Prostate Surgeries and Interventions

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Instructions for Use

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Related Commercial Policies
None

Coverage Rationale

Transurethral ablation of the prostate is proven and medically necessary in certain circumstances. For medical necessity clinical coverage criteria, refer to the InterQual® CP: Procedures, Prostatectomy, Transurethral Ablation.

Click here to view the InterQual® criteria.

Cryoablation of the prostate is proven and medically necessary in certain circumstances. For medical necessity clinical coverage criteria, refer to the InterQual® CP: Procedures, Cryoablation, Prostate.

Click here to view the InterQual® criteria.

Surgical prostatectomy is proven and medically necessary in certain circumstances. For medical necessity clinical coverage criteria, refer to the InterQual® CP: Procedures, Prostatectomy, Radical.

Click here to view the InterQual® criteria.

Prostatic urethral lift (PUL) is proven and medically necessary when performed according to the following U.S. Food and Drug Administration (FDA) labeled indication:

- Treating symptoms due to urinary outflow obstruction secondary to benign prostatic hyperplasia (BPH), including lateral and median lobe hyperplasia; in men 45 years of age or older, and
- The following are not present:
  - Prostate volume of > 100 cc
  - A urinary tract infection
  - Urethra conditions that may prevent insertion of delivery system into bladder
  - Urinary incontinence due to incompetent sphincter
  - Current gross hematuria

High-energy water vapor thermotherapy for the treatment of malignant prostate tissue is unproven and not medically necessary due to insufficient evidence of safety and/or efficacy.

The transperineal placement of biodegradable material, peri-prostatic (via needle) is proven and medically necessary for use with radiotherapy for treating prostate cancer.

The transperineal placement of biodegradable material, peri-prostatic (via needle) is unproven and not medically necessary for all other indications due to insufficient evidence of safety and/or efficacy.

The following procedures are unproven and not medically necessary due to insufficient evidence of safety and/or efficacy:

- Transurethral waterjet ablation of the prostate (aquablation)
- Focal laser ablation
- Insertion of a temporary prostatic urethral stent
- Vascular embolization

Documentation Requirements

CPT Codes*	Required Clinical Information
Prostate Surgeries and Interventions	

52441
52442
53850
53852
55866
55873
55874
	Medical notes documenting the following, when applicable:
	Transurethral Ablation
	• Diagnosis
	• History of the medical condition(s) requiring treatment or surgical intervention
	• Documentation of signs and symptoms; including onset, duration, and frequency
	• Physical exam, including result of digital rectal exam
	• Relevant medical history, including list of all current patient medication
	• Treatments tried, failed, or contraindicated; include the dates and reason for discontinuation
	• Relevant surgical history, including dates
	• Reports of all recent imaging studies and applicable diagnostics including:
	  ○ Results of uroflow test (Q-max and postvoid residual (PVR) test)
	  ○ Results of urinalysis
	  ○ Results of PSA test
	  ○ Results of prostate biopsies
	• Physician treatment plan
	
	Cryoablation of the Prostate
	• Diagnosis, including:
	  ○ Cancer risk group, including stage of disease
	  ○ Life expectancy
	• History of the medical condition(s) requiring treatment or surgical intervention
	• Documentation of signs and symptoms, including onset, duration, and frequency
	• Physical exam
	• Relevant medical history
	• Treatments tried, failed, or contraindicated; include the dates and reason for discontinuation
	• Relevant surgical history, including dates
	• Reports of all recent imaging studies and applicable diagnostics, including:
	  ○ Results of prostate volume via transrectal ultrasound (TRUS)
	  ○ Results of PSA test
	• Physician treatment plan
	
	Surgical - Radical Prostatectomy
	• Diagnosis, including:
	  ○ Results of diagnostic prostate biopsy
	  ○ Cancer risk group, including stage of disease
	  ○ Life expectancy

CPT Codes*	Required Clinical Information
Prostate Surgeries and Interventions	

	• History of the medical condition(s) requiring treatment or surgical intervention
	• Documentation of signs and symptoms, including onset, duration, and frequency
	• Physical exam
	• Relevant medical history
	• Treatments tried, failed, or contraindicated; include the dates and reason for discontinuation
	• Relevant surgical history, including dates
	• Reports of all recent imaging studies and applicable diagnostics, including results of PSA test
	• Physician surgical plan, including plans for pelvic lymph node dissection
	
	Prostatic Urethral Lift (PUL)
	• Diagnosis
	• History of the medical condition(s) requiring treatment or surgical intervention
	• Documentation of signs and symptoms, including onset, duration, and frequency; include presence of the following:
	  ○ Urinary incontinence
	  ○ Gross hematuria
	• Physical exam
	• Relevant medical history, including presence of the following:
	  ○ Urinary tract infection
	  ○ Allergy to nickel
	• Treatments tried, failed, or contraindicated; include the dates and reason for discontinuation
	• Relevant surgical history, including dates
	• Reports of all recent imaging studies and applicable diagnostics, including:
	  ○ Prostate volume
	  ○ Presence of signs or symptoms of obstruction
	  ○ Presence of protruding median lobe of the prostate
	• Physician treatment plan
	
	Transperineal Placement of Biodegradable Material
	• Diagnosis
	• History of the medical condition(s) requiring treatment or surgical intervention
	• Relevant medical history
	• Relevant surgical history, including dates
	• Physician treatment plan including specifics of radiotherapy plan

*For code descriptions, refer to the Applicable Codes section.

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

CPT Code	Description
0421T	Transurethral waterjet ablation of prostate, including control of post-operative bleeding, including ultrasound guidance, complete (vasectomy, meatotomy, cystourethroscopy, urethral calibration and/or dilation, and internal urethrotomy are included when performed)
0582T	Transurethral ablation of malignant prostate tissue by high-energy water vapor thermotherapy, including intraoperative imaging and needle guidance

CPT Code	Description
0655T	Transperineal focal laser ablation of malignant prostate tissue, including transrectal imaging guidance, with MR-fused images or other enhanced ultrasound
37243	Vascular embolization or occlusion, inclusive of all radiological supervision and interpretation, intraprocedural road mapping, and imaging guidance necessary to complete the intervention: for tumors, organ ischemia, or infarction (when performed on prostate tissue)
52441	Cystourethroscopy, with insertion of permanent adjustable transprostatic implant; single implant
52442	Cystourethroscopy, with insertion of permanent adjustable transprostatic implant; each additional permanent adjustable transprostatic implant (List separately in addition to code for primary procedure)
53850	Transurethral destruction of prostate tissue; by microwave thermotherapy
53852	Transurethral destruction of prostate tissue; by radiofrequency thermotherapy
53854	Transurethral destruction of prostate tissue; by radiofrequency generated water vapor thermotherapy
53855	Insertion of a temporary prostatic urethral stent, including urethral measurement
55866	Laparoscopy, surgical prostatectomy, retropubic radical, including nerve sparing, includes robotic assistance, when performed
55873	Cryosurgical ablation of the prostate (includes ultrasonic guidance and monitoring)
55874	Transperineal placement of biodegradable material, peri-prostatic, single or multiple injection(s), including image guidance, when performed

Description of Services

Benign prostatic hyperplasia (BPH) is an enlarged prostate and occurs most often during the second growth phase of the prostate (around age 25 and up). As the prostate enlarges, it presses against the urethra, which can result in the thickening of the bladder wall, the inability to empty the bladder fully, trouble starting urination, a week flow, urgency and needing to push or strain to urinate. In most men, BPH gets worse with age and can lead to bladder and kidney damage and infection.

Several procedures have been proposed for treatment of BPH including transurethral resection of the prostate (TURP), laser vaporization or enucleation, transurethral microwave therapy, transurethral needle ablation, waterjet ablation, thermotherapy prostatic arterial embolization, prostatectomy, prosthetic stents, transurethral incision of the prostate transurethral microwave therapy (TUMT), transurethral holmium laser ablation (HoLAP), and prostatic urethral lift (PUL) (Hayes, Inc., 2020).

In PUL, permanent UroLift® implants are placed to hold open the lateral lobes of the prostate in a minimally invasive procedure to reduce urinary obstruction (Roerborn et al., 2017).

Prostate cancer can be treated by surgery, medications, and / or radiotherapy. Transperineal placement of biodegradable material is sometimes used to protect other pelvic structures during radiotherapy.

Clinical Evidence

High Energy Water Vapor Thermotherapy of Malignant Prostate Tissue

A search of the literature did not identify relevant peer reviewed original data publications.

Prostatic Urethral Lift (PUL)

In 2017, Roehrborn et al. published five-year outcomes of the prospective, multi-center, randomized, blinded sham control trial of the Prostatic Urethral Lift (PUL) in men with bothersome lower urinary tract symptoms (LUTS) due to benign prostatic hyperplasia (BPH). In this 19-center study, 206 subjects ≥ 50 years old with an International Prostate Symptom Score (IPSS) > 12, peak flow rate (Qmax) ≤ 12 mL/s, and prostate volume 30 cc-80 cc were randomized 2:1 to the PUL procedure or blinded sham control. IPSS improvement after PUL was 88% greater than that of sham at 3 months. LUTS and QOL were significantly improved by 2 weeks with return to preoperative physical activity within 8.6 days. Improvement in IPSS, QOL, BPHII, and Qmax

were durable through 5 years with improvements of 36%, 50%, 52%, and 44% respectively. Symptom improvement was commensurate with patient satisfaction. The authors conclude that PUL offers a durable, minimally invasive option in the treatment of LUTS due to BPH.

