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Overview
This Coverage Policy addresses surgical and minimally invasive procedures used in the treatment of benign prostatic hyperplasia (BPH).

Coverage Policy
Prostatic urethral lift (e.g., UroLift) is considered medically necessary for the treatment of symptomatic benign prostatic hyperplasia (BPH) when ALL of the following criteria are met:

- age 45 years or above
- estimated prostate volume < 80 cc
- no obstructive median lobe of the prostate identified on cystoscopy
- failure, contraindication or intolerance to a trial of conventional medical therapy for BPH (e.g., alpha blocker, PDE5 Inhibitor, finasteride/dutasteride)

Water vapor thermal therapy (e.g., Rezūm System) is considered medically necessary for the treatment of symptomatic benign prostatic hyperplasia (BPH) when ALL of the following criteria are met:
• age 50 years or above
• estimated prostate volume $\geq 30 \text{ cm}^3$ and $\leq 80 \text{ cm}^3$
• failure, contraindication or intolerance to a trial of conventional medical therapy for BPH (e.g., alpha blocker, PDE5 Inhibitor, finasteride/dutasteride)

The following treatments for benign prostatic hyperplasia (BPH) are considered experimental, investigational or unproven:

• absolute ethanol injection
• cryosurgical ablation
• high-intensity focused ultrasound (HIFU)
• histotripsy
• interstitial laser coagulation (ILC)
• plasma kinetic vaporization (e.g., PlasmaKinetic™ Tissue Management System)
• prostate artery embolization
• temporary implantable nitinol device (TIND)
• transrectal thermal therapy
• transurethral balloon dilation of the prostatic urethra
• transurethral ultrasound-guided laser incision of the prostate (TULIP)
• water-induced thermotherapy (WIT)
• waterjet tissue ablation (e.g., AquaBeam System)

Note: Pharmacologic therapy is not considered within the scope of this Medical Coverage Policy. Please refer to the applicable pharmacy benefit to determine availability and the terms and conditions of coverage related to the treatment of BPH.

General Background

Benign prostatic hyperplasia (BPH) is a common condition caused by the abnormal growth of non-malignant prostate cells in men that can result in bothersome lower urinary tract symptoms (LUTS) (e.g., urinary urgency and frequency, weak stream and straining, urinary obstruction or retention, renal insufficiency, hydronephrosis, recurrent gross hematuria, recurrent or persistent urinary tract infections, urosepsis, large bladder diverticula, and bladder stones) (Hoffman, 2007). The most frequent indications for surgical management are moderate-to-severe voiding symptoms that are refractory to medical management.

Treatment of BPH is individualized to the patient and involves evaluation of symptoms along with objective findings from examination and laboratory results. Initial treatment for BPH is usually drug therapy (e.g., alpha blocker, PDE5 Inhibitor, finasteride/dutasteride) designed to relieve obstruction, but this often provides only modest relief, and up to 30% of patients require surgical intervention. There are several proposed surgical treatments for BPH that involve burning, cutting, or removal of prostatic tissue (Moul, et al., 2019; American Urological Association [AUA], last updated 2020). Transurethral resection of the prostate (TURP) is considered the gold standard for surgical treatment of BPH. However, several other minimally invasive surgical procedures and therapies have been widely used and are supported by relevant professional societies. Generally, data in the published, peer-reviewed literature demonstrate improved outcomes and support the safety and effectiveness of these other established therapies. These surgeries and therapies include:

• Contact laser ablation of the prostate (CLAP)
• Holmium laser ablation, enucleation, resection (HoLAP, HoLEP, HoLRP)
• Laser vaporization and laser ablation/coagulation
• Open/laparoscopic prostatectomy
• Photoselective vaporization of the prostate (PVP)
• Stents (e.g., UroLume® endourethral prosthesis)
• Transurethral resection of the prostate (TURP)
• Transurethral needle ablation (TUNA), also known as radiofrequency needle ablation (RFNA)
• Transurethral electrovaporization (TUVP, TVP, TUEP), also known as transurethral vapor resection of the prostate (TUVRP)
• Transurethral microwave thermotherapy (TUMT)
• Transurethral incision of the prostate (TUIP)

Prostatic Urethral Lift (PUL)
The UroLift System™ (NeoTract Inc., Pleasanton, CA) is a minimally invasive, prostatic urethral lift (PUL) system that provides anterolateral mechanical traction of the lateral lobes of the prostate, opening the urethral lumen, and reducing urinary obstruction. The delivery device contains a preloaded implant that deploys, self-adjusts, tensions, and trims a permanent tensioning suture. The suture runs from the urethra to the outer prostatic capsule and serves to compress the lateral lobe of the prostate. Implants are delivered bilaterally to separate the encroaching lobes. Four to 5 implants are typically inserted, but this varies with the size and shape of the prostate. The UroLift System is intended for the treatment of symptoms due to urinary outflow obstruction secondary to BPH in men ≥ 45 years of age. The UroLift may be used to treat prostate glands measuring <80 milliliters (mL) in size in the United States. The UroLift System is generally implanted by an urologist in an outpatient or inpatient setting. In order to determine whether a patient is an ideal candidate, the target locations and number of implants, and the ability to perform the procedure in the clinic, a planning cystoscopy and transrectal ultrasound (TRUS) are useful. The transurethral procedure to insert the UroLift is performed with the use of local or general anesthesia and oral sedation. The evidence suggests that the UroLift does not appear to compromise sexual function, which is an advantage of this device compared with the standard BPH treatment, TURP. It has been proposed that the adoption of this device for appropriately selected patients may lead to a reduction in the utilization of inpatient hospital services for more invasive procedures such as TURP (Hayes, 2020; NeoTract, 2020; Roehrborn, et al., 2016, 2015a; Perera, et al., 2015; Barkin, et al., 2012).

Food and Drug Administration (FDA):
In 2013, the FDA granted a de novo classification clearance for the NeoTract® UroLift System (NeoTract, Inc., Pleasanton, CA); the system was classified as an implantable transprostatic tissue retractor system (K130651). The de novo process provides a route to market for medical devices that FDA considers to be low to moderate risk but receive class III classification because FDA has found them to be “not substantially equivalent” to any previous device that is already legally marketed. According to the FDA summary document, the UroLift system “is indicated for the treatment of symptoms due to urinary outflow obstruction secondary to [BPH] in men age 50 and above.” The FDA contraindications state:

The UroLift System should not be used if the patient has:
• prostate volume of >80 cc
• an obstructive or protruding median lobe of the prostate
• a urinary tract infection
• urethra conditions that may prevent insertion of delivery system into bladder
• urinary incontinence
• current gross hematuria
• a known allergy to nickel

In December 2013, FDA granted 510(k) clearance for a modified version of the NeoTract UroLift System, with the prior version serving as the predicate device.

In January 2017, FDA granted 510(k) clearance for UroLift System (UL400 and UL500) for the treatment of symptoms due to urinary outflow obstruction secondary to BPH, including lateral and median lobe hyperplasia, in men 45 years of age or older. The UroLift System includes two generations of the device, the UL400 and the UL500. Both generations use the same UroLift Implant. The only differences are in the delivery device. The median lobe clinical study was the prospective Median Lobe Prostatic UroLift System Procedure (MedLift) study. The FDA contraindications were updated.

The FDA 510(k) summary states that the clinical data demonstrates that treatment of the median lobe with the UroLift System has the same safety and effectiveness as treatment of the lateral lobes (K173087). In addition, literature data and medical opinion support lowering the age indication from 50 years old to 45 years old since
there is no clinical difference between the two patient populations. The overall risk profile remains the same for
the UroLift System. As such, the UroLift System is substantially equivalent to the UroLift System cleared in
K133281 and K172359.

