**Title:** Prostatic Urethral Lift

**Professional**
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<table>
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<th>Populations</th>
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</table>
| Individuals:  
- With lower urinary tract obstruction symptoms due to benign prostatic hyperplasia | Interventions of interest are:  
- Prostatic urethral lift | Comparators of interest are:  
- Transurethral resection of the prostate  
- Minimally invasive prostate resection or ablation  
- Continued medical management | Relevant outcomes include:  
- Symptoms  
- Functional outcomes  
- Health status measures  
- Quality of life  
- Treatment-related morbidity |

**DESCRIPTION**

Benign prostatic hyperplasia is a common condition in older men that can lead to increased urinary frequency, urgency, nocturia, hesitancy, and weak urinary stream. The prostatic urethral lift (PUL) procedure involves the insertion of 1 or more permanent implants into the prostate, which retract prostatic tissue and maintain an expanded urethral lumen.
Background

Benign Prostatic Hyperplasia

Benign prostatic hyperplasia (BPH) is a common disorder among older men that results from hyperplastic nodules in the periurethral or transitional zone of the prostate. BPH prevalence increases with age and is present in more than 80% of men ages 70 to 79.\(^1\) The clinical manifestations of BPH include increased urinary frequency, urgency, nocturia, hesitancy, and weak stream. The urinary tract symptoms often progress with worsening hypertrophy and may lead to acute urinary retention, incontinence, renal insufficiency, and/or urinary tract infection.

Two scores are widely used to evaluate BPH-related symptoms. The American Urological Association Symptom Index (AUASI) is a self-administered 7-item questionnaire assessing the severity of various urinary symptoms.\(^2\) Total AUASI scores range from 0 to 35, with overall severity categorized as mild (≤7), moderate (8-19), or severe (20-35).\(^1\) The International Prostate Symptom Score incorporates questions from the AUASI and a quality of life question or “Bother score.”\(^3\)

Management of BPH

Evaluation and management of BPH includes assessment for other causes of lower urinary tract dysfunction (eg, prostate cancer). Symptom severity and the degree that symptoms are bothersome determine the therapeutic approach.

Medical Therapy

A discussion about medical therapy is generally indicated for patients with moderate-to-severe symptoms (eg, AUASI score, ≥8), bothersome symptoms, or both. Available medical therapies for BPH-related lower urinary tract dysfunction include α-adrenergic blockers (eg, alfuzosin, doxazosin, tamsulosin, terazosin, silodosin), 5α-reductase inhibitors (eg, finasteride, dutasteride), combination α-adrenergic blockers and 5α-reductase inhibitors, anti-muscarinic agents (eg, darifenacin, solifenacin, oxybutynin), and phosphodiesterase-5 inhibitors (eg, tadalafil).\(^1\)

Surgical and Ablative Therapies

Various surgical or ablative procedures are used to treat BPH. Transurethral resection of the prostate (TURP) is generally considered the reference standard for comparisons of BPH treatments.\(^4\) In the perioperative period, TURP is associated with risks of any operative procedure (eg, anesthesia risks, blood loss). Although short-term mortality risks are generally low, 1 large prospective study with 10,654 patients reported the following short-term complications: “failure to void (5.8%), surgical revision (5.6%), significant urinary tract infection (3.6%), bleeding requiring transfusions (2.9%), and transurethral resection syndrome (1.4%).”\(^5\) Incidental carcinoma of the prostate was diagnosed by histologic examination in 9.8% of patients. In the longer term, TURP is associated with risk of sexual dysfunction and incontinence.
Several minimally invasive prostate ablation procedures have also been developed, including transurethral microwave thermotherapy, transurethral needle ablation of the prostate, urethromicroablation phototherapy, and photoselective vaporization of the prostate.

**Prostatic Urethral Lift**

The prostatic urethral lift procedure involves placement of 1 or more implants in the lateral lobes of the prostate using a transurethral delivery device. The implant device is designed to retract the prostate to allow expansion of the prostatic urethra. The implants are retained in the prostate to maintain an expanded urethral lumen.

One device, the NeoTract UroLift System, has been cleared for marketing by the U.S. Food and Drug Administration (see Regulatory Status section). The device has 2 main components: the delivery device and the implant. Each delivery device comes preloaded with 1 UroLift implant.

