Medical Coverage Policy

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Benign Prostatic Hyperplasia (BPH) Surgical Treatments

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for services that are not accompanied by covered code(s) under the applicable Coverage Policy will be denied as not covered. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Overview

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

Coverage Policy

Any of the following treatments are considered medically necessary for the treatment of symptomatic benign prostatic hyperplasia (BPH):

- Urethral lift (e.g., UroLift)
- Water vapor thermal therapy (e.g., Rezūm System)
- Waterjet tissue ablation (e.g., AquaBeam System)

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

- absolute ethanol injection
- high-intensity focused ultrasound (HIFU)
- histotripsy
- prostate artery embolization
- temporary implantable nitinol device (TIND)
- transrectal thermal therapy
- transurethral balloon dilation of the prostatic urethra
- water-induced thermotherapy (WIT)

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) (Franco, et al., 2021). The most frequent indications for surgical management are moderate-to-severe voiding symptoms that are refractory to medical management.

According to a 2020 press release from the American Urological Association (AUA), "race and ethnicity are observed as significant factors associated with disparate higher incidence and poorer outcomes" for BPH. The AUA cited a retrospective cohort study in which information was collected

on age, race, ethnicity, primary insurance, and rural-urban commuting area for patients presenting to Florida emergency departments with reports of lower urinary tract symptoms and acute urinary retention. The study found that men aged 45 years and older were more likely to be of non-white race, have Medicare or private insurance, and live in more urbanized areas. The authors concluded that "African-American and Hispanic patients may be untreated or undertreated for BPH in the outpatient setting". However, data specifically addressing the prevalence of BPH by race/ethnicity are limited and conflicting.

Antoine, et al. (2022) conducted a retrospective review of regional hospital network database information from the University of Colorado Health from January 2011 – October 2018 to determine if race and ethnicity are associated with the likelihood of undergoing surgical treatment for BPH. Male patients (n=30,466) were included in the review if their electronic medical records or billing data showed that they were over the age of 40, on medical therapy for lower urinary tract symptoms (LUTS) associated with BPH, and that they had had two or more provider visits for this diagnosis. The race/ethnicity of the study population consisted of white (n=24,443; 80.2%), Hispanic (n=2715; 8.9%), Black/African American (n=1245; 4.1%), and other race/ethnicity (2073; 6.8%). After adjusting for age, insurance status, major comorbidities, and type of LUTS medication, the authors found that Black/African American patients were significantly less likely than white patients to have been treated with surgery (p=0.011). Similar results were found for individuals who self-identified as other race/ethnicity (p=0.013). The authors postulated that this disparity may be due to implicit bias on the part of the providers, patient differences in attitudes toward medical care, or other structural factors. A limitation of this study is that it is not generalizable to the Black male population in the United States.

In a retrospective cohort study of newly diagnosed Medicare beneficiaries with BPH, Narang et al. (2023) evaluated Medicare claims data from 2009 through 2019 to determine if race has an impact on BPH surgical treatment rates. All eligible beneficiaries with a diagnosis of BPH were followed from their earliest BPH diagnosis until their earliest claim date for BPH surgery, prostate or bladder cancer diagnosis, the end of their continuous enrollment, death, or the end of the study period and were then divided by race (i.e., White or Black, Indigenous, and People of Color (BIPOC)). The median follow-up time was 3.6 years for White men and 2.8 years for BIPOC men. Key outcomes for this study included the type of BPH surgery (i.e., minimally invasive or invasive), time to surgery, and site of surgery. There were 31,699 beneficiaries included in the study, 86.3% were White (n=27,368), and 13.7% were BIPOC (n=4331). A total of 1853 beneficiaries underwent BPH surgery. TURP was the most common surgery type for both groups. BIPOC men were more likely to undergo TURP than White men (p=0.052). BIPOC men had significantly lower BPH surgical rates than White men (p=0.002) by the end of the study period. After controlling for geographical region of residence and comorbidities, BIPOC race was associated with a 19% significantly lower likelihood of receiving BPH surgery than White race (p=0.005). For those men who underwent surgery, BIPOC men were significantly more likely to undergo surgery in an inpatient setting compared to White men (p<0.001). There were no significant differences reported between groups for type of surgical procedure and race. Author reported limitations of the study included: claims data that does not include potential confounders (e.g., physician/patient preferences, symptom severity, medication adherence, socioeconomic and environment factors), potential coding errors, and inability to generalize Medicare claims data to the general population.

