change P-Value			0.0145*	0.6823	0.0622	0.4702	0.8605	0.8254	0.2139	0.8957	0.7343	0.4145
Comparison P-Value			0.3201		0.0689		0.9793		0.3587		0.7709	

*Hochberg method for multiple testing corrected p value > 0.05

Table 2: Percentage of subjects in each study arm who achieved a minimal clinically important difference (MCID) in SF-6D utility score

Visit	PUL	TURP	P-values
2 Weeks	41% (17/41)	25% (8/32)	0.14
1 Month	50% (21/42)	36% (12/33)	0.24
3 Months	51% (21/41)	30% (10/33)	0.07
6 Months	51% (20/39)	37.5% (12/32)	0.25
12 Months	52% (20/39)	50% (16/32)	0.91
24 Months	47% (16/34)	37.5% (12/32)	0.43

Table 3: Jenkins Sleep Score change from baseline over time

	PUL				TURP				Comparison p value
Visit	N	Mean	SD	P-Value	N	Mean	SD	P-Value	
2 Weeks	41	-1.0	5.1	0.33	34	-0.7	5.0	0.85	0.64
1 Month	43	-1.1	5.2	0.18	33	-0.5	4.9	0.71	0.38
3 Months	42	-1.6	5.3	0.08	34	-1.1	5.0	0.35	0.61
6 Months	39	-1.9	5.5	0.03	33	-1.2	4.3	0.14	0.47
12 Months	37	-2.0	5.9	0.04	32	-1.4	4.5	0.10	0.46
24 Months	34	-1.5	6.2	0.05	32	-1.2	4.1	0.10	0.27

Table 4: Nocturia score change from baseline over time

	PUL				TURP				Comparison p value
Visit	N	Mean	SD	P-Value	N	Mean	SD	P-Value	
2 Weeks	42	-0.4	1.6	0.15	34	0.1	1.6	0.67	0.20
1 Month	44	-0.8	1.5	<0.001	33	-0.7	1.2	0.002	0.70
3 Months	43	-0.9	1.5	<0.001	34	-1.1	1.3	<0.001	0.69
6 Months	40	-1.1	1.6	<0.001	33	-1.3	1.6	<0.001	0.56
12 Months	40	-0.8	1.5	0.002	32	-1.5	1.0	<0.001	0.04
24 Months	37	-0.6	1.6	0.02	32	-1.2	1.3	<0.001	0.10

Figure 1: Distribution of Responses to the Patient Global Impression of Improvement (PGI-I) Question and proportion of patients who achieved minimal clinically important difference (Δ) in quality of life (QoL) after PUL or TURP procedure (Note: N/A indicates that the subject did not complete the SF-12 questionnaire and consequently Δ QoL was not assessed.)

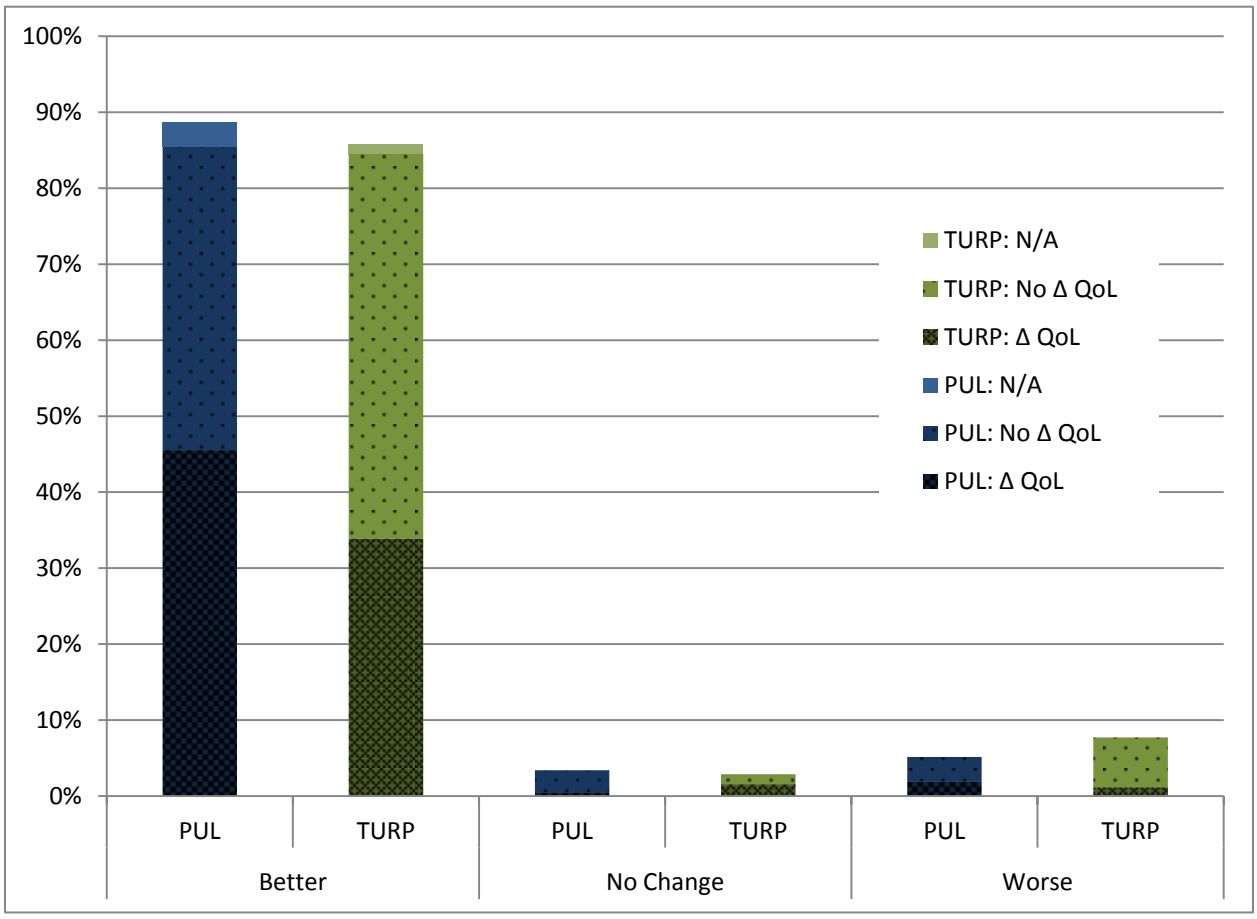

Figure 2: ISI score change from baseline over time (*statistically significant)