Two-year outcomes were reported by Gratzke et al. (2017) for the BPH6 prospective, multicenter, non-blinded randomized study (n=80) which compared PUL to transurethral resection of the prostate (TURP). Inclusion criteria were aged ≥50 years and a candidate for TURP, with IPSS >12, maximum urinary flow rate (Q max) ≤15 mL/s, and prostate volume ≤60 cc on ultrasonography. Parallel 1:1 randomization was performed using permuted blocks of random sizes, stratified by study site. Patients were followed up with visits at 2 weeks, 1 month, 3 months, 6 months, 1 year and 2 years. Significant improvements in IPSS, IPSS QoL, BPH Impact Index (BPHII) and Q max were observed in both arms through 2-year follow-up. IPSS change with TURP was superior to that with PUL at 1 and 2 years, and TURP was superior with regard to Q max at all time points (Table 1). HRQoL and BPHII improvements were not statistically different. Quality of recovery, as defined by at least a score of 70 on the QoR VAS (0–100 scale), was superior for PUL compared with TURP, with 82% of patients in the PUL arm achieving the recovery endpoint by 1 month compared with 53% of patients in the TURP arm (P = 0.008). The results demonstrate that both the PUL and TURP procedures offered significant improvement in symptoms, Q max and HRQoL. The modest patient number may not have provided sufficient statistical power to detect differences in some of the secondary outcome variables.

Transurethral Waterjet Ablation (Aquablation)

Initial treatment for BPH is usually medical therapy, but this often provides only modest relief. Up to 30% of patients require surgical intervention. Aquablation is performed by a medical device that allows rapid removal of prostate tissue without leaving a zone of thermal damage on the treated tissue. It utilizes a waterjet for automated tissue resection as well as for optical energy delivery for cauterization in the treatment of BPH (Hayes, 2018).

In a 2021 Hayes technology assessment regarding aquablation for treating benign prostatic hyperplasia, it was concluded that a low-quality body of evidence suggests it may improve LUTS associated with BPH in the short to intermediate term without impacting sexual or function, and without serious safety concerns. However substantial uncertainty remains due to the scarcity of evidence comparing aquablation to TURP, which is the primary surgical modality for treating BPH in small to moderate sized prostates, as well as limited long-term evidence. Furthermore, clarity is lacking as to which patient populations are likely to benefit the most from aquablation therapy. The report concludes that this technology has a potential but unproven benefit.

A 2020 ECRI clinical evidence assessment of the Aquabeam Robotic System for treating benign prostatic hyperplasia (BPH), reports this is safe, and reduces BPH-related LUTS for up to three years based on evidence from one randomized controlled trial (RCT) and four prospective case series, and this evidence is somewhat favorable. The RCT reported that Aquablation works as well as TURP for improving LUTS at three-year follow-up, but findings need confirmation in additional RCTs. RCTs of sufficient size are needed that compare AquaBeam to other minimally invasive treatments for LUTS due to BPH, as well as report patient-oriented outcomes.

Gilling et al. (2020) reported the results of participants from the Water I clinical trial to report 3-year outcomes for aquablation compared to TURP for the treatment of LUTS related to BPH. Assessments included IPAA, MSHQ-EjD, IIEF and uroflow. Over 3 years of treatment, improvements in IPSS scores were statistically similar across groups. Mean 3-year improvements were 14.4 and 13.9 points in the Aquablation and TURP groups, respectively (difference of 0.6 points, 95% CI -3.3-2.2, p = .6848). Similarly, 3-year improvements in Qmax were 11.6 and 8.2 cc/sec (difference of 3.3 [95% CI -0.5-7.1] cc/sec, p = .0848). At 3 years, PSA was reduced significantly in both groups by 0.9 and 1.1 ng/mL, respectively; the reduction was similar across groups (p = .5983). There were no surgical retreatments for BPH beyond 20 months for either Aquablation or TURP. It was concluded that three-year BPH symptom reduction and urinary flow rate improvement were similar after TURP and Aquablation therapy. No subjects required surgical retreatment beyond 20 months postoperatively. This study is limited by a maximum prostate size of 80cc (however Desai reported on results with larger prostates below), and whether the rigor of clinical trial data can be applied in real world settings. Furthermore, the study may have been too small to detect clinically significant differences at three years, as it was powered for non-inferiority at six months.

Desai et al. (2020) reported the 2-year safety and effectiveness of aquablation in men with larger prostate volumes of 80-150cc in a prospective, multicenter international case series (WATER II). Participants had a mean prostate volume of 107 cc and the results showed IPSS and IPSS quality of life improved from 23.2 to 1.1, and 4.6 to 1.1 from baseline to 2 years respectively. Maximum urinary flow increased from 8.7 to 18.2 cc/sec. By the end of the 2-year study timeframe, all but 2 of the 74 participants stopped taking alpha blockers and all but 32 stopped taking 5α-reducatase inhibitors. During the 2-year study time

frame, adverse urological events were low and included 2 subjects with recurrent BPH symptoms that required retreatment with TURP and HOLEP. The authors concluded that the aquablation procedure is a safe and effective treatment for men with LUTS due to BPH with larger prostate volumes and has an acceptable safety profile and a low retreatment rate. This trial is limited by a lack of a control group which prevented direct comparison to other treatments.

Bach et al. (2020) conducted an international prospective, multicenter, single-arm, open-label, international clinical trial of the efficacy of the Aquablation procedure for the treatment of lower urinary tract symptoms (LUTS) due to BPH in 177 men enrolled at five treatment centers between September 2017 and December 2018. The primary endpoint was the change in total IPSS from baseline to 3 months. Secondary endpoints included the following: (1) Proportion of subjects who were sexually active at the baseline and experienced either ejaculatory or erectile dysfunction at 3 months, change from the baseline to 3 months in maximal flow rate (Qmax), prostate specific antigen (PSA) level, post-void residual (PVR), total MSHQ score, and selected IIEF-5 score. The degree of dysuria was collected on a 0 (not at all) to 5 (almost always) scale. Inclusion criteria was a diagnosis of LUTS due to BPH and a prostate size between 20 and 150 cc. Men were excluded if they were unable to stop anticoagulants and antiplatelet agents perioperatively or had a bleeding disorder, had a history of gross hematuria, were using systemic immune suppressants, had a contraindication to both general and spinal anesthesia, were unwilling to accept transfusion if required, or had any severe illness that could prevent complete follow-up. Patients with prior BPH surgery were not excluded. At baseline and 3 and 12 month follow up, participants completed the International Prostate Symptom Score (IPSS), Incontinence Severity Index, Pain Intensity Scale, Quality of Recovery Visual Analog Scale, International Index of Erectile Function (IIEF-15), the Male Sexual Health Questionnaire (MSHQ-EjD), uroflowmetry and post void residual volume (PVR) measurements. The results showed of the original 177 participants enrolled and had the procedure completed, by month 12, 30 were lost to follow up, three voluntarily withdrew, and one died of an unrelated cause. Mean IPSS improved from 21.7 (7.1) at baseline to 7.1 (5.8) at 3-month follow-up , and 6.4 (4.8) at 12-month follow-up. IPSS QOL scores improved from 4.7 (1.1) at baseline to 1.5 (1.4) at 3-month follow-up, and 1.4 (1.4) at 12-month follow-up. IPSS storage and voiding scales also improved significantly ($p < 0.0001$) at 3 and 12 months (Baseline IPSS scores were unavailable in nine men; of these, seven were using a urinary catheter at the baseline and two cases had incomplete questionnaire responses). Maximum urinary flow rate increased from 9.9 (5.3) cc/sec at baseline to 20.3 (11.4) cc/sec at month 3 and 20.8 (11.2) cc/s at month 12. Postvoid residual improved from 108 (108) to 47 (77) cc at three months and 61 (74) cc at 12 months. Of the 92 men that were sexually active at baseline and 12 months, the MSHQ-EjD score changed by -1 at 3 months, and -1.1 points at 12 months. MSHQ bother/satisfaction changed by −0.3 and −0.7 points at 3 and 12 months respectively. IIEF-15 scores remained stable through month 3. 141 patients had transrectal ultrasound at baseline and after 3 months which showed a decrease in prostate size of 36%. Leakage of urine was reported by 68% of participants at baseline and had reduced to 55% at 12 months, and ISI improved non-significantly. Dysuria of any frequency was reported by 51% at baseline and 29% at 3-month follow-up, and associated pain decreased from 3.5 to 2.4. General pelvic pain decreased from 1.3 at baseline to 0.4 at 3 month follow up. 82 of the participants were taking medication for BPH preoperatively and by month 3, all but 8 had discontinued the medication. There were 69 adverse events reported in 56 participants; 33 grade 1 events, 15 grade 2 events, five grade 3a events and 16 grade 3b events. The authors concluded that Aquablation is safe and effective for men with LUTS due to BPH and replicate results previously seen in a trial setting. This study is limited by a lack of a concurrent control group and a relatively short-term efficacy follow-up.