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. Long-term use of medications for LUTS/BPH has also been associated with cognitive issues and depression. There are several proposed surgical treatments for BPH that involve

burning, cutting, or removal of prostatic tissue. (Moul, et al., 2019; Lerner, et al., 2021). 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)
- Prostatic Urethral lift (e.g., UroLift)
- Stents (e.g., UroLume® endourethral prosthesis)
- Transurethral electrovaporization (TUVP, TVP, TUEP), also known as transurethral vapor resection of the prostate (TUVRP)
- Transurethral incision of the prostate (TUIP)
- Transurethral microwave thermotherapy (TUMT)
- Transurethral needle ablation (TUNA), also known as radiofrequency needle ablation (RFNA)
- Transurethral resection of the prostate (TURP)
- Water vapor thermal therapy (e.g., Rezūm System)
- Waterjet tissue ablation (e.g., AquaBeam System)

Professional Societies/Organizations: In a 2021 guideline on the management of BPH/LUTS (Lerner, et al., 2021), the American Urological Association stated that "surgery is recommended for patients who have renal insufficiency secondary to BPH, refractory urinary retention secondary to BPH, recurrent urinary tract infections (UTIs), recurrent bladder stones or gross hematuria due to BPH, and/or with LUTS/BPH refractory to or unwilling to use other therapies". This recommendation is based upon clinical principle (i.e., widely agreed upon by urologists or other clinicians). The following surgical therapies are recommended by the society:

- "TURP should be offered as a treatment option for patients with LUTS/BPH. (Moderate Recommendation; Evidence Level: Grade B)
    - Clinicians may use a monopolar or bipolar approach to TURP as a treatment option, depending on their expertise with these techniques. (Expert Opinion)
- Open, laparoscopic, or robotic assisted prostatectomy should be considered as treatment options by clinicians, depending on their expertise with these techniques, only in patients with large to very large prostates. (Moderate Recommendation; Evidence Level: Grade C)
- TUIP should be offered as an option for patients with prostates ≤30cc for the surgical treatment of LUTS/BPH. (Moderate Recommendation; Evidence Level: Grade B)
- Bipolar TUVP may be offered as an option to patients for the treatment of LUTS/BPH. (Conditional Recommendation; Evidence Level: Grade B)
- PVP should be offered as an option using 120W or 180W platforms for the treatment of LUTS/BPH. (Moderate Recommendation; Evidence Level: Grade B)
- PUL should be considered as a treatment option for patients with LUTS/BPH provided prostate volume 30-80cc and verified absence of an obstructive middle lobe. (Moderate Recommendation; Evidence Level: Grade C)
    - PUL may be offered as a treatment option to eligible patients who desire preservation of erectile and ejaculatory function. (Conditional Recommendation; Evidence Level: Grade C)
- TUMT may be offered as a treatment option to patients with LUTS/BPH. (Conditional Recommendation; Evidence Level: Grade C)

- WVTT should be considered as a treatment option for patients with LUTS/BPH provided prostate volume 30-80cc. (Moderate Recommendation; Evidence Level: Grade C)
    - WVTT may be offered as a treatment option to eligible patients who desire preservation of erectile and ejaculatory function. (Conditional Recommendation; Evidence Level: Grade C)
- Holmium laser enucleation of the prostate (HoLEP) or thulium laser enucleation of the prostate (ThuLEP) should be considered as an option, depending on the clinician's expertise with these techniques, as prostate size-independent options for the treatment of LUTS/BPH. (Moderate Recommendation; Evidence Level: Grade B)
- Robotic waterjet treatment (RWT) may be offered as a treatment option to patients with LUTS/BPH provided prostate volume 30-80cc. (Conditional Recommendation; Evidence Level: Grade C)
- HoLEP, PVP, and ThuLEP should be considered as treatment options in patients who are at higher risk of bleeding. (Expert Opinion)"

In the 2023 amendment to the guideline on the management of LUTS attributed to BPH (Sandhu, et al., 2023), the AUA removed the statements for TUMT and TUNA as these are now viewed by the AUA as "legacy technologies" that have been historically used but are being "displaced" with newer minimally invasive technologies. Additionally, an expert opinion recommendation was given for the use of temporary implanted prostatic devices (TIPD) (also known as temporary implantable nitinol device; TIND) as "a treatment option for patients with LUTS/BPH provided prostate volume is between 25 and 75cc and lack of obstructive median lobe." Expert opinion recommendations are given by the AUA when there is an absence of sufficient evidence to assign a strength rating of A (high), B (moderate), or C (low).

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 <100 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, 2023; 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 (K173087) 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 (FDA, 2017).

The FDA granted 510(k) clearance (K190377) for the next generation of the UL400 device. The 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. 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 K173087.

"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" (FDA, 2019)

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. Contraindications were updated to disallow the procedure in men with prostate volumes of greater than 100 cc.

"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" (FDA, 2020b)

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 (FDA, 2020c).

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 80cm^3 and European and Australian studies typically ranging up to 100cm^3 (Hayes, 2020; Tanneru, et al., 2020; Jung, et al., 2019; Gratzke, et al., 2017; Rukstalis, et al., 2016, 2019; Jones, et al., 2016; Bozkurt, et al., 2016; Sønksen, et al., 2015; Perera, et al., 2015; Shore, et al., 2014; McVary, et al., 2014; Cantwell, et al., 2014; Roehrborn, et al., 2013, 2015a, 2015b, 2016, 2017a; McNicholas, et al., 2013; Chin, et al., 2012; Woo, et al., 2011, 2012).