**Outcome Measures to Evaluate BPH Symptoms**

A number of health status measures are used to evaluate symptoms relevant to BPH and adverse effects of treatment for BPH, including urinary dysfunction, ejaculatory dysfunction, overall sexual health, and overall quality of life. Some validated scales are shown in Table 1.

| Table 1. Health Status Measures Relevant to Benign Prostatic Hyperplasia |
|-----------------------------|---------------|-------------------|-----------------|
| Measure                                   | Outcome Evaluated | Description                                             | Clinically Meaningful Difference (If Known) |
| Male Sexual Health Questionnaire for Ejaculatory Dysfunction (MSHQ-EjD) | Ejaculatory function | Patient-administered, 4-item scale | |
| Sexual Health Inventory for Men (SHIM) | Erectile function | Patient-administered, 5-item scale; final score range, 1 (worst symptoms) to 25 (fewest symptoms) | |
| American Urological Association Symptom Index (AUASI)<sup>1</sup> | Severity of lower urinary tract symptoms | Patient-administered, 7-item scale; final score range, 0 (no symptoms) to 35 (worst symptoms) | Minimum of 3-point change<sup>1,8</sup> |
| International Prostate Symptom Score (IPSS)<sup>3</sup> | Severity of lower urinary tract symptoms | Patient-administered, 8-item scale | |
| Benign Prostatic Hyperplasia Impact Index (BPH-II)<sup>4,9</sup> | Effect of urinary symptoms on health domains | Patient-administered, 4-item scale; final score range, 0 (best) to 13 (worst) | Minimum of 0.4-point change<sup>8</sup> |

**Regulatory Status**

One implantable transprostatic tissue retractor system has been cleared for marketing by the U.S. Food and Drug Administration (FDA) through the 510(k) process. In December 2013, the NeoTract UroLift® System UL400 (NeoTract, Pleasanton, CA) was cleared (after receiving clearance through FDA’s de novo classification process in March 2013;
K130651/DEN130023). In March 2016, FDA determined that the UL500 was substantially equivalent to existing devices (UL400) for the treatment of symptoms of urinary flow obstruction secondary to benign prostatic hyperplasia in men age 50 years and older. FDA product code: PEW.

**POLICY**
The prostatic urethral lift procedure is considered experimental / investigational for all indications.

**RATIONALE**
This evidence review was created in August 2015 and has been updated regularly with literature search of the MEDLINE database through July 10, 2016.

Assessment of the efficacy of therapeutic interventions such as prostatic urethral lift (PUL) procedures involves a determination of whether the intervention improves health outcomes. The optimal study design for this purpose is a randomized controlled trial (RCT) that includes clinically relevant measures of health outcomes. Well-designed and well-conducted RCTs are needed to demonstrate the efficacy of PUL procedures because of the potential for variable natural history of symptoms related to benign prostatic hypertrophy (BPH) and other potential confounders of outcome. A sham-controlled RCT would be ideal for the assessment of outcome measures that are subjectively reported to control for any placebo effects of treatment. Nonrandomized comparative studies and uncontrolled studies can be useful to determine the rate of short- and long-term adverse effects of treatment and to evaluate the durability of the treatment response. For PUL procedures, the appropriate comparison group could be medical management to demonstrate efficacy; however, to demonstrate that the procedure is at least as good as alternatives, the appropriate comparator would be transurethral resection of the prostate (TURP).

**Systematic Reviews**
Several systematic reviews have been published. They include a similar set of trials and noncomparative studies.

In 2015, Perera et al reported results of a systematic review and meta-analysis10 of studies reporting outcomes after the PUL procedure, which included 7 prospective cohort studies,11-17 1 crossover study (Cantwell et al18), and the LIFT RCT (Roehrborn et al,19 McVary et al20). The pooled standardized mean gain (SMG) estimates for prostate symptoms scores (International Prostate Symptom Score [IPSS], Benign Prostatic Hyperplasia Impact Index [BPH-II]) and sexual health scores used responses from 452 to 680 patients. SMG for prostatic symptoms scores ranged from -1.3 (95% confidence interval [CI], -1.4 to -1.2) to -1.6 (95% CI, -1.7 to -1.3), which translated into a clinically meaningful improvement. The SGM for sexual health scores ranged from 0.3 (95% CI, 0.2 to 0.4) to 0.4 (95% CI, 0.3 to 0.5), suggesting a small improvement.