A 2019 Cochrane review on Aquablation (Hwang et al.) identified only one RCT, the Gilling study described below. The authors concluded that based on short-term (up to 12 months) follow-up, the effect of Aquablation on urological symptoms is probably similar to that of TURP (moderate-certainty evidence). The effect on quality of life may also be similar (low-certainty evidence). There is uncertainty whether patients undergoing Aquablation are at higher or lower risk for major adverse events (very low-certainty evidence). Aquablation may result in little to no difference in erectile function but offer a small improvement in preservation of ejaculatory function (both very low certainty evidence). These conclusions are based on a single study of men with a prostate volume up to 80 mL in size. Longer-term data and comparisons with other modalities appear critical to a more thorough assessment of the role of Aquablation for the treatment of LUTS in men with BPH.

Gilling et al. (2019) compared 2-year safety and efficacy outcomes after Aquablation or TURP for the treatment of LUTS related to BPH. A total of 181 patients with BPH were randomly assigned (2:1 ratio) to either Aquablation or TURP. Patients and follow-up assessors were blinded to treatment. Assessments included the IPSS, MSHQ, IIEF and uroflow. At 2 years, IPSS scores improved by 14.7 points in the Aquablation group and 14.9 points in TURP ($p = 0.8304$, 95 % CI: - 2.1 to 2.6 points). Two-year improvements in Qmax were 11.2 and 8.6 cc/s for Aquablation and TURP, respectively ($p = 0.1880$, 95 % CI: - 1.3 to 6.4). Sexual function as assessed by MSHQ was stable in the Aquablation group and decreased slightly in the TURP group. At 2 years, PSA was reduced in both groups by 0.7 and 1.2 points, respectively; the reduction was similar across groups ($p = 0.1816$). Surgical re-treatment rates after 12 months for Aquablation were 1.7 % and 0 % for TURP. Over 2 years, surgical BPH

retreatment rates were 4.3 % and 1.5 % (p = 0.4219), respectively. The authors concluded that 2-year efficacy outcomes after TURP and Aquablation were similar, and the rate of surgical re-treatment was low and similar to TURP; Aquablation may be an alternative for men who strongly prefer maintenance of ejaculatory function. The sample size may however have been too small to detect clinically important differences.

Reale et al. (2019) performed a systematic review or case series and comparison studies, to evaluate functional outcomes (Qmax, QoL, IPSS, PVR), sexual outcome (erectile dysfunction and anejaculation rate), and adverse events evaluated according to the Clavien-Dindo classification. The functional outcomes, evaluated after water jet dissection, have shown improvement with respect to the baseline in all the selected articles. In the comparison papers with the TURP, the Aquablation has been statistically not inferior regarding functional outcomes. The sexual outcomes have highlighted a better ejaculation rate for water jet dissection than TURP. Regarding the adverse events, water jet dissection documented low rates of adverse events and, in comparison studies, were not statistically superior to TURP. Multicenter randomized trials with larger cohorts and longer follow-up are still needed.

A study to compare urodynamic outcomes between aquablation vs transurethral resection of the prostate (TURP) was performed (Pimentel et al., 2019). Patients (n=66) were randomized 2:1 (aquablation: TURP) in the Waterjet Ablation Therapy for Endoscopic Resection of prostate tissue study. Urodynamics were measured at baseline and 6 months. At mean baseline pDet@qmax was 71 and 73cm H20 in the aquablation and TURP groups, respectively. At 6-month follow-up, pDet@qmax decreased by 35 and 34cm H20, respectively. A large negative shift in bladder outlet obstruction index was observed, consistent with a large reduction in the proportion of subjects with obstruction at follow-up compared to baseline (79% to 22% in aquablation and 96% to 22% in TURP). The authors concluded that in this trial, improvements after aquablation in objective measures of bladder outlet obstruction were similar to those observed after TURP.

Plante et al. (2018) conducted prespecified post hoc exploratory subgroup analyses from a double-blind, multicenter prospective randomized controlled trial that compared transurethral resection of the prostate (TURP) using either standard electrocautery vs surgery using robotic waterjet (aquablation) to determine whether certain baseline factors predicted more marked responses after aquablation as compared with TURP. The primary efficacy endpoint was reduction in International Prostate Symptom Score (IPSS) at 6 months. The primary safety endpoint was the occurrence of Clavien-Dindo persistent grade 1 or grade ≥2 surgical complications. For men with larger prostates (50-80 g), the mean IPSS reduction was four points greater after aquablation than after TURP, a larger difference than the overall result. The primary safety endpoint difference was greater for men with large prostate compared with the overall result. Postoperative anejaculation was also less common after aquablation compared with TURP in sexually active men with large prostates vs the overall results. Exploratory analysis showed larger IPSS changes after aquablation in men with enlarged middle lobes, men with severe middle lobe obstruction, men with a low baseline maximum urinary flow rate, and men with elevated post-void residual urine volume. The authors concluded that in men with moderate-to-severe lower urinary tract symptoms attributable to BPH and larger, more complex prostates, aquablation was associated with both superior symptom score improvements and a superior safety profile, with a significantly lower rate of postoperative anejaculation. The authors noted that the standardized, robotically executed, surgical approach with aquablation may overcome the increased outcome variability in more complex anatomy, resulting in superior symptom score reduction. The RCT reported short-term outcomes and included patients with a prostate size 30 to 80 cc. Therefore, results may not be generalizable for all prostate sizes.

Gilling et al. (2018) conducted a double-blind, multicenter, prospective, randomized, controlled trial (WATER I) to compare safety and efficacy of Aquablation and transurethral prostate resection for the treatment of lower urinary tract symptoms related to benign prostatic hyperplasia. One hundred and eighty-one patients with moderate to severe lower urinary tract symptoms related to benign prostatic hyperplasia underwent transurethral prostate resection or Aquablation. The primary efficacy end point was the reduction in International Prostate Symptom Score at 6 months. The primary safety end point was the development of Clavien-Dindo persistent grade 1, or 2 or higher operative complications. The results showed the mean total operative time was similar for Aquablation and transurethral prostate resection, but resection time was lower for Aquablation. At month 6 patients treated with Aquablation and transurethral prostate resection experienced large I-PSS improvements. The prespecified study noninferiority hypothesis was satisfied. Of the patients who underwent Aquablation and transurethral prostate resection 26% and 42%, respectively, experienced a primary safety end point, which met the study primary noninferiority safety hypothesis and subsequently demonstrated superiority. Among sexually active men the rate of anejaculation was lower in those treated with Aquablation (10% vs 36%) The authors concluded that surgical prostate resection using Aquablation showed noninferior symptom relief compared to transurethral prostate resection but with a lower risk of sexual dysfunction. Larger prostates (50 to 80 ml) demonstrated a more pronounced superior safety and efficacy benefit.

Longer term follow-up would help assess the clinical value of Aquablation. This study was supported by PROCEPT Bio Robotics, the manufacturer of the AquaBeam® device. Several of the authors indicate a financial interest and/or other relationship with PROCEPT BioRobotics. These conflicts of interest may limit the conclusions that can be drawn from the study.

Gilling et al. (2017) performed a prospective, single arm, multicenter trial at a total of 3 centers in Australia and New Zealand with 1-year follow-up to establish the safety and effectiveness of aquablation, an image guided, robotic assisted, water jet tissue ablation technology, for the treatment of benign prostatic hyperplasia. A total of 21 men with moderate to severe lower urinary tract symptoms (LUTS) were included in the study with in-clinic follow up visits at 1, 3, 6 and 12 months. The visits included a review of AEs, uroflow measurements prostate specific antigen (PSA) measurement (at 6 and 12 months only), completion of study questionnaires, and (at 6 months only) urodynamics and transrectal ultrasound (TRUS). Symptoms related to LUTS had significantly improved from baseline at 1 month and were sustained through month 12. At 12 months, the mean international prostatic symptom score (I-PSS) score had improved by 16.2 points. The I-PSS QOL component improved by 3.3 points. Mean maximum urinary flow improved from 8.7 ml per second at baseline to 18.3 ml per second and post-void residual volume (PVR) improved from 136 to 54 ml. Prostate volume decreased from 57 ml at baseline to 35 ml. The bladder outlet obstruction index decreased from 48 at baseline to 13 a month 6. Mean serum PSA, which was measured in 20 subjects, showed no significant change from 3.15 ng/ml at baseline to 2.56 ng/ml at 12 months. No urinary incontinence developed, and sexual function was preserved postoperatively. The authors concluded that this study provides early evidence to support the safety and effectiveness of aquablation for symptomatic benign prostatic hyperplasia by improved symptom scores and other measures of obstruction. The study is of small sample size and lacks a concurrent control group.

Temporary Urethral Stents

Temporary urethral stents are used to maintain urine flow and for short-term use; they are commonly used in males with BPH. These temporary devices can be either removable or absorbable.