Professional Societies/Organizations:
The 2018 (revised 2021) American Urological Association (AUA) evidence-based guideline, "Surgical 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 2021) AUA evidence-based Guideline: Surgical Management of Benign Prostatic Hyperplasia/Lower Urinary Tract Symptoms with the following statement:

- "PUL should be considered as a treatment option for patients with LUTS/BPH provided prostate volume 30–80cc and verified absence of an obstructive middle lobe. (Moderate Recommendation; Evidence Level: Grade C)
- PUL may be offered as a treatment option to eligible patients who desire preservation of erectile and ejaculatory function. (Conditional Recommendation; Evidence Level: Grade C)"

Body of Evidence Strength Grading:

Strong Recommendation (Net benefit or harm substantial)
- Evidence Strength A (High Certainty): Benefits > Risks/Burdens (or vice versa); Net benefit (or net harm) is substantial; Applies to most patients in most circumstances and future research is unlikely to change confidence

- Evidence Strength B (Moderate Certainty): Benefits > Risks/Burdens (or vice versa); Net benefit (or net harm) is substantial; Applies to most patients in most circumstances but better evidence could change confidence
- Evidence Strength C (Low Certainty): Benefits > Risks/Burdens (or vice versa); Net benefit (or net harm) appears substantial; Applies to most patients in most circumstances but better evidence is likely to change confidence (rarely used to support a Strong Recommendation)

Moderate Recommendation (Net benefit or harm moderate)

- Evidence Strength A (High Certainty): Benefits > Risks/Burdens (or vice versa); Net benefit (or net harm) is moderate; Applies to most patients in most circumstances and future research is unlikely to change confidence
- Evidence Strength B (Moderate Certainty): Benefits > Risks/Burdens (or vice versa); Net benefit (or net harm) is moderate; Applies to most patients in most circumstances but better evidence could change confidence
- Evidence Strength C (Low Certainty): Benefits > Risks/Burdens (or vice versa); Net benefit (or net harm) appears moderate; Applies to most patients in most circumstances but better evidence is likely to change confidence

Conditional Recommendation (No apparent net benefit or harm)

- Evidence Strength A (High Certainty): Benefits = Risks/Burdens; Best action depends on individual patient circumstances; Future research unlikely to change confidence
- Evidence Strength B (Moderate Certainty): Benefits = Risks/Burdens; Best action appears to depend on individual patient circumstances; Better evidence could change confidence
- Evidence Strength C (Low Certainty): Balance between Benefits & Risks/Burdens unclear; Alternative strategies may be equally reasonable; Better evidence likely to change confidence

Clinical Principle

- A statement about a component of clinical care that is widely agreed upon by urologists or other clinicians for which there may or may not be evidence in the medical literature
- A statement, achieved by consensus of the Panel, that is based on members' clinical training, experience, knowledge, and judgment for which there is no evidence

The AUA stated that there have been retrospective chart reviews evaluating PUL in a small number of men with prostate volumes between 81–100cc. The AUA recognizes that many devices do not necessarily lack efficacy in prostate volumes above or below the recommended treatment parameters, however, insufficient evidence prevents the AUA from making formal recommendations beyond those sizes identified.

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 (K150786). 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 cm^3 and ≤ 80 cm^3. 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 of 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; McVary, et al., 2021).

Professional Societies/Organizations:
Water vapor thermal therapy (WVTT) is discussed in the updated 2018 (amended 2021) 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:

- WVTT should be considered as a treatment option for patients with LUTS/BPH provided prostate volume 30–80cc. (Moderate Recommendation; Evidence Level: Grade C)
- WVTT may be offered as a treatment option to eligible patients who desire preservation of erectile and ejaculatory function. (Conditional Recommendation; Evidence Level: Grade C)

Body of Evidence Strength Grading:

Strong Recommendation (Net benefit or harm substantial)
- Evidence Strength A (High Certainty): Benefits > Risks/Burdens (or vice versa); Net benefit (or net harm) is substantial; Applies to most patients in most circumstances and future research is unlikely to change confidence
- Evidence Strength B (Moderate Certainty): Benefits > Risks/Burdens (or vice versa); Net benefit (or net harm) is substantial; Applies to most patients in most circumstances but better evidence could change confidence
- Evidence Strength C (Low Certainty): Benefits > Risks/Burdens (or vice versa); Net benefit (or net harm) appears substantial; Applies to most patients in most circumstances but better evidence is likely to change confidence (rarely used to support a Strong Recommendation)

Moderate Recommendation (Net benefit or harm moderate)
- Evidence Strength A (High Certainty): Benefits > Risks/Burdens (or vice versa); Net benefit (or net harm) is moderate; Applies to most patients in most circumstances and future research is unlikely to change confidence
- Evidence Strength B (Moderate Certainty): Benefits > Risks/Burdens (or vice versa); Net benefit (or net harm) is moderate; Applies to most patients in most circumstances but better evidence could change confidence

- Evidence Strength C (Low Certainty): Benefits > Risks/Burdens (or vice versa); Net benefit (or net harm) appears moderate; Applies to most patients in most circumstances but better evidence is likely to change confidence

Conditional Recommendation (No apparent net benefit or harm)

- Evidence Strength A (High Certainty): Benefits = Risks/Burdens; Best action depends on individual patient circumstances; Future research unlikely to change confidence
- Evidence Strength B (Moderate Certainty): Benefits = Risks/Burdens; Best action appears to depend on individual patient circumstances; Better evidence could change confidence
- Evidence Strength C (Low Certainty): Balance between Benefits & Risks/Burdens unclear; Alternative strategies may be equally reasonable; Better evidence likely to change confidence

Clinical Principle

- A statement about a component of clinical care that is widely agreed upon by urologists or other clinicians for which there may or may not be evidence in the medical literature
- A statement, achieved by consensus of the Panel, that is based on members' clinical training, experience, knowledge, and judgment for which there is no evidence

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 that is commonly seen 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) (DEN170024) 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.