In 2016, Jones, et al performed a systematic review of UroLift studies with at least 12 months of follow-up.21 Seven studies were identified, which included 4 noncomparative studies (Woo et al,17 Chin et al,15 McNicholas et al,14 Bozkurt et al22), 1 crossover study (Cantwell et al18), and 2 RCTs
The review included data from 440 patients. Only the data from men in the UroLift arms of these RCTs were included. Results were combined to create summaries but the meta-analytic methods used to combine the data were not described and precision estimates were not given. The authors reported that mean peak urinary flow rate (Qmax) increased from 8.4 mL/s to 11.8 mL/s, mean IPSS improved from 24.1 to 14, mean quality of life (QOL) improved from 4.5 to 2.3, and mean 5-item International Index of Erectile Function score improved from 17.7 to 18.2. The most frequent complications reported were dysuria, hematuria and pelvic pain.

The National Institute for Health and Care Excellence (NICE) published a technical guidance on prostatic lift procedures in 2016. The NICE External Assessment Centre (EAC) performed a literature search and data synthesis to support development of the guidance. Studies selected were the same studies included in Perera et al, except for the exclusion of Hoffman et al and the inclusion of Abad et al in the analysis. Comparators for the review were TURP and holmium laser enucleation of prostate (HoLEP). When the literature search was performed, there were no studies directly comparing PUL to either TURP or HoLEP. Therefore the NICE EAC extracted data from a TURP versus HoLEP systematic review to perform a “pragmatic indirect comparison” of these comparators to prostatic lift procedures. The conclusion of the review was that PUL provides significant improvement in IPSS, BPH-II, and QOL (estimates of effect similar to Perera et al) but with improvements that were smaller than those seen with TURP or HoLEP; however, the PUL procedure was associated with a slight improvement in erectile or ejaculatory function.

Randomized Controlled Trials

BPH6 Study
In 2016, Sonksen et al reported results of a multicenter RCT comparing the PUL procedure with TURP among men ages 50 and older with lower urinary tract symptoms secondary to benign prostatic obstruction. Eligible patients had an IPSS above 12, a Qmax of 15 mL/s or less for a 125-mL voided volume, a postvoid residual volume less than 350 mL, and prostate volume of 60 cm³ or less on ultrasound. The study used a novel composite end point, referred to as the BPH6, which included lower urinary tract symptom relief measured by the IPSS, recovery experience measured on a visual analog scale (VAS), erectile function measured by the Sexual Health Inventory for Men (SHIM) scale, ejaculatory function measured by the Male Sexual Health Questionnaire for Ejaculatory Dysfunction (MSHQ-EjD), continence preservation measured by the Incontinence Severity Index, and safety measured by no treatment-related adverse event greater than grade 1 on the Clavien-Dindo classification system. Patients were considered treatment responders if they met all 6 composite criteria. The study used a noninferiority design with a margin of 10% for the primary end point, BPH6. Study investigators modified 2 of the original end point definitions in the study's analysis, including changing the sexual function element assessment from a single time point (12 months) to assess sustained effects during 12 months of follow-up, and lowering the threshold of quality of recovery on VAS from 80 to 70.

Ninety-one patients were randomized to TURP (n=45) or PUL (n=46). Ten patients in the TURP group and 1 patient in the PUL group declined treatment, leaving an analysis group of 80 subjects. Analysis was per-protocol, including 35 in the TURP group and 44 in the PUL group (87% of those randomized; 1 patient was excluded for violation of the active urinary retention exclusion criterion). Groups were similar at baseline, with the exception of MSHQ-EjD Function score. For procedure recovery, 82% of the PUL group achieved the recovery end point by 1 month compared with 53% of the TURP group (p=0.008). For the study's primary outcome, the
proportion of participants who met the original BPH6 primary end point was 34.9% for the PUL group and 8.6% for the TURP group (noninferiority $p<0.001$; superiority $p=0.006$). The modified BPH6 primary end point was met by 52.3% of the PUL group and 20.0% of the TURP group (noninferiority $p<0.001$; superiority $p=0.005$). Both groups demonstrated improvements over IPSS, IPSS Quality of Life score, BPH-II score, and Qmax over time. IPSS, Qmax, and postvoid residual volumes were better for the TURP group than for the PUL group. The TURP group demonstrated declines in ejaculatory function (average MSHQ-EjD score) compared with baseline (9 at baseline vs 5.6 at 12-month follow-up; $p<0.001$), while the PUL group demonstrated a slight improvement (11 at baseline vs 11.9 at 12-month follow-up, $p=0.03$) for an overall difference between groups of -5.0 (95% CI, -6.9 to -3.1; $p<0.001$). Intention-to-treat (ITT) analyses were not reported.