The UroLift System should not be used if the patient has:
- prostate volume of >80 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

In June 2020, FDA granted 510(k) clearance for the UroLift Advanced Tissue Control (ATC) System (K200441)
for the treatment of 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. The UroLift ATC System
is substantially equivalent to the predicate UL400 device with the exception that there was a modification made
to the distal tip allowing for a larger footprint during the procedure and effective mobilization of tissue when
needed.

The UroLift System should not be used if the patient has:
- 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

In July 2020, FDA granted 510(k) clearance for the NeoTract UroLift 2 (UL2) System (K201837) for the treatment
of 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. The UL2 System is substantially equivalent to the
predicate UroLift UL500 System by NeoTract. Minor modifications were made to the device including the delivery
handle and the implant cartridge that do not affect the overall safety and effectiveness of the UroLift procedure.
Contraindications remain the same as the ATC System.

Literature Review:
Prostatic Urethral Lift (PUL) has been widely used and is supported by relevant professional societies. Evidence
in the published, peer-reviewed scientific literature consists of randomized controlled trials and smaller
prospective, retrospective, and case series studies. The evidence suggests that PUL using the UroLift System
relieves symptoms in men age 50 years or older who have urinary outflow obstruction secondary to BPH
however there is a lack of large randomized studies with long-term outcomes data comparing PUL with other
established BPH treatments including TURP. Studies on the PUL procedure have been conducted in the United
States, Canada, Europe, and Australia. Patient inclusion and exclusion criteria were relatively consistent
between the large trials, with patients 50 years old or older, in International Prostate Symptom Score (IPSS)
greater than 12, and Qmax less than 12 to 15 mL/s. Prostate volume ranges have varied, with the US studies
ranging from 30 to 80cm³ and European and Australian studies typically ranging up to 100cm³ (Woo, et al., 2011,
2012; Chin, et al., 2012; McNicholas, et al., 2013; Roehrborn, et al., 2013, 2015a, 2015b, 2016, 2017a; Cantwell,
et al., 2014; McVary, et al., 2014; Shore, et al., 2014; Perera, et al., 2015; Sønksen, et al., 2015; Bozkurt, et al.,

Professional Societies/Organizations:
Management of Benign Prostatic Hyperplasia/Lower Urinary Tract Symptoms” addresses surgical and minimally
invasive procedures used in the treatment of benign prostatic hyperplasia (BPH). The AUA states that clinical
scenarios exist where conservative management (e.g., medications), used alone or in combination with a
minimally invasive surgery, is either inadequate or inappropriate (e.g., renal insufficiency, patient preference) in
which case consideration of one of the more invasive treatment modalities is warranted. Prostatic Urethral Lift
(PUL) is discussed in the updated 2018 (amended 2020) AUA evidence-based Guideline: Surgical Management
of Benign Prostatic Hyperplasia/Lower Urinary Tract Symptoms with the following statement:
• 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.

• PUL may be offered to eligible patients who desire preservation of erectile and ejaculatory function.

**Use Outside of the US:**

European Association of Urology (EAU) guidelines on management of non-neurogenic male LUTS include prostatic urethral lift recommendations stating to offer prostatic urethral lift (Urolift®) to men with LUTS interested in preserving ejaculatory function, with prostates < 70 mL and no middle lobe (Strength Rating: Strong) (Gravas et al., 2019).

The updated 2018 Canadian urological Association (CUA) guideline on male lower urinary tract symptoms/benign prostatic hyperplasia (MLUTS/BPH) recommendation for PUL states: We suggest that prostatic urethral lift (Urolift) may be considered an alternative treatment for men with LUTS interested in preserving ejaculatory function, with prostates <80 cc and no middle lobe (conditional recommendation based on moderate-quality evidence) (Nickel, et al., 2018).

In September 2015, the National Institute for Clinical Excellence ([NICE] United Kingdom) published a Medical Technology Guidance on UroLift for Treating Lower Urinary Tract Symptoms of Benign Prostatic Hyperplasia. The guidance stated that surgical options should be considered after the failure of conservative management and medication. The NICE Committee concluded that “the UroLift system is effective in relieving symptoms of benign prostatic hyperplasia. It noted that the degree of symptom relief outcomes is slightly less than that after transurethral resection of the prostate (TURP) or holmium laser enucleation (HoLEP), but it is sufficient and clinically important. The Committee recognized that the duration of symptom relief after using the UroLift system is uncertain. It concluded that it is similar in the medium term (up to 3 years) to the comparators but that further evidence on durability and the need for subsequent procedures would be useful.”

NICE recommendations state:

• “The clinical case for adopting the UroLift system for treating lower urinary tract symptoms of benign prostatic hyperplasia is supported by the evidence. The UroLift system relieves lower urinary tract symptoms while avoiding the risk to sexual function associated with transurethral resection of the prostate (TURP) or holmium laser enucleation of the prostate (HoLEP). Using the system reduces the length of a person’s stay in hospital. It can also be used in a day-surgery unit.

• 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.”

**Water Vapor Thermal Therapy (e.g., Rezūm System):** A new approach to thermal therapy using convective radiofrequency (RF) water vapor energy has emerged to treat men with moderate-to-severe lower urinary tract symptoms (LUTS). The principles of RF-generated water vapor thermal energy are based on the thermodynamic properties of water and the use of convective versus conductive heat transfer to ablate tissue. Examples of conductive heat transfer technologies include TUNA using RF and TUMT using microwaves to generate thermal energy.

**Food and Drug Administration (FDA):**

In August 2015, the Rezūm ® System (NxThera, Inc., Maple Grove, MN) received FDA 510(k) approval. The Rezūm System is classified by the FDA as an endoscopic electrosurgical unit. The FDA indications for use state: The Rezūm System is intended to relieve symptoms, obstructions, and reduce prostate tissue associated with BPH. It is indicated for men ≥ 50 years of age with a prostate volume ≥ 30 cm³ and ≤ 80 cm³. The Rezūm System is also indicated for treatment of prostate with hyperplasia of the central zone and/or median lobe. Per the FDA 510(k) Summary the device has also been tested in three clinical studies to evaluate the safety and effectiveness of the Rezūm device: 65 patients in the feasibility and pilot open label studies and in a 197 patient randomized placebo controlled study. All these studies showed that the device is safe and effective. The device
converts water into vapor outside of the body and the vapor is delivered to the prostate tissue via a needle within the sterile Delivery Device. The vapor ablates the targeted tissue within the prostate via thermal ablation as energy is transferred from the vapor to the prostate tissue. The amount of vapor delivered is controlled by an RF Generator which also controls the amount of saline flush used to cool the urethra (FDA, 2015, 2016). The procedure can be performed in an office or outpatient treatment setting.

**Literature Review:**
Although there is a paucity of data in the peer-reviewed scientific literature comparing water vapor thermal therapy (e.g., Rezūm System) to other treatment options for BPH such as microwave TUMT and radiofrequency TUNA, the therapy has been widely used and is supported by relevant professional societies. The evidence in the peer-reviewed scientific literature provides consistent results suggesting that the Rezūm System may be an effective treatment for LUTS associated with BPH. Improvements in urinary symptoms and BPH-related quality of life from baseline were generally consistent across studies. Treatment with the Rezūm System is generally safe and not associated with loss of sexual function (Dixon, et al., 2015b, 2016; McVary, et al., 2016a; Darson, et al., 2017; Roehrborn, et al., 2017b; Hayes, 2018, annual review 2020; McVary and Roehrborn, 2018).