Ahn et al. (2020) retrospectively investigated the clinical effectiveness between two temporary urethral stents in the treatment of traumatic bulbar urethral strictures. 30 patients diagnosed with complete bulbar urethral rupture following blunt trauma underwent temporary urethral stent placement. Fifteen patients were treated with a thermo-expandable nickel-titanium alloy urethral stent (Memokath) and the other fifteen with the Allium Bulbar Urethral Stent (BUS). After placement, all stents were removed at 6 months with participant follow up at 1, 3, 6 and 12 months. The follow-up visits included patient assessment with uroflowmetry and ureteroscopy. While the BUS had a lower incidence of stent-related complications than Memokaths, the authors concluded both stents were effective for managing traumatic complete bulbar urethral rupture. This review is limited by lack of randomization, lack of comparison group undergoing traditional open urethroplasty, small sample size and short duration of follow-up; further investigation is warranted.

Chughai et al. (2020) conducted a RCT that compared a temporarily implanted nitinol device (iTind; aka ITIND or Tind) to that of a sham on 175 males with lower urinary tract symptoms due to benign prostatic hyperplasia (BPH). Inclusion criteria for the participants were males 50 years of age or older, an International Prostate Symptoms Score (IPSS) of ≥10, peak urinary flow rate (PFR) of ≤12 mL/sec with a 125 mL voided volume, and prostate volume between 25 and 75 cc. Subjects were randomized into either insertion of the iTIND or a sham control group; the sham group received the insertion of a foley catheter to simulate both implantation and retrieval of a temporary implanted device. The a priori primary outcome was changes in IPSS score at three months post procedure. In the intention to treat patient population, the iTind arm improved IPSS by -9.0 ± 8.5 (22.1-13.0) while the sham arm improved -6.6 ± 9.5 (22.8-15.8) (p = 0.063) at 3 months. A total of 78.6% of patients in the iTind arm showed a reduction of ≥3 points in IPSS, vs 60% of patients in the control arm at 3 months (p= .029). Adverse events occurred in 38.1% of patients in the iTind arm and 17.5% in the control arm. The study failed to identify significant differences between groups in peak urinary flow rate, quality of life, or sexual function. The authors found iTIND to be durable for twelve months with only 4.7% of participants having undergone another surgical intervention for BPH. 78.6% of the patients receiving the iTIND had improvement of their IPSS score. Limitations included mixed results, loss to follow-up of almost 30% of participants, and specific inclusion criteria that could or could not be applied to all males with BPH.

Porpiglia et al. (2018) reported 3-year outcomes from a prospective case series study involving the temporary implantable nitinol device (iTIND) implantation for the treatment of BPH. Thirty-two patients with LUTS were enrolled. Follow-up assessments were made at 3 and 6 weeks, and 3, 6, 12, 24 and 36 months after the implantation. The change from baseline in IPSS, QOL score and Qmax was significant at every follow-up time point. After 36 months of follow-up, a 41% rise in Qmax was achieved (mean 10.1 mL/s), the median (IQR) IPSS was 12 (6-24) and the IPSS QoL was 2 (1-4). Four early complications (12.5%) were recorded, including one case of urinary retention (3.1%), one case of transient incontinence due to device

displacement (3.1%), and two cases of infection (6.2%). No further complications were recorded during the 36-month follow-up. In the authors' opinion, the extended follow-up period supports the temporary stent to be safe, effective, and well-tolerated. Lack of comparison group or randomization and small patient population are limitations to this study.

Kimata et al. (2015) conducted a small prospective case series (n=37 elderly male patients) to evaluate the use of the Memokath in patients who required long-term urination management with Foley catheters. Patients were followed for a mean of approximately 33 months. A total of 21 patients (56.7%) were able to urinate without assistance after insertion of the Memokath stent. This study was hampered by several limitations, including lack of randomization and appropriate control group.

Kim et al. (2014) conducted a small cohort study (n=27) to compare patients who received treatment with a Memokath stent and a self-expandable covered metallic stent (UVENTA) for managing ureteral obstructions. Study results showed no significant differences between the two types of stents for benign and malignant ureteral obstructions. However, the clinical success rate was higher for the UVENTA stent (82.4%) compared with the Memokath stent (42.9%) (P=0.031). Patients who received the Memokath stent experienced tumor progression (n=2), stent migration (n=6), flank pain (n=1), and acute pyelonephritis (n=1). The study is limited by lack of comparison with other established treatments or randomization between the two stent types.

Jordan et al. (2013) investigated the ability of the Memokath™ 044TW stent to maintain urethral patency after dilation or internal urethrotomy for recurrent urethral stricture. A total of 92 patients with recurrent bulbar urethral strictures were treated with dilation or internal urethrotomy and randomized to short-term urethral catheter diversion (n=29) or insertion of a Memokath 044TW stent (n=63). The primary end point was urethral patency, as assessed by passage of a calibrated endoscope. Secondary end points included urinary symptoms and uroflowmetry parameters. Stents were scheduled to remain in situ for 12 months. The rate of successful stent insertion was 93.6%. In stented patients, patency was maintained significantly longer than controls (median 292 vs 84 days). Patency was reflected in significantly improved uroflowmetry and symptom scores. The stent was removed in 100% of patients. The most frequently noted side effects in stented patients were bacteriuria, hematuria and penile pain, which were usually mild and transient. Stent dislocation and occlusion were observed in 8 and 3 patients, respectively. The authors concluded that patients with recurrent bulbar urethral strictures treated with dilation or urethrotomy and a Memokath 044TW stent maintained urethral patency significantly longer than those treated with dilation or urethrotomy alone. The Memokath stent is not FDA approved and should be considered investigational. Based on differences in stent design, these findings may not be generalizable to FDA-approved devices.

Goh et al. (2013) assessed the ease of insertion and removal of a temporary prostatic stent (the Spanner) following the use of a prostatic urethral measuring device (the Surveyor™) in patients with bladder outflow obstruction or urinary retention awaiting definitive surgery. 16 patients had the Spanner inserted following use of the Surveyor. All insertions were uncomplicated. No symptomatic infection was reported. The stents stayed in situ for a median of 10 days. 12 stents were removed prematurely due to severe symptoms or retention. A total of 12 stents had to be removed endoscopically. The authors concluded that the Spanner is easy to insert. Stent removal via the retrieval suture has been difficult necessitating the use of endoscopy in the majority of cases. Possible causes of stent failure include underestimation of the prostatic urethral length by the Surveyor leading to obstruction by apical prostatic tissue, excessive suture length between the stent and distal anchor permitting proximal migration or inadequate suture length leading to urinary incontinence. According to the authors, further design modifications are suggested.

Following transurethral microwave thermotherapy, 186 patients were randomized to receive a Spanner (n=100) or the standard of care (n=86). The stent group reported significantly superior improvement in symptoms at the one-week follow-up visit. Thereafter, there was no significant difference between the stent and control groups. The investigators concluded that the Spanner is a safe, effective and well tolerated temporary stent for severe prostatic obstruction resulting from therapy induced edema after transurethral microwave thermotherapy (Dineen et al., 2008). Shore et al. published the same study in 2007. The study results are limited in demonstrating meaningful improvement in clinical outcomes in the group that received the temporary prostatic stent compared to the patients in the control group.

Egilmez et al. (2006) evaluated the efficacy of intraurethral metal stents in preventing or eradicating urinary-tract infections (UTI) during the management of bladder outlet obstruction (BOO) by comparing the frequency and nature of the infections with indwelling-catheter-associated UTI. The SAS relative-risk test was used to compare the risks of UTI in 76 patients with temporary urethral stents, 60 patients with BOO who had never been catheterized nor stented, and 34 patients with a permanent indwelling urethral catheter (PIUC). Infection was assessed 1 month after placement of the devices. After insertion of the catheter, UTI developed in 79.4% of the patients who originally had sterile urine. However, after insertion of the stent, UTI

developed in only 40.9% of the patients with sterile urine. In 21 (44.6%) of the catheterized patients who had infected urine, UTI was eradicated after stent insertion. The investigators concluded that urinary infection is a significant problem in patients with PIUC but is significantly less frequent and less severe in patients with urethral stents. These findings require confirmation in larger randomized controlled trials.

A series of 43 consecutive patients were stented with the Spanner temporary prostatic stent and reviewed retrospectively. Stents were removed and replaced every 3 months if tolerated. More than half of the patients (63%) had an unsatisfactory outcome, namely, immediate or delayed retention or elective removal because of unbearable symptoms. The remaining 37% of patients had a satisfactory outcome and either continued to have the stent in situ after a mean of five changes or are stent free after a successful voiding trial (Grimsley et al., 2007).

The National Institute for Health and Care Excellence (NICE) 2018 medical technology guidance on use of the Memokath-051 stent for ureteric obstruction concludes that the quality of reporting across all the studies was generally poor. None of the studies provided adequate details on patient characteristics, stent insertion procedures, follow-up, statistical analyses and uncertainty around the results. Migration rates and clinical success were the most commonly reported outcomes, but definitions of clinical success varied, so statistical pooling could not be done.

For information on current and completed trials studying the use of temporary prostatic urethral stents refer to ClinicalTrials.gov. (Accessed May 5, 2021)

Transperineal Focal Laser Ablation

Standard treatments for prostate cancer such as surgery and radiation involve the whole gland, even if the tumor is small and localized. These treatment modalities are associated with significant urinary and sexual dysfunction. Focal laser ablation (FLA) has been proposed as an alternative, as it allows the treatment of only the tumor, sparing the rest of the gland.