On March 11th, 2021, the FDA granted 510(k) approval (K202961) as a class II device for the AquaBeam Robotic System (PROCEPT BioRobotics Corporation, Redwood City, CA) for the same indication as the de novo approval that served as the predicate device. The AquaBeam system is capable of mapping the prostatic treatment area and uses a pressurized jet of fluid to cut the desired tissue (FDA, 2021c).

Literature Review:
Several peer reviewed studies have been published comparing Aquablation to the gold standard of TURP. Studies consist of several randomized controlled trials including the pivotal WATER trial reporting up to three years of data, a systematic review, an open-label study, and a retrospective review. The studies are limited by small patient populations, however, no serious safety concerns have been reported. The literature demonstrates neutrality when comparing Aquablation to the hold standard of TURP and the technology is supported by relevant professional societies. The literature suggests that Aquablation may be an effective treatment option for LUTS associated

with BPH in men ≥ 45 years old with prostate volumes between 30–80 cm3 (Bach, et al., 2020; Gilling, et al., 2020; Kasraeian, et al. 2020; Gilling, et al., 2019; Hwang, et al., 2019; Pimentel, et al., 2019; Gilling, et al., 2018; Kasivisvanathan, et al., 2018; AUA, 2021).

Elterman et al. (2021) conducted a pooled meta-analysis of four international studies including one randomized controlled trial, two single-arm controlled trials, and one observational study to evaluate outcomes in men (n=425) with benign prostatic hyperplasia (BPH) and various prostate volumes who underwent Aquablation. The average age for participants across all four studies was 66.9 years old. Studies were included if they had a minimum of one year follow-up. Individual study inclusion criteria varied in regards to prostate size (i.e., 20-150mL), International Prostate Symptom Score (IPSS) (i.e., ≥12 or diagnosed with lower urinary tract symptoms due to BPH), and Qmax (i.e., <15mL/s or diagnosed with lower urinary tract symptoms due to BPH). Individual study exclusion criteria varied as well in regards to post-void residual (i.e., >300mL, none), history of urinary retention (i.e., yes, none, only if catheter use exceeded 90 days), previous prostate surgery (i.e., yes, none), and American Society of Anesthesiologists classification (i.e., III or higher, none). Additionally, studies with less than one year follow-up were excluded. The intervention was waterjet ablation in men with prostate volumes of 20–150mL. Transurethral resection of the prostate served as the comparator in the randomized controlled trial. The primary outcome measures were IPSS, uroflowmetry, postoperative Incontinence Severity Index (ISI) and surgical retreatment. A statistically significant improvement of 16 points was noted at one year in IPSS scores. Qmax improved by 9.4mL at one year. Post-void residual urine volumes improved at one year by 42–68% depending on baseline PVR. Surgical re-treatment occurred in 0.7% of patients. All improvements were independent of prostate size and the presence or absence of a median lobe. Author noted limitations include the fact that data past one year was not available in all studies, heterogeneity of inclusion and exclusion criteria between studies. An additional limitation of the study is the small patient population.

In 2020, Gilling et al. reported on the three-year results of the WATER study which was a prospective, double-blinded, multicenter, international, randomized controlled trial to compare efficacy and safety outcomes between the gold standard of transurethral resection of the prostate (TURP) to Aquablation in men with lower urinary tract symptoms (LUTS) attributed to benign prostatic hypertrophy (BPH). Three year follow-up data was obtained on 97 Aquablation patients and 55 TURP patients. Reductions in mean International Prostate Symptom Scores (IPSS) were maintained at three years in both the Aquablation and TURP groups. There was not a significant difference in scores between groups with the exception of men with prostates ≥ 50 cc who averaged 3.5 points higher in the IPSS test in the Aquablation group compared to the TURP group (p=0.0125). Quality of life scores were also similar across groups at three years (p=0.7845). A statistically significant reduction in mean ejaculatory function scores were noted in the TURP group compared to the Aquablation group (p=0.0008). There were no statistically significant differences between groups for erectile function. In both groups, maximum urinary flow rates increased and post-void residual and PSA decreased over the course of three years. These results were maintained at three years but did not show a statistically significant difference between groups as was the case for post-void residual and PSA as well. Adverse events were similar across both groups with the exception of anejaculation which was statistically significantly reduced in the Aquablation group (p=0.0039). One patient in the Aquablation group and four patients in the TURP group experienced a urethral stricture (p=0.0567). Retreatment rates were 4.3% in the Aquablation group and 1.5% in the TURP group (p=0.4219) at three years. An author noted limitation of the study is the inability to generalize data to men with prostates larger than 80 cc.