**LIFT Study**

In 2013, Roehrborn et al reported results of the pivotal LIFT study, an RCT comparing PUL with sham control among 206 men ages 50 and older with lower urinary tract symptoms secondary to BPH. Eligible patients had an American Urological Association Symptom Index (AUASI) score of 13 or greater, Qmax of 12 mL/s or less for a 125-mL voided volume, and a prostate volume between 30 and 80 mL. Patients were randomized to PUL ($n=140$) or sham control ($n=66$) and evaluated at 3 months postprocedure for the study's primary efficacy end point. After that, all patients were unblinded and sham control patients were permitted to undergo the PUL procedure. Fifty-three control subjects eventually underwent a PUL procedure. Analysis was ITT. The study met its primary efficacy end point that the reduction in AUASI score at 3 months postprocedure was at least 25% greater after the PUL than that seen with sham ($p=0.003$). The AUASI score decreased from 24.4 at baseline to 18.5 at 3-month follow-up for sham control patients and from 22.2 at baseline to 11.2 at 3-month follow-up for PUL patients. The 3-month change in Qmax was 4.28 mL/s for PUL patients and 1.98 mL/s for sham control patients ($p=0.005$). Compared with sham control patients, PUL patients had greater improvements in QOL scores (note that specific QOL scoring device was not specified) and BPH-II score.

McVary et al reported on sexual function outcomes in a subset of patients from the LIFT study. At baseline, 53 (38%) PUL subjects and 23 (53%) sham control subjects were sexually inactive or had severe erectile dysfunction and were censored from the primary sexual function analysis. Scores on the SHIM and MSHQ-EjD Function scale and the MSHQ-EjD Bother scale did not differ significantly between groups.

In 2014, Cantwell et al reported outcomes for the 53 subjects in the LIFT sham control group who underwent PUL after unblinding at 3 months postprocedure. Crossover (unblinded) patients had a change in IPSS from 23.4 to 12.3 at 3 months postprocedure compared with the change in IPSS from 25.2 to 20.2 at 3 months after the sham procedure. Subjects had greater improvements in BPH-II score in the crossover period (-3.3) than in the sham period (-1.9; $p=0.024$), but did not report significant differences in improvement in Qmax. Change in sexual function scores did not differ significantly after sham procedure compared with after active procedure.

In 2015, Roehrborn et al reported 3-year results from patients randomized to PUL in the LIFT study. After exclusion of 11 subjects who were lost to follow-up, 36 subjects with missing data, protocol deviations, medication treatment for BPH, or other prostate procedures, and 15 subjects who underwent surgical retreatment for lower urinary tract symptoms (6 with repeat PUL
procedures, 9 with TURP or laser vaporization), the 3-year effectiveness analysis included 93 (66%) of the original 140 subjects. For subjects included in the follow-up data, change in IPSS was -8.83 (95% CI, -10.35 to -7.30; p<0.001). Significant improvements were also reported for QOL score, BPH-II score, and Qmax. Sexual function was unchanged. Implants were removed from 10 participants. No analyses were performed to assess how sensitive the results were to changes in the assumptions about the considerable amount of missing data.

In 2016, Roehrborn et al reported 4-year results from patients randomized to PUL in the LIFT study.26 Of the 140 originally randomized patients, 32 were lost by the 4-year follow-up visit (6 losses were deaths). Of the remaining 108 patients for whom data were available, an additional 29 patients were excluded from analysis for BPH retreatment or protocol deviations. For the 79 (56%) of the 140 subjects included in the analysis, change in IPSS score was -8.8 (precision not given) or -41% (95% CI, -49% to -33%; p<0.001). Significant improvements compared to baseline were also reported for QOL, BPH-II, and Qmax. Fourteen percent of the 140 participants had surgical retreatment by 4 years. SHIM scores did not differ statistically from baseline.

Noncomparative Studies
Other noncomparative studies have described outcomes after the PUL procedure in sample sizes ranging from 17 to 102.13-17,22 The study reporting the longest follow-up (Chin et al) reported outcomes for 64 men at 6 Australian institutions up to 24 months postprocedure.15 At the time of publication, 33 patients had reached 24-month follow-up. At 24 months, for IPSS, patients had improved by -9.2 over baseline. Other outcome parameters, including QOL scores, BPH-II score, and Qmax, had similar magnitudes of improvement at 24 months postprocedure.