Bates et al. (2021) conducted a systematic review (SR) to compare the clinical effectiveness of primary focal ablative therapy (FT) to standard current treatment options for clinically localized prostate cancer (PCa) to make clinical practice recommendations, and identify gaps, providing recommendations for further research. Four primary studies (1 randomized controlled trial [RCT] and 3 retrospective studies) including 3,961 patients, (and ten eligible SRs were identified) reporting on different types of FT. The results showed the following: The RCT compared photodynamic therapy (PDT) with active surveillance and found PDT was associated with a significantly lower rate of treatment failure at 2 years, no difference in functional outcomes, and was associated with worse transient adverse events. A retrospective matched-pair study comparing focal high-intensity focused ultrasound (HIFU) with robotic radical prostatectomy (RP) found no significant differences in treatment failure at 3 years, while the focal HIFU group had better recovery of continence and erectile function. Two retrospective SEER-based, propensity- matched cohort studies compared focal laser ablation (FLA) against radical prostatectomy (RP) and external beam radiotherapy (EBRT), reporting significantly worse overall survival with FLA on adjusted analysis. Overall, the evidence in support of FT as an alternative to either AS or radical interventions for localized PCa is limited. Data regarding the oncological effectiveness were mixed and inconsistent. For FLA specifically, limited quality data suggest harm, as compared to alternative, established therapies. Overall, for FT, the vast majority of primary studies were small and uncontrolled; others were comparative studies with serious methodological flaws with extremely low internal and external validity. Most studies had significant clinical heterogeneity, with poorly defined populations, interventions (e.g., intermingling of whole-gland and FT as a single index intervention), different definitions of retreatments with different intervals, different imaging and follow-up schedules, different comparators, outcome measures with different definitions of treatment failure measured at different time points, and a lack of long-term data. The overview of SRs confirmed these findings, and none showed high-certainty evidence. The authors concluded that the routine use of FT in clinical practice is currently not recommended and should ideally be restricted to a clinical trial or prospective comparative study involving comprehensive data capture using standardized definitions and appropriate outcome measures.

In a 2019 Delphi consensus project following a systematic review of the literature, van Luijtelaar et al. presented the evidence-based consensus of 37 international experts in the field of focal therapy for prostate cancer (PCa). Consensus was agreed upon in 39/43 topics. Clinically significant PCa (csPCa) was defined as any volume Grade Group 2 [Gleason score (GS) 3+4]. Focal therapy was specified as treatment of all csPCa and can be considered primary treatment as an alternative to radical treatment in carefully selected patients. In patients with intermediate-risk PCa (GS 3+4) as well as patients with MRI-visible and biopsy-confirmed local recurrence, the experts felt that FLA is optimal for targeted ablation of a specific magnetic resonance imaging (MRI)-visible focus. However, FLA should not be applied to candidates for active surveillance and close follow-up is required.

Suitability for FLA is based on tumor volume, location to vital structures, GS, MRI-visibility, and biopsy confirmation. The expert consensus concluded that FLA is a promising technique for treatment of clinically localized PCa and should ideally be performed within approved clinical trials. They noted that there are only a few studies have reported on FLA and further validation with longer follow-up is mandatory before widespread clinical implementation is justified.

Valerio et al. (2017) completed a systematic review summarizing the evidence regarding the specific sources of energy used in focal ablative therapy for prostate cancer. Thirty-seven articles reporting on 3230 patients undergoing focal therapy were selected. Thirteen reported on high-intensity focused ultrasound, 11 on cryotherapy, three on photodynamic therapy, four on laser interstitial thermotherapy, two on brachytherapy, three on irreversible electroporation, and one on radiofrequency. Laser interstitial thermotherapy has been evaluated in up to Stage 2a studies. Median follow-up varied between 4 months and 61 months, and the median rate of serious adverse events ranged between 0% and 10.6%. Padfree leak-free continence and potency were obtained in 83.3–100% and 81.5–100%, respectively. In series with intention to treat, the median rate of significant and insignificant disease at control biopsy varied between 0% and 13.4% and 5.1% and 45.9%, respectively. The authors concluded that while focal therapy seems to have a minor impact on quality of life and genito-urinary function, the oncological effectiveness has not been defined against the current standard of care. The author identified limitations of this SR include the length of follow-up, the absence of a comparator arm, and study heterogeneity.

Transperineal Placement of Biodegradable Material

The SpaceOAR is used to temporarily position the anterior rectal wall away from the prostate during radiotherapy for prostate cancer and in creating this space it is the intent to reduce the radiation dose delivered to the anterior rectum. The absorbable spacer maintains space for the entire course of prostate radiotherapy treatment and is completely absorbed by the patient's body over time.

A Hayes report (2020) summarized that while published evidence suggests a potential benefit of an absorbable perirectal spacer (APS) during radiation therapy for prostate cancer, there is substantial uncertainty regarding its safety and efficacy; future studies are needed to assess the APS clinical usefulness and cost-effectiveness.

In a custom product brief, ECRI (2020) concludes that SpaceOAR hydrogel is well tolerated and works as intended to reduce rectal irradiation long-term, but not acute, rectal toxicity, and it improves bowel quality of life (QOL), based on one randomized controlled trial and four prospective nonrandomized comparative studies.

Afkhami Ardekani and Ghaffari (2020) evaluated the effect of dosimetry and procedure toxicity of polyethylene glycol (PEG)-based hydrogel spacers during prostate brachytherapy. There were twelve studies included in the systematic review involving 615 patients. The approach used to place the hydrogel spacers was hydrodissection and considered one of the most common techniques. Ultrasonography is used to insert a large gauge needle where saline water is injected to create potential space between the prostate and anterior rectal wall; PEG hydrogel is then injected into the created space. The DuraSeal and SpaceOar then polymerize within 3 and 10 seconds after injection. The authors found the data of several studies revealed the rectal dosimetry was significantly reduced with the use of the PEG hydrogel spacers and that the procedure was safe. The authors concluded the implantation of PEG hydrogel spacers is practical and safe with well tolerance of the procedure. The use of PEG hydrogels for prostate brachytherapy has a very high success rate, however the advantages of these spacers should be weighed against possible risks of complications. Additional RCTs should be done to further clarify rectal dose reduction on toxicity and quality of life.

A systematic review was conducted by Vaggers et al. (2020) from nine full text articles reviewing polyethylene glycol-based hydrogel rectal spacers for prostate brachytherapy. Four studies used the DuraSeal Spinal Sealant and five studies used SpaceOar. Primary outcomes included procedure complications, failures, prostate-rectum separation, rectal dosimetry and GI toxicities for hydrogel insertion. There was little variation in technique used throughout the articles reviewed. The authors found the studies demonstrated a significant reduction in rectal dosimetry and concluded that the polyethylene glycol-based hydrogel rectal spacers appear to be safe and easy. Even though the spaces appear to reduce rectal toxicity, further studies are needed to confirm these findings. Limitations include the review as retrospective and non-randomization along with small sample size.

Paetkau et al. (2019) retrospectively evaluated 13 patients with SpaceOAR implant to determine future planning needs for patients with prostate cancer undergoing radiation therapy. Computerized tomography (CT) scans were taken pre- and post-implant. A prescription of 60 Gy in 20 fractions was planned on both scans. Six treatment plans were produced per anonymized dataset using either a structure of rectum plus the hydrogel, termed composite rectum wall (CRW), or rectal wall (RW) as an

inverse optimization structure and intensity modulated radiotherapy (IMRT) or volumetric modulated arc therapy (VMAT) as a treatment technique. Dose-volume histogram metrics were compared between plans to determine which optimization structure and treatment technique offered the maximum rectal dose sparing. RW structures offered a statistically significant decrease in rectal dose over CRW structures, whereas the treatment technique (IMRT vs VMAT) did not significantly affect the rectal dose. There was improvement seen in bladder and penile bulb dose when VMAT was used as a treatment technique. The authors concluded that overall, treatment plans using the RW optimization structure offered the lowest rectal dose while VMAT treatment technique offered the lowest bladder and penile bulb dose.

Wu et al. (2018, included in Afkhami Ardekani and Ghaffari (2020) and Vaggers et al. (2020) systematic reviews above) evaluated 18 consecutive patients underwent transperineal ultrasound-guided placement of 10 cc of SpaceOAR hydrogel prior to HDR brachytherapy in the treatment of prostate cancer. Treatment plans were generated using an inverse planning simulated annealing algorithm. Rectal dosimetry for these 18 patients was compared with the 36 preceding patients treated with HDR brachytherapy without SpaceOAR. There was no difference in age, pretreatment prostate-specific antigen, Gleason score, clinical stage, prostate volume, or contoured rectal volume between those who received SpaceOAR and those who did not. Patients who received SpaceOAR hydrogel had significantly lower dose to the rectum as measured by percent of contoured organ at risk (median, V80 < 0.005% vs. 0.010%, p = 0.003; V75 < 0.005% vs. 0.14%, p < 0.0005; V70 0.09% vs. 0.88%, p < 0.0005; V60 = 1.16% vs. 3.08%, p < 0.0005); similar results were seen for rectal volume in cubic centimeters. One patient who received SpaceOAR developed a perineal abscess 1 month after treatment. The authors concluded that transperineal insertion of SpaceOAR hydrogel at the time of HDR brachytherapy is feasible and decreases rectal radiation dose. Further investigation is needed with well-designed clinical trials and larger patient populations to further assess the clinical impact.