Bach et al. (2020) conducted a prospective, multicenter, single-arm, open-label, international clinical trial to assess the safety and effectiveness of waterjet-based prostate resection (Aquablation procedure) for the treatment of benign prostatic hyperplasia (BPH). A total of 178 men with a mean age of 67.7 years were included in the study. Thirty men were lost to follow-up.

Men were included in the study if they had a diagnosis of lower urinary tract symptoms (LUTS) attributable to BPH and had a prostate size of 20–150 cc. Men were excluded if they: had a bleeding disorder or were unable to stop anticoagulants or antiplatelet agents perioperatively, had a history of gross hematuria, were on systemic immune suppressants, had a contraindication to general and spinal anesthesia, were unwilling to accept a transfusion if needed, or if they had a severe illness that could prevent complete follow-up. All patients underwent the aquablation procedure by a trained surgeon. The change in International Prostate Symptom Score (IPSS) from baseline to three months served as the primary outcome measure. Secondary outcomes measured as a comparison between baseline and three months follow-up included: the proportion of patients who experienced ejaculatory or erectile dysfunction, maximal flow rate (Qmax), prostate specific antigen (PSA) level, post-void residual (PVR), total Male Sexual Health Questionnaire (MSHQ) score, International Index of Erectile Function (IIEF-15) score, and subjective reporting of dysuria on a 0–5 scale. Follow-up occurred at three and 12 months. IPSS scores improved significantly by 14.5 points at three months follow-up compared to baseline ($p<0.0001$) and 15.3 points at 12 months follow-up ($p<0.0001$). Qmax significantly improved from 9.9 cc/ sec at baseline to 20.3 cc/sec at three months and 20.8 cc/sec at 12 months ($p<0.0001$). PVR significantly improved from 108 cc at baseline to 47 cc at three months and 61 cc at 12 months ($p<0.0001$). Significant reductions in mean prostate size were noted at three months follow-up compared to baseline (35 cc vs. 59 cc; $p<0.0001$). Significant improvements in MSHQ scores were not reported. Reports of dysuria significantly decreased at three month follow-up (29%) compared to baseline (51%) ($p<0.0001$). Five patients (n=2.7%) underwent transfusion in the first week after the procedure, 14 (n=7.9%) returned to the operating room for post-procedure bleeding, one patient returned to the operating room for clot evacuation, one patient had a rectal perforation requiring a temporary colostomy, three patients had a meatal stenosis or stricture requiring a procedure, 15 patients (n=8%) experienced ejaculatory dysfunction, and one patient experienced erectile dysfunction. Author noted limitations of the study included the lack of a comparator and short-term follow-up. Additional limitations of the study include the small sample size and non-blinded design of the study.

Kasraeian et al. (2020) conducted an all-comers, single-center retrospective review of prospectively collected data to assess the safety and efficacy of robotically guided waterjet-based prostate resection in patients with lower urinary tract symptoms associated with BPH. Patients (n=55) ranged in age from 50–84 years and had a mean prostate volume of 100cc. Patients were excluded if they were unable to stop anticoagulation prior to surgery. Patients underwent Aquablation using the AquaBeam Robotic System. Outcome measures included: operative time, preoperative to postoperative change in hemoglobin, length of hospital stay, BPH symptom score, post-void residual measurements, and sexual function. Follow-up occurred at three months. Significant improvements were noted in IPSS ($p<0.0001$), quality of life ($p<0.0001$), and maximum urinary flow rate ($p=0.0001$). Adverse events included: hematuria (n=5), bladder spasms (n=1), dehydration (n=1), intolerance of Foley catheter (n=1), and temporarily elevated creatinine (n=1). Limitations of the study include the small sample size, lack of a comparator, and short-term follow-up.

Desai et al. (2020) conducted a prospective, multicenter, single-arm study, known as the WATER II trial, to assess the safety and efficacy of the Aquablation procedure in men with lower urinary tract symptoms associated with BPH and with prostate volumes of 80–150 cc. Men (n=101) aged 45-80 years were included if they had: a prostate volume of 80–150 cc, a baseline International Prostate Symptom Scores (IPSS) of ≥ 12, a maximum urinary flow rate (Qmax) of <15 mL/sec, a serum creatinine of < 2 mg/dL, a history of failure of medical management, and a capacity to participate. Exclusion criteria were: body mass index ≥ 42 kg/m2, history of prostate or bladder cancer, significant bladder calculus or diverticulum, active infection, previous urinary tract surgery, urinary catheter use for 90 or more days, chronic pelvic pain, urethral stricture, meatal stenosis, use of anticholinergic agents, and any condition that would prevent follow-up.