**Professional Societies/Organizations:**
Water vapor thermal therapy is discussed in the updated 2018 (amended 2020) American Urological Association (AUA) evidence-based Guideline: Surgical Management of Benign Prostatic Hyperplasia/Lower Urinary Tract Symptoms. The recommendations were based on results of the randomized controlled trial conducted by McVary et al. (2016a). The guideline recommendation states:

- Water vapor thermal therapy may be offered to patients with LUTS attributed to BPH provided prostate volume <80g. (Conditional Recommendation; Evidence Level: Grade C)
- Water vapor thermal therapy may be offered to eligible patients who desire preservation of erectile and ejaculatory function. (Conditional Recommendation; Evidence Level: Grade C)

**Use Outside of the US:**
The 2019 European Association of Urology (EAU) guideline on Management of Non-neurogenic Male LUTS addresses techniques under consideration including convective water vapor energy (WAVE) ablation: The Rezūm system. The guideline practical considerations state that further RCTs against a reference technique are needed to confirm the first promising clinical results and to evaluate mid- and long-term efficacy and safety of water vapor energy treatment (Gravas et al., 2019).

The updated 2018 Canadian Urological Association (CUA) guideline on male lower urinary tract symptoms/benign prostatic hyperplasia (MLUTS/BPH) recommendation for convective water vapor energy ablation states that Rezūm system of convective water vapor energy ablation may be considered an alternative treatment for men with LUTS interested in preserving ejaculatory function, with prostates <80 cc, including those with median lobe (conditional recommendation based on moderate-quality evidence) (Nickel, et al., 2018).

In 2020, the National Institute for Clinical Excellence ([NICE] (United Kingdom) published a Medical Technologies Guidance on Rezūm for the treatment of lower urinary tract symptoms secondary to benign prostatic hyperplasia. The guidance included the following recommendations:

- Evidence supports the case for adopting Rezūm for treating LUTS caused by benign prostatic hyperplasia (BPH) in the National Health Service.
- Rezum is a minimally invasive procedure. It should be considered as a treatment option for people with:
  - moderate to severe LUTS (International Prostate Symptoms Score [IPSS] typically 13 or over) and
  - a moderately enlarged prostate (typically between 30 cm3 and 80 cm3).

**Additional Therapies:**
Numerous other therapies have been proposed for the treatment of BPH however, to date there is insufficient evidence in the published peer-reviewed scientific literature to demonstrate safety and effectiveness of these therapies.
**Absolute Ethanol Injection:** Absolute Ethanol Injection is a minimally invasive procedure that can be performed in an outpatient setting and has been proposed as a treatment for benign prostatic hypertrophy (BPH). Ethanol injection is performed using dehydrated ethanol injected with a flexible injection needle through the side channel of a cystoscope and into the targeted tissue. The result is coagulation necrosis (chemoablation) aimed at destroying the enlarged tissue (Sakr, et al., 2009).

**Literature Review:**
Randomized controlled trials data are lacking regarding the safety and effectiveness of absolute ethanol injection compared to standard therapy for the treatment of BPH. Two small prospective nonrandomized studies without comparators and a case series study totaling 123 patients demonstrated improvements in International Prostate Symptom Score (IPSS), quality of life scores, and significant differences in peak flow volumes and post void residual after therapy (Arslan, et al., 2014; Sakr, et al., 2009; Magno, et al., 2008).

**Use Outside of the US:**
The National Institute for Clinical Excellence (NICE) (United Kingdom) (NICE, 2015) does not recommend absolute ethanol injection for the treatment of BPH. Absolute ethanol injection for the treatment of BPH is not discussed in published guidelines of the AUA, CUA and EUA (Nickel, et al., 2018; Gravas et al., 2019).

**Cryosurgical Ablation:** Cryosurgical ablation is a minimally invasive therapy that aims to destroy prostate tissue through local freezing and has been proposed for the treatment of benign prostatic hypertrophy.

**Literature Review:**
There are scarce data in the published peer-reviewed scientific literature to support the safety and effectiveness of cryosurgical ablation for the treatment of BPH. At this time the role of this therapy has not yet been established.

**High-Intensity Focused Ultrasound (HIFU):** High-intensity focused ultrasound (HIFU) is a procedure which uses a small probe to produce bursts of ultrasound that creates coagulation necrosis in a specific area of tissue. Frequencies range from 4–10 MHz, although 4 MHz is most frequently used. HIFU devices use imaging ultrasound for treatment planning and monitoring, and they deliver targeted high-intensity ultrasound that rapidly elevates the temperature in a precise focal zone. The increased tissue temperature is designed to kill excess prostate tissue (in the case of BPH). The same probe can be used for imaging, which allows both diagnostic and therapeutic testing at the same time.

**Literature Review:**
There are scarce data in the published peer-reviewed scientific literature regarding the safety and effectiveness of HIFU for the treatment of BPH.

**Use Outside of the US:**
The National Institute for Clinical Excellence (NICE) (United Kingdom) (NICE, 2015) does not recommend HIFU as an appropriate treatment for benign prostatic hyperplasia (BPH). At this time the role of high-intensity focused ultrasound for the treatment of BPH has not been established.

**Histotripsy:** Histotripsy is an extracorporeal ultrasound technology that has been proposed to treat BPH. Histotripsy is a form of focused ultrasound therapy that utilizes cavitation mechanisms to produce tissue necrosis in prostatic tissue.

**Literature Review:**
There are scarce data in the published peer-reviewed scientific literature to support the safety and effectiveness of histotripsy for the treatment of BPH. At this time the role of this therapy has not yet been established (Schuster et al., 2018; Lusuardi, et al., 2013; Hempel, et al., 2011).

**Interstitial Laser Coagulation (ILC):** ILC of the prostate by the transurethral route has been attempted using several laser and delivery devices. The laser enters the prostate and tissue is coagulated. Intraprostatic lesions reabsorb and the tissue atrophies. Consequently, some volume reduction occurs (AUA, 2010/2014).
U.S. Food and Drug Administration (FDA):
The Indigo® OPTIMA Laser System (Ethicon Endo-Surgery, Inc., Cincinnati, OH) was noted by the FDA (December, 2001) to be substantially equivalent to the Indigo LaserOptic Treatment System which received FDA clearance in December, 1997. It is intended to be used in the non-contact mode to photocoagulate, vaporize/ablate soft tissue (muscle, connective tissue, organ) and for cutting, incision, excision, and for coagulation in the contact mode for open/closed surgical procedures. The Diffuser Tip Fiberoptic is intended for ILC treatment of BPH.

Literature Review:
Indigo 830e has been studied in the United States; however, its role in treating lower urinary tract symptoms has yet to be defined. The lack of randomized controlled studies comparing ILC to other approaches has resulted in no consensus on the ILC technique.

Ng et al. (2005) conducted a study to evaluate the impact of improvements in surgical techniques and patient selection of overall outcomes of ILC of the prostate. Over a four-year period, 66 patients underwent interstitial coagulation (ILC) using the Indigo 830e. They were stratified into two groups: group one consisted of those treated during the first two years (n=47) and those treated during the latest two years (n=19) were labeled as group two. At 12 months, maximum flow rates improved by 47% in group one and 85% in group two. Subjective measures were significantly improved from baseline in both groups but did not differ between groups. The incidence of adverse events was similar in the two groups. In a prospective study of 49 men with symptomatic benign prostatic hyperplasia (BPH) who underwent ILC, Daehlin et al. (2007) reported a decrease in International Prostate Symptom Scores (IPSS), and an increase in peak urinary flow; however, twenty-two patients (50%) required retreatment.