Chao et al. (2018) conducted a prospective case series analysis to report on the dosimetric benefits and late toxicity outcomes following injection of a hydrogel spacer between the prostate and rectum in 76 patients with T1-T3a prostate cancer treated with radiotherapy. There were no postoperative complications reported. Mean prostate size were 66.0cc (25.0cc - 187.0cc). Rectal dose volume parameters were observed with volume of rectum receiving 70Gy (rV70), 75Gy (rV75) and 78Gy (rV78) were 7.8%, 3.6% and 0.4%. 21% (16/76) developed acute grade 1 GI toxicities but all were resolved completely by 3 months post-treatment. 3% (2/76) developed late grade 1 GI toxicities. No patients experienced acute or late grade 2+ GI toxicities. The authors concluded that injection of hydrogel spacer resulted in a reduction of irradiated rectal dose volumes along with minimal GI toxicities, irrespective of prostate size. Additional studies with longer-term outcomes are needed to evaluate long-term toxicities. The findings are limited by lack of comparison group.

Taggar et al. (2018, included in Afkhami Ardekani and Ghaffari (2020) and Vaggers et al. (2020) systematic review above) conducted a prospective cohort study to evaluate placement of an absorbable rectal hydrogel spacer in 74 patients with prostate cancer undergoing low-dose-rate brachytherapy with palladium-103. Rectal dosimetry was compared with a consecutive cohort of 136 patients treated with seed implantation without a spacer. On average, 11.2-mm (SD 3.3) separation was achieved between the prostate and the rectum. The resultant mean rectal volume receiving 100% of prescribed dose (V100%), dose to 1 cc of rectum (D1cc), and dose to 2 cc of rectum (D2cc) were 0 (SD 0.05 cc), 25.3% (SD 12.7), and 20.5% (SD 9.9), respectively. All rectal dosimetric parameters improved significantly for the cohort with spacer placement as compared with the non-spacer cohort. Injection of rectal spacer is feasible in the post-LDR brachytherapy setting and reduces dose to the rectum with minimal toxicity. Prostate and urethral dosimetries do not appear to be affected by the placement of a spacer.

Pinkawa et al. (2017a) reported 5-year outcomes of a cohort study after prostate cancer radiation therapy with and without the use of a hydrogel spacer. Fifty-four patients were selected to receive a hydrogel spacer. Patients were surveyed before RT; at the last day of RT; and a median time of 2 months, 17 months, and 63 months after RT. For patients treated with a hydrogel spacer, mean bowel function and bother score changes of >5 points in comparison with baseline levels were found only at the end of RT (10-15 points; P<.01). No spacer patient reported moderate or big problems with his bowel habits overall. Mean bother score changes of 21 points at the end of RT, 8 points at 2 months, 7 points at 17 months, and 6 points at 63 months after RT were found for patients treated without a spacer. A bowel bother score change >10 points was found in 6% versus 32% (P<.01) at 17 months and in 5% versus 14% (P=.2) at 63 months with versus without a spacer. The authors conclude that hydrogel spacer application demonstrates excellent treatment tolerability, in particular regarding bowel problems. They encourage further studies with dose-escalated or re-irradiation concepts.

Pinkawa et al. (2017b) evaluated in a cohort study of 167 consecutive patients who received prostate RT with 2 Gy fractions up to 76 Gy (without hydrogel, n = 66) or 76-80 Gy (with hydrogel, n = 101). The numbers of interventions resulting from bowel problems during the first 2 years after RT were compared. Patients were surveyed prospectively before RT, at the last day of RT, and at a median of 2 and 17 months after RT using a validated questionnaire (Expanded Prostate Cancer Index Composite). Treatment for bowel symptoms (0 vs. 11 %; p < 0.01) and endoscopic examinations (3 vs. 19 %; p < 0.01) were performed less frequently with a spacer. Mean bowel function scores did not change for patients with a spacer in contrast to patients without a spacer (mean decrease of 5 points) >1 year after RT in comparison to baseline, with 0 vs. 12 % reporting a new moderate/big problem with passing stools (p < 0.01). It was noted that statistically significant differences were found for the items "loose stools", "bloody stools", "painful bowel movements" and "frequency of bowel movements". The authors concluded that spacer injection is associated with a significant benefit for patients after prostate cancer RT.

Hamstra et al. (2017) reported the final outcomes from their single-blind phase III trial of image guided intensity modulated radiation therapy (n=222). The 3-year incidence of grade ≥1 (9.2% vs 2.0%; P=.028) and grade ≥2 (5.7% vs 0%; P=.012) rectal toxicity favored the spacer arm. Grade ≥1 urinary incontinence was also lower in the spacer arm (15% vs 4%; P=.046), with no difference in grade ≥2 urinary toxicity (7% vs 7%; P=0.7). From 6 months onward, bowel QOL consistently favored the spacer group (P=.002), with the difference at 3 years (5.8 points; P<.05) meeting the threshold for a MID. The control group the authors reported that the benefit of a hydrogel spacer in reducing the rectal dose, toxicity, and QOL declines after image guided intensity modulated radiation therapy for prostate cancer was maintained or increased with a longer follow-up period, providing stronger evidence for the benefit of hydrogel spacer use in prostate radiation therapy. Additional long-term outcomes are needed to determine the benefits of hydrogel spacers.

In a prospective, randomized patient-blinded clinical study, Karsh et al. (2017) compared image-guided intensity modulated prostate radiotherapy (79.2Gy in 44 fractions) in men with or without insertion of prostate-rectum hydrogel spacer (SpaceOar). The mean additional space created between the prostate and the rectum was just over 1cm, which allowed significant rectum and penile bulb radiation dose reduction resulting in less acute pain, lower rates of late rectal toxicity, and improved bowel and urinary QOL scores from 6 months through the 3-year follow-up period as compared to the control group. The authors concluded that spacer application significantly reduced rectal radiation dose, resulting in long-term reductions in rectal toxicity, as well as improvements in bowel, urinary, and sexual QOL. Patient sample volumes were not reported.

Yeh et al. (2016, included in Afkhami Ardekani and Ghaffari (2020) and Vaggers et al. (2020) systematic reviews above) studied rectal toxicity rates in 326 patients administered a polyethylene glycol (PEG) hydrogel rectal spacer in conjunction with combination high-dose-rate brachytherapy at 16 Gy (average dose 15.5 Gy; standard deviation [SD] = 1.6 Gy) and external beam radiotherapy of 59.4 Gy (average dose 60.2 Gy; SD = 2.9 Gy). Clinical efficacy was determined by measuring acute and chronic rectal toxicity using the National Cancer Center Institute Common Terminology Criteria for Adverse Events v4.0 grading scheme. Median follow-up was 16 months. The mean anterior-posterior separation achieved was 1.6 cm (SD = 0.4 cm). Rates of acute Grade 1 and 2 rectal toxicity were 37.4% and 2.8%, respectively. There were no acute Grade 3/4 toxicities. Rates of late Grade 1, 2, and 3 rectal toxicity were 12.7%, 1.4%, and 0.7%, respectively. There were no late Grade 4 toxicities. The authors concluded that acute and chronic rectal toxicities are low despite aggressive dose escalation. Longer term outcomes are needed to evaluate impact.

Mariados et al. (2015) conducted a prospective multicenter randomized controlled pivotal trial to assess outcomes following absorbable spacer (SpaceOAR system) implantation. The study included 222 patients with clinical stage T1 or T2 prostate cancer who underwent computed tomography (CT) and magnetic resonance imaging (MRI) scans for treatment planning, followed with fiducial marker placement. Patients were randomized to receive spacer injection or no injection (control). Spacer safety and impact on rectal irradiation, toxicity, and QOL were assessed throughout 15 months. Spacer application had a 99% hydrogel placement success rate. The authors reported that there were no device-related AEs, rectal perforations, serious bleeding, or infections within either group. Overall acute rectal adverse event rates were similar between groups, with fewer spacer patients experiencing rectal pain (P=.02). There was no late rectal toxicity greater than grade 1 in the spacer group. At 15 months 11.6% and 21.4% of spacer and control patients, respectively, experienced 10-point declines in bowel QOL. MRI scans at 12 months verified spacer absorption. The authors concluded that spacer application was well tolerated. Increased perirectal space reduced rectal irradiation, reduced rectal toxicity severity, and decreased rates of patients experiencing declines in bowel QOL. The spacer appears to be an effective tool, potentially enabling advanced prostate radiation therapy protocols. However, the short follow-up period is a study limitation, as researchers have published the median time to late gastrointestinal grade >2 toxicity onset was 17 months. The study was also limited by the exclusion of patients with prostate volumes >80 mL, patients with extracapsular extension, and those with prior radiation or surgery. Patients with extracapsular

extension have the theoretical risk of pushing posterior extracapsular disease farther from the prostate during radiation therapy, whereas patients with prior radiation or surgery may have perirectal scar formation, limiting space creation. The authors noted that the use of spacers in these populations should proceed cautiously in separate clinical trials.