Aquablation was performed in all patients using the AquaBeam Robotic System. The following assessments were taken at baseline: IPSS, Incontinence Severity Index, Pain Intensity Scale, International Index of Erectile Function (IIEF-15), the Male Sexual Health Questionnaire (MSHQ-EjD), uroflometry, serum prostate-specific antigen (PSA), transrectal ultrasound prostate size, Qmax, and post-void residual (PVR). Two year follow-up included assessment of IPSS and uroflowmetry. PSA follow-up occurred at six, 12, and 24 months. Transrectal ultrasound prostate size follow-up occurred at three months post-operatively. Fifteen patients were lost to the two year follow-up. Mean IPSS scores showed statistically significant improvement from a baseline of 23.2 to 5.8 at two years ($p<0.0001$) regardless of prostate size. Quality of life scores showed a significant improvement of 3.4 points at two year follow-up ($p<0.0001$). Qmax significantly improved by 9.7 cc/ sec at two years ($p<0.0001$). PVR volume decreased from 131 cc at baseline to 45 cc at two years. PSA decreased from a baseline of 7.1 to 4.9 at two years while men with a PSA of ≥ 4 at baseline observed a significant 38% reduction at two years ($p<0.0001$). Two patients required surgical retreatment with TURP and HOLEP. An author noted limitation of the study was the lack of a comparator. Additional limitations of the study include the small patient population and the predominantly white (87.1%) make-up of the patient population compared to Asian (5%), Black (5.9%), and other (2%). Additional high quality studies are needed to evaluate the safety and efficacy of Aquablation in patients with larger prostate volumes.

Gilling et al. (2019) reported one year safety and efficacy outcomes for the WATER study. 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 men 45-80 years old with a prostate between 30-80 gm as measured by transrectal ultrasound, moderate to severe symptoms as indicated by IPSS 12 or greater and a maximum urinary flow rate less than 15 ml per second. Men were excluded from analysis if they had a history of prostate or bladder cancer, neurogenic bladder, bladder calculus or clinically significant bladder diverticulum, active infection, treatment for chronic prostatitis, diagnosis of urethral stricture, meatal stenosis or bladder neck contracture, a damaged external urinary sphincter, stress urinary incontinence, post-void residual urine greater than 300 ml or urinary retention, self-catheterization use or prior prostate surgery. Men receiving anticoagulants or bladder anticholinergics and those with severe cardiovascular disease were also excluded. Mean total operative time was similar for Aquablation and transurethral prostate resection (33 vs 36 minutes, p=0.2752) but resection time was lower for Aquablation (4 vs 27 minutes, p<0.0001). Mean IPSS had decreased from baseline by 16.9 points for Aquablation and 15.1 points for TURP. The mean difference in the change score at six months was 1.8 points greater for Aquablation (noninferiority p<0.0001 and superiority p=0.1347). At six months 100% of Aquablation vs 98% of TURP cases showed I-PSS improvement. Of the patients who underwent Aquablation and transurethral prostate resection 26% and 42%, respectively, experienced a three-month primary safety end point, which met the study primary noninferiority safety hypothesis and subsequently demonstrated superiority (p=0.0149). Among sexually active men the rate of anejaculation was lower in those treated with Aquablation (10% vs 36%, p=0.0003). In men with a prostate greater than 50 ml, the rate of persistent grade 1 events was (2% vs 26%, p=0.0003), the rate of persistent grade 1 events was substantially lower (2% vs 26%, p=0.0003) and the rate of Clavien-Dindo grade 2 and greater events trended in favor of Aquablation (19% vs 29%, p=0.3146). Each group achieved significant symptom relief compared to baseline with similar rates of Clavien-Dindo 2 or greater complications. The risk of anejaculation was lower with Aquablation. Larger prostates (50 to 80 ml) demonstrated a more pronounced safety and efficacy benefit. This study was limited by the short-term six-month follow-up (ClinicalTrials.org: NCT02505919).

In a cohort study (n=90), Kasivisvanathan et al. (2018) reported the efficacy and safety at one year for the treatment of LUTS related to benign prostatic hyperplasia (BPH) in the United States cohort from the WATER study. Sixty individuals were treated with Aquablation and 30 were treated with TURP. A total of 87 individuals completed one year follow-up. The efficacy objective was reduction in IPSS. The safety objective was the occurrence of Clavien-Dindo persistent grade 1 or grade 2 or higher operative complications. Change in IPSS at one year between Aquablation and TURP was similar (14.5 vs13.8, respectively, p=0.7117). The number of subjects experiencing persistent Clavien-Dindo grade 1 or Clavien-Dindo grade 2 or higher adverse events was lower in the Aquablation group compared to the TURP group (20% vs 47% respectively, p=0.0132). Amongst sexually active subjects, the rate of an ejaculation was lower in patients treated with Aquablation than TURP (9% vs 45%, respectively, p=0.0006). The authors reported that further follow-up is needed to assess the durability of Aquablation. This study is limited by small sample size and short-term follow-up.

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) signaling 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 but offer a small improvement in preservation of ejaculatory 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).