At present there is insufficient evidence in the published peer-reviewed scientific literature to support the effectiveness of interstitial laser coagulation (ILC); its role in the treatment of benign prostatic hyperplasia (BPH) has not yet been established.

Plasma Kinetic Vaporization using the PlasmaKinetic™ Tissue Management System: The PlasmaKinetic™ Tissue Management System (Gyrus ACMI, Southborough, MA) uses plasma energy to vaporize tissue with minimal thermal spread and enhanced hemostasis.

U.S. Food and Drug Administration (FDA):
In July 2003, the PlasmaKinetic Superpulse System (Gyrus, Maple Grove, MN) received 510K premarket notification that the device is substantially equivalent to predicate devices and is safe and effective in its intended use. It is intended for use for ablation, removal, resection and coagulation of soft tissue and where associated hemostasis is required. Predicate devices are the PlasmaKinetic Generator, the PlasmaKinetic Endourology Generator, and the Endourology AxiPolar Resectoscope Electrode.

Literature Review:
There are scarce data in the published, peer-reviewed scientific literature regarding the safety or effectiveness of this therapy and its role in the treatment of BPH has not yet been established.

Prostate Artery Embolization: Prostatic arterial embolization (PAE) is proposed as a minimally invasive procedure and as an alternative to transurethral resection of the prostate (TURP) or open prostatectomy for the treatment of benign prostatic hypertrophy (BPH). PAE for BPH has been proposed to reduce the blood supply of the prostate gland, causing some of it to undergo necrosis with subsequent shrinkage. The procedure is performed under local anesthesia and sedation using a percutaneous transfemoral approach by an interventional radiologist, in consultation with the urologist. The arterial occlusion may be achieved through the use of polyvinyl alcohol particles, coil embolizers, or microspheres (Hayes, 2019).

Literature Review:
Short and limited mid-term data in the published, peer-reviewed literature demonstrate improved outcomes of PAE as a minimally invasive procedure for the treatment of BPH. Additional large, well-designed studies with longer follow-up are needed to validate results (Hayes, 2019; Jiang et al., 2019; Zumstein, et al., 2018;
Insausti et al. (2020) conducted a non-inferiority randomized controlled trial (n=45) to assess the efficacy and safety of prostate artery embolization (PAE) versus Transurethral Resection of the Prostate (TURP) in the treatment of lower urinary tract symptoms (LUTS) related to BPH. Patients were included if: age >60 years, TURP was indicated; the International Prostate Symptom Score (IPSS) was ≥8, quality of life (QoL) related to LUTS was ≥3, and the peak flow rate (Qmax) was ≤ 10 mL/s or urinary retention. Patients were also included if LUTS related to BPH was refractory to medical treatment for at least six months or the patient could not tolerate medical treatment. Patients were excluded if they had: advanced atherosclerosis and tortuosity of the iliac arteries, non-visualization of the prostatic artery or other accessory arteries supplying the prostate on computed tomography angiography, urethral stenosis, detrusor failure or neurogenic bladder, glomerular filtration rate of less than 30 mL/min, and the presence of prostate cancer. The intervention was PAE (n=23) performed with 300- to 500-μm microspheres under local anesthesia. Bipolar TURP (n=22) under spinal or general anesthesia served as the comparator. Primary outcomes were changes in Qmax and IPSS score. QoL and prostate volume (PV) changes were secondary outcomes. Follow up occurred at three months, six months, and 12 months post procedure. Results showed a nonsignificant 3.31mL/second difference in Qmax in favor of TURP (p=0.862) and a 3.04 point difference in IPSS score in favor of PAE (p=0.080). A significant difference was seen in QoL in favor of PAE (p=0.002), and a 22.1 cm3 difference in PV in favor of TURP (p=<0.001). Adverse events for TURP were urethral stricture, retrograde ejaculation, erectile dysfunction, decreased ejaculatory volume, and mild hematuria. Adverse events for PAE were rectal ischemia; radiodermatitis; urinary retention, irritation, pain, discomfort; erectile dysfunction; and transient changes in the color of the penis. Author noted limitations were: small sample size, patient attrition, non-blinding of patients, and short term follow-up.

Pisco et al. (2020) conducted an RCT (n=80) to assess the safety and efficacy of prostatic artery embolization (PAE) compared with sham in the treatment of lower urinary tract symptoms (LUTS) caused by benign prostatic hypertrophy (BPH). Patients ranged in age from 48-76 years. Inclusion criteria were as follows: age greater than 45 years; maximum urine flow rate (Qmax) <12 ml/s; prostate volume (PV) ≥ 40 cm3, and diagnosis of severe LUTS/BPH refractory to medical management. The exclusion criteria included: computed tomography (CT) angiography showing that prostatic arteries were not feasible for PAE; previous surgical or invasive prostate treatments; prostatitis or suspected prostatitis; history of prostate or bladder cancer or pelvic irradiation; active or recurrent urinary tract infections; history of neurologic condition or disease causing or impacting LUTS; advanced atherosclerosis and tortuosity of iliac and prostatic arteries; secondary renal insufficiency; large bladder diverticula or stones; detrusor failure; history of acute urinary retention; current severe, significant, or uncontrolled disease; bleeding disorder; hypersensitivity or contraindication to tamsulosin use; mental condition or disorder that would interfere with the patient’s ability to provide informed consent; participation in a study of any investigational drug or device in the previous three months; and administration of the 5-ARIs finasteride and dutasteride in the previous two week and four months respectively. The intervention was PAE (n=40) performed with 300-500 μm microspheres. Sham PAE without embolization (n=40) served as the comparator. After six months follow-up, the sham group also underwent PAE and were then followed for another six months. Primary outcome measures included: change from baseline International Prostate Symptom Score (IPSS) and quality of life (QoL) score. The secondary outcomes measured were changes from baseline in: the BPH Impact Index, the 15-item International Index of Erectile Function (IIEF-15), PV, Qmax, postvoid residual urine volume (PVR), and PSA. Follow up occurred at one, three, and six months post treatment. Statistically significant improvement was shown in IPSS (p<0.0001) and QoL (p<0.0001) scores at the 6- month follow up. Secondary outcome results at six months also showed statistically significant improvement with a decrease in BPH-II scores of 2.28 and 6.33 points in the sham and PAE groups respectively (p<0.0001), a decrease in prostate volume of 0.06 cm3 and 17.6 cm3 in the sham and PAE groups respectively (p=0.002), an increase in Qmax of 2.80 ml/s and 6.82 ml/s in the sham and PAE groups respectively (p=0.005), an increase in PVR volume in the sham group of 8.63 ml and a decrease of 59.9 ml in the PAE group (p=0.03), and a decrease in PSA of 0.02 ng/dl and 1.51 ng/dl in the sham and PAE groups respectively (p=0.01). A statistically significant improvement was not shown in IIEF-15 scores with an increase of 5.95 and 9.53 points in the sham and PAE groups respectively (p=0.29). The following adverse events were reported: perineal pain, urethral pain, dysuria, ecchymosis, hematospermia, hematuria, inguinal hematoma, expelled prostate fragment, rectorrhagia, and UTI. Author noted limitations included: inclusion of severe LUTS only, the large PVs of the participants, small sample sizes, and short term follow-up.
A 2019 (reviewed 2020) Hayes comparative effectiveness review of PAE for treatment of BPH summarized that low-quality, consistent evidence for PAE is associated with significant improvements in lower urinary tract symptoms, although improvements were significantly less robust than those associated with transurethral resection of the prostate (TURP) or open prostatectomy. The evidence suggests that PAE is associated with fewer complications than TURP or open prostatectomy. Uncertainty remains regarding optimal patient selection criteria for PAE versus TURP and the long-term safety and efficacy of PAE beyond two years. The evidence base for this report included ten studies that evaluated PAE for the treatment of BPH; five randomized controlled trials including a post hoc analysis of an RCT and five prospective or retrospective cohort studies. The 2020 Hayes annual review identified eight new relevant publications that did not change the Hayes conclusion.