Prostate Artery Embolization

Embolization places medications or synthetic materials through a catheter into a blood vessel to block blood flow to an area of the body. It may be used to control or prevent abnormal bleeding, close off vessels supplying blood to a tumor, eliminate abnormal connections between arteries and veins, or to treat aneurysms. When performed for the prostate in patients with benign prostatic hyperplasia (BPH), microspheres are injected into the prostate blood vessels, occluding the vessels which results in the gradual shrinking of the prostate tissue which widens the urethra, alleviating urinary difficulties. Evidence from several randomized controlled trials show inconclusive findings or inferiority of prostate artery embolization as compared to established treatments for effectiveness, with some apparent benefit for adverse events. Therefore, the evidence is currently insufficient to consider this technology to be proven as non-inferior or superior to established approaches.

In a 2021 systematic review and meta-analysis, Xiang et al. investigated the efficacy and safety of PAE versus TURP in patients with BPH. Eleven randomized controlled trials (RCTs) met the selection criteria, and ten independent patient series were included in the final analysis. Pooled estimates were inconclusive for the difference between TURP and PAE for patient-reported outcomes including International Prostate Symptom Score (2.32 (- 0.44 to 5.09)) and quality of life (0.18 (- 0.41 to 0.77)) at 12 months. PAE was less effective regarding improvements in most functional outcomes such as maximum flow rate, prostate volume, and prostate-specific antigen. PAE may however be associated with relatively fewer complications, lower cost, and shorter hospitalization. After the PAE procedure, the overall weighted mean differences for all outcomes except sexual health scores were significantly improved from baseline during follow-up to 24 months. The authors concluded that PAE is non-inferior to TURP with regard to improving patient-reported outcomes, though most functional parameters undergo more improvement after TURP than after PAE. They also concluded that PAE can significantly continue to relieve symptoms for 24 months without causing serious complications. The findings are limited by the overall sample size that may have been too small to demonstrate non-inferiority. For example, the upper limit of the pooled estimate for the International Prostate Symptom Score was 5 on a scale from 0 to 35. Furthermore, inferiority of PEA, compared to TURP was shown on other outcomes, with the exception of adverse events.

Xu et al. (2021) conducted a small case series to assess the safety and efficacy of PAE for large BPH and severe LUTS in 28 patients over the age of 80 who were not suitable candidates for open or endoscopic surgical procedures . PAE was performed using microspheres and functional outcomes including International Prostate Symptom Score (IPSS), quality of life (QoL), maximum urine flow rate (Qmax), post-void residual urine volume, prostate volume and total prostate-specific antigen level were evaluated at 1, 3, 6, and 12 months postoperatively. Safety was evaluated using perioperative data and included operative time, fluoroscopy time, changes in hemoglobin within 24 hours postoperatively, hospitalization days, postoperative duration, as well as complications. Bilateral PAE was performed in 25 patients, and 2 received unilateral PAE. The results showed technical success with PAE in 27 of the 28 participants. All of the functional outcomes results were significantly improved at 12 months postoperatively compared to baseline. The overall complication rate was 46.4%, and included post-embolization syndrome, hematuria, urinary tract infection, and acute urinary retention. The authors concluded that PAE may be an effective treatment option for patients with BPH that are not suitable candidates for open or endoscopic procedures following failed treatments. This study is limited by a lack of comparison group, a small number of participants and a short follow up period. Furthermore, radiation doses and fluoroscopy time were not examined.

In 2021, Abt et al. reported the two-year safety and efficacy outcomes of the open label, randomized non- inferiority trial they conducted in 2018 for which 12-week outcomes were reported previously. In the 2018 trial ((included in the Xiang systematic review), 103 participants aged 40 or greater with refractory LUTS secondary to benign prostatic obstruction (BPO) were treated with either PAE using 250-400 μm microspheres under local anesthesia, or monopolar transurethral resection of the prostate (TURP) under spinal or general anesthesia. International Prostate Symptoms Score (IPSS) and other patient reported outcomes, functional measures, prostate volume, and adverse events were evaluated. Changes from baseline to 2 years were tested for differences between the two interventions with standard two-sided tests. For the participants that received PAE, the results showed the mean reduction in IPSS was 9.21 points, and 12.09 points after TURP (difference of 2.88 [95% confidence interval 0.04–5.72]; p = 0.047) . TURP showed superiority for most other patient reported outcomes as well (except erectile dysfunction), including maximum urinary flow rate, reduction of postvoid residual urine, and reduction of prostate volume. Adverse events were less frequent after PAE than after TURP, but the severity was similar. 21% of participants who initially received PAE required TURP within 2 years due to unsatisfactory results. The authors concluded that PAE for the treatment of

BPH remains investigational due to inferior functional outcomes and a relevant re-treatment rate found 2 years after PAE compared with TURP. These disadvantages should be considered for patient selection and counselling.

In 2020, a Cochrane systematic review was performed to assess the effects of prostatic arterial embolization (PAE) compared to transurethral resection of the prostate (TURP) for the treatment of lower urinary tract symptoms in men with benign prostatic hyperplasia (BPH). Mean age, IPSS, and prostate volume of participants were 66 years, 22.8, and 72.8 mL, respectively. Primary outcomes assessed were urological symptom scores, quality of life and major adverse events. Based on the 6 RCTs with up to 12 month follow up (short term), as measured by the International Prostatic Symptom Score (IPSS), the authors found little to no difference in urological symptom score, and quality of life, ((with improvement mean difference (MD) 1.55, 95% confidence interval (CI) -0.40 to 3.50 in 369 participants in 6 RCTs with 75% low-certainty evidence on a scale from 0 to 35. Quality of Life (QOL) results also showed little to no difference with MD 0.16, 95% CI -0.37 to 0.68 in 309 participants in 5 RCTs with 56% low-certainty evidence on a scale from 0-6.)) There is low certainty evidence regarding the effects of PAE on major adverse events, with perineal pain, hematuria, and acute urinary retention commonly reported. Additionally, there was inconsistency in reporting and classifying the adverse events. PAE may increase the need for retreatment, with 47 or more (0 more to 214 more) per 1000 men receiving PAE compared to 18 re-treatments per 1000 men who received TURP. Regarding the effects of PAE on erectile dysfunction, the authors reported very low certainty evidence as measured by the International Index of Erectile Function (IIEF) that PAE may reduce ejaculatory disorders. Only one RCT reported 13-24 month (long term) follow up and the results showed in 95 participants very low certainty evidence on urological symptom scores and QOL compared to TURP, as well as major adverse events. There was no evidence regarding erectile function and ejaculation disorders. 56 re-treatments per 1000 men in the TURP group were identified, compared to 143 more (25 more to 430 more) per 1, 000 in the PAE group. The authors concluded that the evidence for the main outcomes assessed is low to very low and this procedure needs future research. (Jung et al., 2020)

In a May 2020 Hayes comparative effectiveness review of prostatic artery embolization (PAE) for the treatment of benign prostatic hypertrophy (BPH), it was concluded that based on a moderately large body of evidence, albeit low quality due to individual study limitations, PAE is reasonable safe, but long-term efficacy has not been adequately evaluated.

In a 2019 systematic review and meta-analysis, Zumstein et al. performed a systematic review and meta-analysis of clinical trials comparing the efficacy and safety of prostate artery embolization (PAE) to established surgical therapies. Functional parameters assessed included maximum urinary flow, post void residual, and reduction of prostate volume. There were 5 comparative studies consisting of 708 patients, some of which had an unclear risk of bias in patient selection, blinding, and incomplete outcome data. Reporting of complications varied widely and was poor in some. The results showed that compared to standard surgical therapies PAE showed less improvement in the International Prostate Symptom Score and was less efficient in a in all functional parameters assessed. Conversely, patient reported erectile function was better after PAE and there were significantly fewer adverse events overall. The authors concluded that PAE is safe and effective in the short term, particularly regarding safety and sexual function, but clear disadvantages for all other patient reported and functional outcomes assessed compared to established surgical therapies were identified. This suggests PAE is not as effective as established surgical therapies. The authors recommend large scale randomized controlled trials that include longer follow up, as well as defining ideal indications are mandatory before PAE can be considered a standard treatment option.

Abt et al. (2018) conducted a randomized, open label, non-inferiority trial in the urology and radiology departments of a Swiss tertiary care center. 103 patients aged ≥40 years with refractory lower urinary tract symptoms secondary to benign prostatic hyperplasia were randomized to receive prostatic artery embolization (PAE) with 250-400 μm microspheres under local anesthesia, or monopolar transurethral resection of the prostate (TURP) under spinal or general anesthesia. 48 and 51 patients reached the primary endpoint 12 weeks after PAE and TURP, respectively. Primary outcome was change in international prostate symptoms score (IPSS) from baseline to 12 weeks after surgery (a difference of less than 3 points between treatments was defined as non-inferiority for PAE and tested with a one-sided t test). Secondary outcomes included further questionnaires functional measures, magnetic resonance imaging findings and adverse events. Changes from baseline to 12 weeks were compared between treatments with two sided tests for superiority. The authors failed to prove non-inferiority for the primary outcome (1.54 points in favor of TURP (95% confidence interval −1.45 to 4.52)), but fewer adverse events occurred after PAE than after TURP (36 v 70 events; P=0.003). (This trial was included in the systematic review by Xiang et al. 2021, and Jung et al. 2020)

The 2018 NICE guidelines for prostate artery embolization for lower urinary tract symptoms caused by BPH states that the current evidence of the safety and efficacy is adequate to support the use of this procedure provided that standard

arrangements are in place for clinical governance, consent and audit. Furthermore, patient selection should be done by a urologist and an interventional radiologist. This procedure is technically demanding and should only be done by an interventional radiologist with specific training and expertise in prostatic artery embolization.