Professional Societies/Organizations:
Robotic waterjet treatment (RWT) (e.g., Aquablation) is discussed in the 2021 amended American Urological Association (AUA) evidence-based Guideline: Surgical Management of Benign Prostatic Hyperplasia/Lower Urinary Tract Symptoms. Several publications from a single low risk of bias randomized controlled trial (n=181) assessing Aquablation was evaluated by the panel. The guideline recommendation states:

- Robotic waterjet treatment RWT may be offered as a treatment option to patients with LUTS/BPH provided prostate volume 30–80cc. (Conditional Recommendation; Evidence Level: Grade C)

Body of Evidence Strength Grading:

Strong Recommendation (Net benefit or harm substantial)
- Evidence Strength A (High Certainty): Benefits > Risks/Burdens (or vice versa); Net benefit (or net harm) is substantial; Applies to most patients in most circumstances and future research is unlikely to change confidence
- Evidence Strength B (Moderate Certainty): Benefits > Risks/Burdens (or vice versa); Net benefit (or net harm) is substantial; Applies to most patients in most circumstances but better evidence could change confidence
- Evidence Strength C (Low Certainty): Benefits > Risks/Burdens (or vice versa); Net benefit (or net harm) appears substantial; Applies to most patients in most circumstances but better evidence is likely to change confidence (rarely used to support a Strong Recommendation)

Moderate Recommendation (Net benefit or harm moderate)
- Evidence Strength A (High Certainty): Benefits > Risks/Burdens (or vice versa); Net benefit (or net harm) is moderate; Applies to most patients in most circumstances and future research is unlikely to change confidence
- Evidence Strength B (Moderate Certainty): Benefits > Risks/Burdens (or vice versa); Net benefit (or net harm) is moderate; Applies to most patients in most circumstances but better evidence could change confidence
- Evidence Strength C (Low Certainty): Benefits > Risks/Burdens (or vice versa); Net benefit (or net harm) appears moderate; Applies to most patients in most circumstances but better evidence is likely to change confidence

Conditional Recommendation (No apparent net benefit or harm)
- Evidence Strength A (High Certainty): Benefits = Risks/Burdens; Best action depends on individual patient circumstances; Future research unlikely to change confidence

- Evidence Strength B (Moderate Certainty): Benefits = Risks/Burdens; Best action appears to depend on individual patient circumstances; Better evidence could change confidence
- Evidence Strength C (Low Certainty): Balance between Benefits & Risks/Burdens unclear; Alternative strategies may be equally reasonable; Better evidence likely to change confidence

Clinical Principle

- A statement about a component of clinical care that is widely agreed upon by urologists or other clinicians for which there may or may not be evidence in the medical literature
- A statement, achieved by consensus of the Panel, that is based on members' clinical training, experience, knowledge, and judgment for which there is no evidence

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).

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.

Histotripsy: Histotripsy is an extracorporeal ultrasound technology that has been proposed to treat BPH. Histotripsy is a form of focused ultrasound therapy that utilizes cavitational 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).

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, annual review 2020).

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 (Knight, et al., 2021; Hayes, 2019, annual review 2020; Jiang et al., 2019; Zumstein, et al., 2018; Carnevale, et al., 2017; Kuang et al, 2017; Pyo et al., 2017; Wang et al, 2016; de Assisi, et al., 2015; Wang, et al., 2015; Russo, et al., 2015; Gao, et al., 2014; Bagla, et al., 2014; Pisco, et al., 2013).

Knight et al. (2021) conducted a systematic review and meta-analysis of four randomized controlled trials and two non-randomized comparative studies to compare the safety and efficacy of prostatic artery embolization (PAE) to transurethral resection of the prostate (TURP) for benign prostatic hyperplasia (BPH). The number of participants in each study ranged from 30–260. Studies were included for analysis if they compared PAE and TURP in the treatment of LUTS secondary to BPH. Abstracts, reviews, editorials, guidelines, protocols, economic evaluations, studies not reporting on relevant clinical outcomes, studies that included additional procedures for BPH, and studies that included fewer than 10 participants were excluded. Outcomes included the difference between groups for maximum urinary flow rate (Qmax), prostate volume, prostate-specific antigen (PSA), International Prostate Symptoms Score (IPSS), IPSS quality of life (IPSSQoL), International Index of Erectile Function (IIEF-5), post-void residual (PVR), and hospital and procedural times. Follow-up ranged from three months to 12 months. Significant improvements were reported in the TURP group for Qmax ($p<0.0001$), prostate volume ($p<0.00001$), and PSA ($p=0.02$) compared to the PAE group. Significant differences between groups were not reported for changes in International Prostate Symptoms Score (IPSS), IPSS quality of life (IPSS-QoL), International Index of Erectile Function (IIEF-5), and postvoid residual (PVR). Significantly fewer adverse events and shorter hospital times were reported in the PAE group ($p<0.00001$ and $p<0.00001$, respectively). Adverse events occurred in both treatment groups and included hematuria, UTI, dysuria, urinary retention, and urinary incontinence. Author noted limitations of the review included the small number of studies and short-term follow-up. An additional limitation is the heterogenous study protocols used between studies.