In a 2019 meta-analysis, Jiang et al. evaluated studies comparing PAE to TURP and evaluated short-term outcomes with at least 12 months follow-up. Four studies were included in the review (n=506), two randomized controlled trials (Gao, et al., 2014; Carnevale, et al., 2016) and two comparative observational studies (Qiu, et al., 2017; Ray, et al., 2018). In a pooled analysis of data from two studies, there was no significant difference in post-operative IPSS. The post-operative peak flow rate (Qmax) was significantly higher in the TURP group than the PAE group. Similarly, the post-operative prostate volume and quality of life improved significantly more in the TURP group. Data from two studies found no statistically significant differences in complications in the two groups. The authors reported that additional multi-center high quality randomized controlled trials with large sample sizes are needed to verify the clinical efficiency of TURP and PAE for the treatment of BPH.

Malling et al. (2019) conducted a systematic review and meta-analysis of 10 studies (randomized controlled trials and prospective studies) (n=1,046) to review the efficacy and safety of prostate artery embolization (PAE) in the treatment of benign prostatic hyperplasia (BPH) with lower urinary tract symptoms (LUTS). The number of patients in each study ranged from 22-630 and the mean age was 68.6 years. Studies evaluating the efficacy of PAE to treat BPH were included. Studies with less than ten participants, short-term follow-up (<6 months) or indications for PAE other than BPH were excluded. The intervention was PAE to treat BPH and TURP served as a comparator. The primary outcome measure was mean change in the International Prostate Symptom Score (IPSS). Secondary outcome measures were quality of life (QoL), prostate volume (PV), prostate-specific antigen (PSA), post-void residual (PVR), peak urinary flow (Qmax), International Index of Erectile function (IIEF-5), complications, and technical and clinical success rates. Follow-up for nine of the studies was 12 months while one study, with an unreported number of participants, was followed for 6.5 years. Meta-analysis showed statistically significant improvement in IIEF (p=0.005) and all other outcomes (p<0.001) at 12 months follow up. Adverse events included: transient dysuria, increased urinary frequency, post embolization syndrome, bladder ischemia, UTI, and persistent perineal pain for three months. Author noted limitations included: heterogeneity of IPSS measurement thresholds, patient selection, embolization technique, small sample sizes, short-term follow-up, and one long-term follow-up that is based on a small sample size. Additional, high quality studies are needed to support the safety and efficacy of PAE.

In a 2018 meta-analysis and systematic review, Zumstein et al. evaluated studies comparing PAE with TURP for patients with BPH. The authors included five studies (n=708); (Gao et al., 2014; Russo et al., 2015; Carnevale et al., 2016; Abt et al., 2018; Ray, et al., 2018) with at least 12 month follow-up. The authors concluded that PAE was less effective than TURP and had less favorable IPSS scores, peak urinary flow, prostate volume reduction, and prostate void residual. In contrast, International Index of Erectile function scores were better and complications were fewer for PAE versus TURP. The authors reported that additional randomized controlled trials with longer follow-up periods are needed to evaluate the mid- and long-term efficacy and safety of PAE and to assess its ideal spectrum of indications, also compared to less invasive procedures such as TUMT, TUNA, or prostatic urethral lift.

In a systematic review and meta-analysis, Wang et al. (2016) evaluated the efficacy and safety of PAE on LUTS related to BPH. Twelve prospective and retrospective studies involving 840 participants were included. Compared with baseline, the International Index of Erectile Function (IIEF-5; International Prostate Symptom Score) scores, the quality of life scores, peak urinary flow rate (Qmax) and post void residual volume all had significant improvements during the 24-month follow-up (all P<0.0001). Both prostate volume (PV) and prostate-specific antigen had significant decrease during the 12-month follow-up (p<0.0001 and p=0.005, respectively), except postoperative 24 months (p=0.47 and p=0.32, respectively). The IIEF-5 short form scores had significant increase at postoperative six months (p=0.002) and 12 months (p<0.0001), except postoperative
one month (p=0.23) and 24 months (p=0.21). For large volume (PV ≥ 80 mL) BPH, the results were similar. There were no life-threatening complications. The major limitations of this study include heterogeneity in the participants chosen, different materials and sizes of embolic agents and bilateral or unilateral embolization. Additional limitation is the small sample sizes of some included studies with no long-term follow-up. Data in the studies covered by this meta-analysis are insufficient to determine whether or not PAE is as good as TURP. Similar conclusions were reported in a systematic review and meta-analysis of PAE for LUTS related to BPH by Pyo et al. (2017) and in a 2017 systematic review of PAE in the treatment of symptomatic BPH (Kuang, et al., 2017).

In a prospective series matched study (n=160), Russo et al. (2015) evaluated one-year surgical and functional results and morbidities of prostatic artery embolization (PAE) vs open prostatectomy (OP). Inclusion criteria included lower urinary tract symptoms or benign prostatic obstruction, IPSS ≥ 12, prostate-specific antigen (PSA) <4 ng/mL, or PSA between 4 and 10 ng/mL but negative prostate biopsy, total prostate volume >80 cm³, and peak flow (PF) <15 mL/s. Follow-up was performed at one month, six months, and one year. Primary end points of the study were the comparison regarding IPSS, International Index of Erectile Function-5, PF, post voidal residual (PVR), and IPSS quality of life (IPSS-QoL) after one year of follow-up. The authors reported that PAE was inferior to OP in terms of one-year functional outcomes such as the reduction of IPSS and PVR and the increase of PF. Further clinical trials comparing PAE with other minimally invasive surgical are required.

In a prospective randomized study (n=114), Gao et al. (2014) compared prostatic arterial embolization (PAE) (n=57) and transurethral resection of the prostate (TURP) (n=57) in the care of patients with benign prostatic hyperplasia (BPH). The groups were compared regarding relevant adverse events and complications. Functional results including improvement of International Prostate Symptom Score (IPSS), quality of life (QOL), peak urinary flow, postvoiding residual urine volume, prostate-specific antigen (PSA) level, and prostate volume were assessed at one-, three-, six-, 12-, and 24-month follow up. Overall technical success rates for TURP and PAE were 100% and 94.7%, respectively; the clinical failure rates were 3.9% and 9.4%, respectively. The six functional results showed improvements after TURP and PAE at all follow-up time points when compared with preoperative values (p=0.001). The TURP group showed greater degrees of improvement in the IPSS, QOL, peak urinary flow, and postvoiding residual urine volume at one and three months, as well as greater reductions in the PSA level and prostate volume at all follow-up time points, when compared with the PAE group (p<0.05). The PAE group showed more overall adverse events and complications (p=0.029), mostly related to acute urinary retention (25.9%), postembolization syndrome (11.1%), and treatment failures (5.3% technical; 9.4% clinical). The authors reported that “the advantages of the PAE procedure must be weighed against the potential for technical and clinical failures in a minority of patients.”

**Professional Societies/Organizations:**
The 2020 updated American Urological Association (AUA) evidence-based guideline on the “Surgical Management of Benign Prostatic Hyperplasia/Lower Urinary Tract Symptoms” stated that:

Artery Embolization (PAE) for the treatment of LUTS secondary to BPH is not supported by current data and trial designs, and benefit over risk remains unclear; therefore, PAE is not recommended outside the context of clinical trials.