Ongoing and Unpublished Clinical Trials
Some currently unpublished trials that might influence this review are listed in Table 2.

Table 2. Summary of Key Trials

<table>
<thead>
<tr>
<th>NCT No.</th>
<th>Trial Name</th>
<th>Planned Enrollment</th>
<th>Completion Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ongoing</td>
<td>Luminal Improvement Following Prostatic Tissue Approximation for the Treatment of Lower Urinary Tract Symptoms</td>
<td>206</td>
<td>Feb 2017</td>
</tr>
</tbody>
</table>

NCT: national clinical trial.
* Denotes industry-sponsored or cosponsored trial.

Summary of Evidence
For individuals who have lower urinary tract obstruction symptoms due to benign prostatic hyperplasia who receive prostatic urethral lift (PUL), the evidence includes systematic reviews, randomized controlled trials (RCTs), and noncomparative studies. Relevant outcomes are symptoms, functional outcomes, health status measures, quality of life, and treatment-related morbidity. The LIFT study was an RCT comparing PUL with sham control that reported the PUL procedure is associated with greater improvements in lower urinary tract symptoms than medical management, without worsened sexual function. One publication from this trial reported that functional improvements were durable over 3- and 4-year follow-ups in a subset of patients, but this conclusion is limited because only treated patients were included in the longer follow-up and there was a high loss to follow-up in the treated group. Another RCT, the BPH6 study, compared the PUL procedure with transurethral resection of the prostate (TURP) and reported that PUL was noninferior for the study’s composite end point, which included multiple measures of symptoms.
and complications combined into a single score. While TURP was associated with greater improvements in urinary tract obstruction symptom outcomes, it was also associated with greater declines in sexual function than PUL. This small trial was limited by unequal dropout rates between groups after enrollment, and uncertainty about the validity of its primary composite outcome measure. The composite measure was composed mostly of safety items, and may have therefore favored the PUL group. Because of limitations with the BPH6 trial, its results do not definitively demonstrate the noninferiority of PUL to TURP; more evidence is needed to corroborate these results. In addition, follow-up in the available studies was inadequate to identify longer term adverse events. The evidence is insufficient to determine the effects of the technology on health outcomes.

**Practice Guidelines and Position Statements**

**National Institute for Health and Care Excellence**

In 2014, the National Institute for Health and Care Excellence (NICE) published interventional procedural guidance on urethral lift implants to treat lower urinary tract symptoms secondary to benign prostatic hyperplasia. These guidelines state: “Current evidence on the efficacy and safety of insertion of prostatic urethral lift implants to treat lower urinary tract symptoms secondary to benign prostatic hyperplasia is adequate to support the use of this procedure provided that normal arrangements are in place for clinical governance, consent and audit.”

In 2015, NICE published a medical technology guidance on use of UroLift for treating lower urinary tract symptoms of benign prostatic hyperplasia. The guidelines state: “the UroLift system is effective in relieving symptoms of benign prostatic hyperplasia” and “the UroLift system should be considered as an alternative to current surgical procedures for use in a day-case setting in men with lower urinary tract symptoms of benign prostatic hyperplasia who are aged 50 years and older and who have a prostate of less than 100 ml without an obstructing middle lobe.”

**American Urological Association**

The 2010 (reaffirmed 2014) American Urological Association guideline on the management of benign prostatic hyperplasia does not address the PUL procedure.

**U.S. Preventive Services Task Force Recommendations**

Not applicable.

**CODING**

The following codes for treatment and procedures applicable to this policy are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement. Please refer to the member’s contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

**CPT/HCPCS**

52441 Cystourethroscopy, with insertion of permanent adjustable transprostatic implant; single implant


*Contains Public Information*
52442  Cystourethroscopy, with insertion of permanent adjustable transprostatic implant; each additional permanent adjustable transprostatic implant (List separately in addition to code for primary procedure)

C9739  Cystourethroscopy, with insertion of transprostatic implant; 1 to 3 implants

C9740  Cystourethroscopy, with insertion of transprostatic implant; 4 or more implants

ICD-10 Diagnoses
Experimental / Investigational for all diagnoses related to this medical policy.

REFERENCES