Clinical Practice Guidelines

American Urological Association (AUA)

In 2020, the AUA (Parsons et al.) amended their clinical guidelines on the surgical management of BPH/LUTS. Included in their guideline statements are the following:

- PUL may be offered as an option for patients with LUTS attributed to BPH provided prostate volume <80g and verified absence of an obstructive middle lobe (Moderate Recommendation; Evidence Level: Grade C).
- PUL may be offered to eligible patients who desire preservation of erectile and ejaculatory function (Conditional Recommendation; Evidence Level: Grade C).
- Aquablation may be offered to patients provided prostate volume >30/<80g. (Conditional Recommendation; Evidence Level: Grade C)
- Water vapor thermal therapy:
  - May be offered to patients with LUTS/BPH with a prostate volume of <80g. patients should be informed that evidence of efficacy, including longer-term retreatment rates, remains limited. (Conditional Recommendation; Evidence Level: Grade C)
  - Patients who desire preservation of erectile and ejaculatory function (Conditional Recommendation; Evidence Level: Grade C)
- Prostate artery embolization is not recommended for the treatment of LUTS/BPH outside the context of a clinical trial until sufficient evidence from rigorous studies is available that show benefit over well-established therapies (Expert Opinion)

American Urological Association/ American Society for Radiation Oncology (ASTRO)/ Society of Urologic Oncology (SUO)

In a 2017 AUA/ASTRO/SUO practice guideline for clinically localized prostate cancer states that if focal therapy is offered as an alternative treatment modality for localized prostate cancer, it should only be done within the context of a clinical trial. Initial studies with short term follow up suggest that effective disease eradication in the treated volume can be attained, however, it should be noted that long-term follow up data is lacking. The Panel recognizes that concern exists about the potential for undetected and, therefore, occult untreated clinically significant multifocal disease. The also state that confirmation of oncologic effectiveness is currently lacking and will require prospective studies with long-term follow up. Additionally, this practice guideline states that prostate cancer is often multifocal, clinicians should inform localized prostate cancer patients considering focal therapy that focal therapy may not be curative and that further treatment for prostate cancer may be necessary.

The clinical guidelines on advanced prostate cancer (Lowrance et al., 2020), and clinically localized prostate cancer (Sanda et al., 2017) do not include water vapor therapy as a treatment option.

The National Comprehensive Cancer Network (NCCN)

Clinical practice guidelines for the treatment of prostate cancer (v21.2021) states “biocompatible and biodegradable perirectal spacer materials may be implanted between the prostate and rectum in patients undergoing external radiotherapy with organ-confined prostate cancer in order to displace the rectum from high radiation dose regions. Perirectal spacer materials may be employed when the other techniques are insufficient to improve oncologic curet rates and/or reduce side effects due to anatomic geometry or other patient related factors, such as medication usage and/or comorbid conditions. Patients with obvious rectal invasion or visible T3 and posterior extension should not undergo perirectal spacer implantation.

NCCN Clinical Practice Guidelines in Oncology do not mention water vapor thermotherapy for the treatment of prostate cancer (2021).

Society of Interventional Radiology (SIR)

In a 2020 multi-society, evidence -based position statement regarding PAE for the treatment of lower urinary tract symptoms due to BPH, the SIR states that PAE is a safe and effective treatment, has good short and intermediate term efficacy and is a treatment option for the following:

- For appropriately selected men with BPH and moderate to severe LUTS (strong recommendation)
- In patients with BPH and moderate to severe LUTS who have very large prostate glands (> 80 cm3), without an upper limit of prostate size (moderate recommendation)
- In patients with BPH and acute or chronic urinary retention in the setting of preserved bladder function as a method of achieving catheter independence (moderate recommendation)
- In patients with BPH and moderate to severe LUTS who wish to preserve erectile and/or ejaculatory function (weak recommendation)
- In patients with hematuria of prostatic origin as a method of achieving cessation of bleeding (strong recommendation)
- in patients with BPH and moderate to severe LUTS who are deemed not to be surgical candidates for any of the following reasons: advanced age, multiple comorbidities, coagulopathy, or inability to stop anticoagulation or antiplatelet therapy (moderate recommendation)
- PAE should be included in the individualized patient centered discussions regarding treatment options (strong recommendation)

SIR also gives a strong recommendation that Interventional radiologists, given their knowledge of arterial anatomy, advanced microcatheter techniques, and expertise in embolization procedures, are the specialists best suited for the performance of PAE. (McWilliams et al., 2019)

U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

Prostate surgeries are procedures and, therefore, not regulated by the FDA. However, devices and instruments used during the surgery may require FDA approval. See the following website for additional information: http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm. (Accessed June 3, 2021)

On September 13, 2013, the FDA approved the UroLift® System (Teleflex Inc., Pleasanton, CA) for marketing through a de novo classification as a class II device used as a permanent implant to relieve low or blocked urine flow in men with BPH. Since that time, additional FDA clearances have been granted. For additional information see the following, using the product code PEW: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm?ID=K193269. (Accessed June 3, 2021)

On August 2, 2019, The U.S. Food and Drug Administration (FDA) cleared the Rezūm™ Water Vapor Therapy system (Boston Scientific Corp.) under 510(k) premarket notification for treatment of symptoms of benign prostatic hyperplasia (BPH), and treatment of the prostate with hyperplasia of the central zone and/or a median lobe. It is not approved for treatment of malignant prostate tissue. For additional information, see: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm?ID=K191505. (Accessed April 16, 2021)

The U.S. Food and Drug Administration (FDA) has cleared powered laser devices under 510(k) Premarket Notification. For device specific information, search product code GEX here: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm. (Accessed April 15, 2021)

The U.S. Food and Drug Administration (FDA) cleared SpaceOAR Vue hydrogel (Boston Scientific Corporation) (K182971) under its 510(k) premarket notification process as substantially equivalent to predicate devices on June 19, 2019. For additional information see the following: https://www.accessdata.fda.gov/cdrh_docs/pdf18/K182971.pdf. (Accessed May 20, 2021)

The U.S. Food and Drug Administration (FDA) approved the Spanner® Temporary Prostatic Stent (SRS Medical, North Billerica, MA) on December 14, 2006. Refer to the following website for additional information:
- https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma_template.cfm?id=p060010
- https://www.accessdata.fda.gov/cdrh_docs/pdf6/p060010a.pdf

(Accessed May 5, 2021)

In December 2017, the FDA granted a De Novo request for the ITind system (Olympus America, Center Valley, PA) (DEN190020), a temporarily-placed system for the urethra to treat urinary symptoms associated with BPH. Refer to the following

website for additional information: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/denovo.cfm. (Accessed May 5, 2021)

On March 3, 2021 the Aquabeam® Robotic System (Procept BioRobotics, Redwood City, CA) received 510(k) approval as a Class II device. Refer to the following for further information: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm?ID=K202961. (Accessed May 21, 2021).

In June 2017, the FDA granted a De Novo request for Embosphere® Microspheres (Merit Medical Systems, Jordan, UT) for embolization of prostatic arteries for symptomatic benign prostatic hyperplasia. Refer to the following website for additional information: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/denovo.cfm?id=DEN160040. (Accessed June 10, 2021).

For additional information on microsphere products with 510(k) premarket notification, refer to the following website and search by product code NOY: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm. (Accessed June 10, 2021)

The Memokath has not yet received FDA approval.

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Policy History/Revision Information

Date	Summary of Changes
06/01/2022	**Coverage Rationale** • Removed references to specific InterQual® release dates; refer to the most current InterQual® criteria **Supporting Information** • Archived previous policy version 2022T0618C

Instructions for Use

This Medical Policy provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the member specific benefit plan document must be referenced as the terms of the member specific benefit plan may differ from the standard plan. In the event of a conflict, the member specific benefit plan document governs. Before using this policy, please check the member specific benefit plan document and any applicable federal or state mandates. UnitedHealthcare reserves the right to modify its Policies and Guidelines as necessary. This Medical Policy is provided for informational purposes. It does not constitute medical advice.

This Medical Policy may also be applied to Medicare Advantage plans in certain instances. In the absence of a Medicare National Coverage Determination (NCD), Local Coverage Determination (LCD), or other Medicare coverage guidance, CMS allows a Medicare Advantage Organization (MAO) to create its own coverage determinations, using objective evidence-based rationale relying on authoritative evidence (Medicare IOM Pub. No. 100-16, Ch. 4, §90.5).

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