In 2018, the Society of Interventional Radiology (SIR) updated their 2014 position statement on PAE for treatment of LUTS attributed to BPH. The updated position statement addresses the global experience with PAE stating the joint position and recommendations of SIR, the Cardiovascular and Interventional Radiological Society of Europe, Society Française de Radiologie, and the British Society of Interventional Radiology. The societies made the following recommendations for PAE (McWilliams, et al., 2018):

- PAE is an acceptable minimally invasive treatment option for appropriately selected men with BPH and moderate to severe LUTS. (Level of evidence: B; strength of recommendation: strong.)
- PAE can be considered as a treatment option in patients with BPH and moderate to severe LUTS who have very large prostate glands (> 80 cm³), without an upper limit of prostate size. (Level of evidence: C; strength of recommendation: moderate.)
• PAE can be considered as a treatment option in patients with BPH and acute or chronic urinary retention in the setting of preserved bladder function as a method of achieving catheter independence. (Level of evidence: C; strength of recommendation: moderate.)

• PAE can be considered as a treatment option in patients with BPH and moderate to severe LUTS who wish to preserve erectile and/or ejaculatory function. (Level of evidence: C; strength of recommendation: weak.)

• PAE can be considered in patients with hematuria of prostatic origin as a method of achieving cessation of bleeding. (Level of evidence: D; strength of recommendation: strong.)

• PAE can be considered as a treatment option 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. (Level of evidence: E; strength of recommendation: moderate.)

• PAE should be included in the individualized patient-centered discussion regarding treatment options for BPH with LUTS. (Level of evidence: E; strength of recommendation: strong.)

• 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. (Level of evidence: E; strength of recommendation: strong.)

Use Outside of the US:
The updated 2018 Canadian Urological Association (CUA) guideline on male lower urinary tract symptoms/benign prostatic hyperplasia (MLUTS/BPH) recommendation for PAE states that PAE should not be offered at this time for the treatment of LUTS due to BPH (conditional recommendation based on moderate-quality evidence). The guideline authors note that PAE performed by interventional radiologists, at specialized centers, is associated with significant clinical improvements from baseline to one year. However, outcomes are inferior compared with TURP and open simple prostatectomy. Further, non-targeted embolization is associated with ischemic complications (e.g., bladder ischemia, transient ischemic proctitis, urethral and ureteral stricture, or seminal vesicles ischemia) (Nickel, et al., 2018).

The 2019 European Association of Urology (EAU) guideline on Management of Non-neurogenic Male LUTS states that the selection of LUTS patients who will benefit from PAE needs to be defined. Several studies evaluating PAE have been published but there is a lack of long-term randomized controlled trials. To define the role of PAE as a potential option among established treatment modalities, a multidisciplinary approach involving urologists and interventional radiologists is needed (Gravas et al., 2019).

In 2018 National Institute for Clinical Excellence (NICE) (United Kingdom) published an Interventional Procedure Guidance Prostate Artery Embolisation for Lower Urinary Tract Symptoms caused by benign prostatic hyperplasia which includes the following recommendations:

• Current evidence on the safety and efficacy of prostate artery embolisation for benign prostatic hyperplasia is adequate to support the use of this procedure provided that standard arrangements are in place for clinical governance consent and audit.

• Patient selection should be done by a urologist and an interventional radiologist.

• This technically demanding procedure should only be done by an interventional radiologist with specific training and expertise in prostatic artery embolization.

Temporary implantable nitinol device (TIND): A TIND is a device proposed to provide a minimally invasive means of increasing prostatic urethral patency to relieve the symptoms of urinary outflow obstruction secondary to benign prostatic hypertrophy (BPH). The TIND is crimped and delivered through a cystoscope sheath, and then, when placed in the urethra, it is released from the cystoscope sheath to assume its expanded configuration, thereby reshaping the urethra and the bladder neck. It is removed after a few days under local anesthesia. (Magistro, et al., 2018; 2018; Marcon, et al., 2018; Nickels, et al., 2018; Porpiglia, et al., 2015).

Food and Drug Administration (FDA):
In 2020, the FDA granted a de novo classification clearance (DEN190020) for the iTind System (Medi-Tate Ltd, Or Akiva, IL). The system was classified as a temporarily-placed urethral opening system for symptoms of
benign prostatic hyperplasia. According to the FDA summary document, the iTind System “is intended for the
treatment of symptoms due to urinary outflow obstruction secondary to benign prostatic hyperplasia (BPH) in
men age 50 and above.” The self-expanding implant is deployed at the bladder neck between the obstructed
prostatic lobes by means of a pre-mounted device on a dedicated guide wire. The implant provides continuous
pressure for 5–7 days and is removed using a Foley catheter (FDA, 2020).

**Literature Review:**
There are scarce data in the published peer-reviewed scientific evidence to determine the safety and efficacy of
the TIND as a treatment option for BPH.

Porpiglia et al. (2019) conducted a prospective single-arm, multicenter study (n=81) to assess the feasibility,
safety and efficacy of a second-generation of temporary implantable nitinol device (iTIND; Medi-Tate Ltd, Or-
Akiva, Israel) for the treatment of lower urinary tract symptoms (LUTS) due to benign prostatic hyperplasia
(BPH). The mean age of participants was 65 years. The inclusion criteria were: LUTS, International Prostate
Symptom Score (IPSS) ≥10, maximum urinary flow rate (Qmax) ≤12 mL/s, and prostate volume <75 mL. The
exclusion criteria were: hemostatic disorders, neurogenic bladder and/or sphincter abnormalities, impaired renal
function, history of urethral strictures, post-void residual urine volume (PVR) >250 mL, urinary bladder stones,
bladder cancer, obstructive median lobe, active UTI, and previous prostate surgery. After discontinuation of
pharmacological therapy, patients underwent implantation of the iTIND within the bladder neck and the prostatic
urethra under light sedation. The device was removed five to seven days later. There were no comparators in
this single arm study. The outcome measures were maximum urinary flow rate (Qmax), International Prostate
Symptom Score (IPSS), quality of life (QoL), and post-void residual urine volume (PVR). Follow-up was
conducted at one, three, six, and 12 months postoperatively. Statistical significance was shown with an
improvement in Qmax from a baseline of 7.3 ml/s to 11.2 ml/s at one month, 12.4 ml/s at three months, 13.69
ml/s at six months, and 14.7 ml/s at one year follow up (p<0.001); an improvement in total IPSS from a baseline
of 26.22 to 13.81 at one month, 11.61 at three months, 11.57 at six months, and 10.38 at one year (p<0.001); an
improvement in QoL from a baseline of 4 to 2 at one, three, and six months, and one at one year follow up
(p<0.001); and an overall improvement in PVR from a baseline of 76.17 mL to 49.84 mL at one month, 46.75 mL
at three months, 48.84 mL at six months, and 34.03 at one year follow up (p<0.001). The authors reported a 5%
treatment failure rate (n=4). Adverse events included: hematuria, urinary urgency, urinary retention, pain,
dysuria, and UTI. Author noted limitations of the study include: short term follow-up, lack of a control, selection
bias, and patient attrition.

**Use Outside of the US:**
The temporary implantable nitinol device (TIND) has CE mark approval. The manufacturer website for the TIND
device states the device is available in the European Union, UK, Israel, Australia, Brazil, and the USA.

In an interventional procedures guidance document for prostatic urethral temporary implant insertion for lower
urinary tract symptoms (LUTS) cause by benign prostatic hyperplasia (BPH), the National Institute for Health and
Clinical Excellence (NICE) (United Kingdom) (2019) stated that the safety and efficacy of prostatic urethral
temporary implant insertion for LUTS caused by BPH is insufficient and lacking quality. As such, further research
is needed in the form of quality randomized controlled trials.

The 2018 Canadian Urological Association (CUA) guideline on male lower urinary tract symptoms/benign
prostatic hyperplasia (MLUTS/BPH) recommends that TIND should not be offered at this time for the treatment
of LUTS due to BPH.

**Transrectal Thermal Therapies:** There are scarce data in the published peer-reviewed scientific evidence to
determine the safety and efficacy of thermal therapy via the rectum as a treatment option for BPH. At this time
the role of this therapy has not yet been established.

**Transurethral Balloon Dilation of the Prostatic Urethra:** Transurethral balloon dilation of the prostatic urethra,
also known as endoscopic balloon dilation of the prostatic urethra, involves the insertion of a balloon catheter
through the urethra into the prostatic urethra where it is inflated to stretch the urethra where it has been
narrowed by the prostate.
Literature Review:
There are scarce data regarding the safety and effectiveness of this therapy for the treatment of BPH and its role has not yet been established.

Transurethral Ultrasound Guided Laser Incision of the Prostate (TULIP): TULIP is a procedure that is similar to transurethral incision of the prostate except that cuts are made with a laser. Laser energy is delivered under ultrasound guidance, producing necrosis. TULIP is a difficult procedure with a very high incidence of incontinence, a delayed onset of improvement, and no ability to obtain tissue for histological examination. TULIP is rarely used by urologists because it has been surpassed by instruments that are easier to use (Fitzpatrick, 2011).

Literature Review:
There are scarce data in the published, peer-reviewed scientific literature regarding the effectiveness of TULIP and the role of this therapy in the treatment of BPH has not yet been established.

Water-Induced Thermotherapy (WIT): WIT is a minimally-invasive therapy that uses hot water circulating through a urethral balloon catheter to deliver heat energy to prostate tissue and thereby shrink the prostate and treat symptoms of BPH. It is generally considered only for patients who cannot undergo TURP or who require less invasive treatments, however the long-term safety and effectiveness of this treatment in this or other proposed subsets of individuals has not been proven.

U.S. Food and Drug Administration (FDA):
The AquaTherm device, formerly known as the Thermoflex™ Water-Induced Thermotherapy System (ACMI, Southborough, MA, previously Argomed, Inc., Cary, NC) is a catheter-based thermal therapy device for the treatment of symptoms due to urinary outflow obstruction secondary to BPH. FDA 510(k) class II approval was received in 1999.

Literature Review:
There are scarce data in randomized controlled clinical trials or comparative studies regarding outcomes of WIT as a treatment for BPH. Minardi et al. (2004) reported that WIT resulted in a reduction of prostatic volume of 5.2% compared with a decrease of 48.4% when transurethral resection of the prostate (TURP) was performed. The urine flow rate increased more after TURP (75.3%) than after WIT (16.7%). Residual prostate volume decreased more after TURP (89.8%) than after WIT (25.2%), an increase of maximum flow rate of 16.7% and a decrease of residual volume of 25.2%. The relief of bladder outlet obstruction was indicated by the decrease of detrusor pressure at maximum flow rate in comparison to baseline values; decreases of 27.5% were noted for WIT compared with decreases of 48% for transurethral resection of the prostate (TURP).

At this time there is insufficient evidence in the peer-reviewed scientific evidence to determine the safety and effectiveness of WIT for the treatment of BPH. Additionally, there is insufficient direct comparison of WIT to other treatment options for BPH; optimal protocols have not been established and long-term information regarding duration of treatment effect or adverse effects is lacking.

Use Outside of the US:
The National Institute for Clinical Excellence (United Kingdom) does not recommend WIT as an appropriate option for the treatment of BPH (NICE, 2010, 2015).

Waterjet Tissue Ablation using the AquaBeam System: Waterjet tissue ablation using the AquaBeam System has been proposed as the first minimally invasive medical device that allows rapid removal of prostate tissue without leaving a zone of thermal damage on the treated tissue. The AquaBeam System uses proprietary heat-free high-velocity waterjet technology for automated tissue resection as well as for optical energy delivery for cauterization in the treatment of BPH. No heat sources are used for cutting. The AquaBeam system consists of three components: a single-use probe, a robotic hand piece, and a console. The procedure is carried out under transrectal ultrasound imaging. The AquaBeam probe is attached to the hand piece and inserted in the urethra; cystoscopic visualization is available continuously during the procedure. After mapping the desired tissue to be ablated, high-velocity sterile saline is delivered to the prostate tissue via the AquaBeam probe, which also provides a channel for aspiration of ablated tissue during the procedure. After excision of tissue from the
prostate, the jet’s pressure is reduced so that it can be used to carry a laser light beam to cauterize the excised area. The aim is to reduce the heat damage to adjacent tissue common in other available interventions.

**Food and Drug Administration (FDA):**
On December 21, 2017 the FDA granted a de novo classification for the AquaBeam system (PROCEPT BioRobotics Corporation, Redwood Shores, CA) for the resection and removal of prostate tissue for males suffering from LUTS due to BPH. FDA clearance was supported by the international WATER randomized controlled trial (NCT02505919) comparing AquaBeam with TURP in patients with LUTS due to BPH.

**Literature Review:**
There is a paucity of evidence in the published peer-reviewed literature addressing waterjet tissue ablation and its role in the treatment of BPH. Evidence in the peer-reviewed literature for waterjet tissue ablation using the AquaBeam system includes an RCT (n=181) (Gilling, et al., 2019; 2018), a follow-up cohort study (n=90) (Kasivisvanatha, et al., 2018) and a prospective study (n=66) of the RCT (Pimentel, et al., 2019), an additional prospective study (n=21) (Gilling, et al., 2017) and a safety and feasibility study (n=15) (Gilling, et al., 2016). Longer-term data and comparisons with similar modalities such as the Holmium laser enucleation of the prostate (HOLeP) are needed to establish the safety and efficacy of the Aquabeam system. Although professional society recommendations state that Aquablation may be offered to patients with LUTS attributed to BPH, they note that patients should be informed that long term evidence of efficacy and retreatment rates remains limited.

Gilling et al. (2019) reported one year safety and efficacy outcomes for the WATER study above. BPH symptom score improvements were similar across groups with 12-month reduction of 15.1 points after TURP or Aquablation. In both groups, mean maximum urinary flow rates increased markedly postoperatively, with mean improvements of 10.3 cc/s for Aquablation versus 10.6 cc/s for TURP (p=0.8632). At one year, Prostate-specific antigen (PSA) was reduced significantly (p<0.01) in both groups by one point; the reduction was similar across groups (p=0.9125). Surgical retreatment for BPH rates for TURP were 1.5% and Aquablation 2.6% within one year from the study procedure (p=not significant [NS]). The rate of late complications was low, with no procedure-related adverse events after six months. The authors concluded that Aquablation for LUTS due to BPH provides sustained, 12-month, symptom-reduction efficacy with a low rate of late adverse events in men with prostates between 30 and 80 cc.

In a blinded, prospective, randomized multicenter study, Pimentel et al. (2019) compared urodynamic outcomes between aquablation vs transurethral resection of the prostate (TURP). Patients (n=66) were randomized 2:1 (aquablation [n=43]; TURP [n=23]) in the Waterjet Ablation Therapy for Endoscopic Resection (WATER) of prostate tissue study. Of 17 participating trial sites, seven centers performed urodynamic studies preoperatively and at a month after treatment. Urodynamic studies were optional; study centers that routinely performed urodynamic studies in clinical practice included these assessments in the trial. The primary urodynamic outcome measures were detrusor pressure at maximal flow rates (pDet@Qmax) and mean change in the Bladder Outlet Obstruction Index (BOOI). Urodynamics were measured at baseline and six months. At mean baseline pDet@qmax was 71 and 73cm H20 in the aquablation and TURP groups, respectively. At six-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. Reported limitations include that urodynamics were optional in the WATER study. This analysis had limited subjects at the seven sites performing such evaluations in the trial, which could have introduced a bias. While sample size was large enough to detect statistically significant and clinically important changes from baseline in each group, it is possible that smaller differences in urodynamic responses across treatment groups might not be detectable due to limited sample size.

In a double-blind, multicenter, prospective, randomized, controlled trial or the WATER (Waterjet Ablation Therapy for Endoscopic Resection of Prostate Tissue) trial (n=181), Gilling et al. (2018) reported on individuals with moderate to severe lower urinary tract symptoms related to BPH who underwent the gold standard transurethral prostate resection (n=116) or Aquablation (n=65). The primary efficacy end point was the reduction in International Prostate Symptom Score (IPSS) at six months. The primary safety end point was the development of Clavien-Dindo persistent grade 1, or 2 or higher operative complications. The study included...
A 2019 Cochrane Systematic Review on Aquablation of the prostate for the treatment of LUTS in men with BPH included one RCT with 184 participants comparing Aquablation to TURP (Gilling, et al., 2018). The authors did not find other prospective, comparative studies comparing Aquablation to TURP or other procedures such as laser ablation, enucleation, or other minimally invasive therapies. The conclusions state that based on short-term 12 month 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) signalling major uncertainty about the true effect size. Reported adverse events include postoperative pain, hematuria, urinary tract infections, urethral stricture disease, acute urinary retention and one instance of blood transfusion (Gilling, et al., 2018). The reported rates of reoperations is 2.5% (Gilling, et al., 2018). The authors are very uncertain whether Aquablation may result in little to no difference in erectile function (both very low-certainty evidence). The 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 (Hwang, et al., 2019).

**Medical Coverage Policy:** 0159

**Professional Societies/Organizations:**
Aquablation is discussed in the 2020 amended American Urological Association (AUA) evidence-based Guideline: Surgical Management of Benign Prostatic Hyperplasia/Lower Urinary Tract Symptoms. One low risk of bias randomized controlled trial (n=181) assessing Aquablation was evaluated by the panel. The guideline
recommendation states: Aquablation may be offered to patients with LUTS attributed to BPH provided prostate volume >30/<80g. (Conditional Recommendation; Evidence Level: Grade C) (AUA, 2020).

Use Outside of the US:
The updated 2018 Canadian Urological Association (CUA) guideline on male lower urinary tract symptoms/benign prostatic hyperplasia (MLUTS/BPH) recommends that aquablation be offered to men with LUTS interested in preserving ejaculatory function, with prostates <80 cc, with or without middle lobe. (Conditional recommendation based on moderate quality evidence). (Nickel, et al., 2018).

The 2019 European Association of Urology (EAU) guideline on Management of Non-neurogenic Male LUTS states that the first clinical experience provides encouraging results, with a low risk of sexual dysfunction, but further modifications of the AquaBeam system may be necessary. Longer term follow up would help assess the clinical value of Aquablation (Gravas et al., 2019).

In an interventional procedures guidance on transurethral water jet ablation for lower urinary tract symptoms caused by benign prostatic hyperplasia, the National Institute for Health and Clinical Excellence (NICE) (United Kingdom) (2018) stated that this procedure raises no major safety concerns; however, the evidence on this procedure is limited in quality. NICE encourages further, quality research on this procedure.

Medicare Coverage Determinations

<table>
<thead>
<tr>
<th>Contractor</th>
<th>Determination Name/Number</th>
<th>Revision Effective Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>LCD National Government Services, Inc.</td>
<td>Water Vapor Thermal Therapy for LUTS/BPH (L37808)</td>
<td>12/01/2019</td>
</tr>
<tr>
<td>LCD CGS Administrators, LLC</td>
<td>Laser Ablation of the Prostate (L34090)</td>
<td>09/19/2019</td>
</tr>
<tr>
<td>LCD CGS Administrators, LLC</td>
<td>Fluid Jet System in the Treatment of Benign Prostatic Hyperplasia (BPH) (L38378)</td>
<td>06/01/2020</td>
</tr>
<tr>
<td>LCD National Government Services, Inc.</td>
<td>Fluid Jet System in the Treatment of Benign Prostatic Hyperplasia (BPH) (L38367)</td>
<td>06/01/2020</td>
</tr>
</tbody>
</table>

Note: Please review the current Medicare Policy for the most up-to-date information.

Coding/Billing Information

Note: 1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

<table>
<thead>
<tr>
<th>CPT® Codes</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>52441</td>
<td>Cystourethroscopy, with insertion of permanent adjustable transprostatic implant; single implant</td>
</tr>
<tr>
<td>52442</td>
<td>Cystourethroscopy, with insertion of permanent adjustable transprostatic implant; each additional permanent adjustable transprostatic implant (List separately in addition to code for primary procedure)</td>
</tr>
<tr>
<td>53854</td>
<td>Transurethral destruction of prostate tissue; by radiofrequency generated water vapor thermotherapy</td>
</tr>
<tr>
<td>HCPCS Codes</td>
<td>Description</td>
</tr>
<tr>
<td>------------</td>
<td>----------------------------------------------------------------------------</td>
</tr>
<tr>
<td>C9739</td>
<td>Cystourethroscopy, with insertion of transprostatic implant; 1 to 3 implants</td>
</tr>
<tr>
<td>C9740</td>
<td>Cystourethroscopy, with insertion of transprostatic implant; 4 or more implants</td>
</tr>
</tbody>
</table>

Considered Experimental/Investigational/Unproven when used to report any procedure listed in this policy as Experimental/Investigational/Unproven for the treatment of benign prostatic hyperplasia (BPH):

<table>
<thead>
<tr>
<th>CPT® Codes</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>37242</td>
<td>Vascular embolization or occlusion, inclusive of all radiological supervision and interpretation, intraprocedural roadmapping, and imaging guidance necessary to complete the intervention; arterial, other than hemorrhage or tumor (eg, congenital or acquired arterial malformations, arteriovenous malformations, arteriovenous fistulas, aneurysms, pseudoaneurysms)</td>
</tr>
<tr>
<td>53852</td>
<td>Transurethral destruction of prostate tissue; by radiofrequency thermotherapy</td>
</tr>
<tr>
<td>53899</td>
<td>Unlisted procedure, urinary system</td>
</tr>
<tr>
<td>55873</td>
<td>Cryosurgical ablation of the prostate (includes ultrasonic guidance and monitoring)</td>
</tr>
<tr>
<td>55899</td>
<td>Unlisted procedure, male genital system</td>
</tr>
<tr>
<td>76999</td>
<td>Unlisted ultrasound procedure (eg, diagnostic, interventional)</td>
</tr>
<tr>
<td>0421T</td>
<td>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).</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>HCPCS Codes</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>C2596</td>
<td>Probe, image-guided, robotic, waterjet ablation</td>
</tr>
<tr>
<td>C9747</td>
<td>Ablation of prostate, transrectal, high intensity focused ultrasound (HiFU), including imaging guidance</td>
</tr>
<tr>
<td>C9769</td>
<td>Cystourethroscopy, with insertion of temporary prostatic implant/stent with fixation/anchor and incisional struts</td>
</tr>
</tbody>
</table>


References


137. van Melick H, van Venrooij G, Eckhardt G, Boon T. A randomized controlled trial comparing transurethral resection of the prostate, contact laser prostatectomy and electrovaporization in men with benign