Jung et al. (2022) conducted a Cochrane systematic review of randomized controlled trials and prospective cohort studies to evaluate the effects of prostate artery embolization (PAE) on the treatment of lower urinary tract symptoms in men with benign prostatic hyperplasia (BPH). Nine studies comparing either PAE to TURP (7 studies; n=300) or PAE to sham (2 studies; n=120) were included in the review. The primary outcome measured was the International Prostate Symptom Score (IPSS). Secondary outcomes included were: maximal flow rate (Qmax), post void residual (PVR), quality of life (QoL), chronic prostatitis symptoms index, prostate volume, prostate-specific antigen (PSA), and the International Index of Erectile Function-5 questionnaire (IIEF-5). Short (i.e., ≤ 12 months) and long-term (i.e., 13–24 months) follow-up data showed little to no difference in the improvement of IPSS, QoL, or erectile function scores compared to TURP. The quality of evidence was rated very low to low certainty. The authors were uncertain about major adverse events but concluded that PAE results in an increase in retreatment rates compared to TURP. The quality of evidence used to reach this conclusion was rated moderate. The authors

concluded that the evidence for the use of PAE for the treatment of LUTS in men with BPH should be better informed by larger studies with longer follow-up.

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 size 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 IEEF (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 $P<0.00001$). Both prostate volume (PV) and prostate-specific antigen had significant decrease during the 12-month follow-up ($p<0.00001$ 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 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 cm^3, 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 void 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 American Urological Association (AUA) evidence-based guideline on the management of benign prostatic hyperplasia associated with lower urinary tract symptoms (Lerner, et al., 2021) stated that:

PAE for the routine treatment of LUTS is not supported by current data, and benefit over risk remains unclear; therefore, PAE is not recommended outside the context of clinical trials. (Expert Opinion)

Body of Evidence Strength Grading:

Strong Recommendation (Net benefit or harm substantial)
- Evidence Strength A (High Certainty): Benefits > Risks/Burdens (or vice versa); Net benefit (or net harm) is substantial; Applies to most patients in most circumstances and future research is unlikely to change confidence
- Evidence Strength B (Moderate Certainty): Benefits > Risks/Burdens (or vice versa); Net benefit (or net harm) is substantial; Applies to most patients in most circumstances but better evidence could change confidence
- Evidence Strength C (Low Certainty): Benefits > Risks/Burdens (or vice versa); Net benefit (or net harm) appears substantial; Applies to most patients in most circumstances but better evidence is likely to change confidence (rarely used to support a Strong Recommendation)

Moderate Recommendation (Net benefit or harm moderate)
- Evidence Strength A (High Certainty): Benefits > Risks/Burdens (or vice versa); Net benefit (or net harm) is moderate; Applies to most patients in most circumstances and future research is unlikely to change confidence
- Evidence Strength B (Moderate Certainty): Benefits > Risks/Burdens (or vice versa); Net benefit (or net harm) is moderate; Applies to most patients in most circumstances but better evidence could change confidence
- Evidence Strength C (Low Certainty): Benefits > Risks/Burdens (or vice versa); Net benefit (or net harm) appears moderate; Applies to most patients in most circumstances but better evidence is likely to change confidence

Conditional Recommendation (No apparent net benefit or harm)
- Evidence Strength A (High Certainty): Benefits = Risks/Burdens; Best action depends on individual patient circumstances; Future research unlikely to change confidence
- Evidence Strength B (Moderate Certainty): Benefits = Risks/Burdens; Best action appears to depend on individual patient circumstances; Better evidence could change confidence
- Evidence Strength C (Low Certainty): Balance between Benefits & Risks/Burdens unclear; Alternative strategies may be equally reasonable; Better evidence likely to change confidence

Clinical Principle
- A statement about a component of clinical care that is widely agreed upon by urologists or other clinicians for which there may or may not be evidence in the medical literature

- A statement, achieved by consensus of the Panel, that is based on members' clinical training, experience, knowledge, and judgment for which there is no evidence

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 cm^3), 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.)

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, 2020a). In June 2021, the iTind System (Medi-Tate Ltd, Philadelphia, PA) received FDA 510(k) approval (K210138) using the prior version as the predicate device. Indications for use were unchanged (FDA, 2021b).

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.

Chughtai et al. (2021) conducted a randomized controlled trial to evaluate the safety and efficacy of the iTind system on lower urinary tract symptoms (LUTS) in men with benign prostatic hyperplasia. A total of 175 men with a mean age of 61.1 years were randomized 2:1 and assigned to either treatment with iTind (n=118) or sham control (n=57). Criteria for inclusion were as follows: men ≥ 50 years, International Prostate Symptoms Score (IPSS) ≥ 10; peak urinary flow rate (PFR) ≤ 12 mL/sec with a 125 mL voided volume; prostate volume between 25–75c; and a normal urinalysis, CBC, and biochemistry. Participants were excluded if they had: a post void residual volume (PVR) > 250 mL, an obstructive median lobe (OML), prostate specific antigen (PSA) > 10 ng/mL or free PSA < 25% without a subsequent negative prostate biopsy, previous prostate surgery, prostate or bladder cancer, neurogenic bladder and/or sphincter abnormalities, or confounding bladder pathologies based on medical history, recent cystolithiasis or hematuria, active urinary tract infection, compromised renal function, severe respiratory disorders, known immunosuppression, active antithrombotic or antiplatelet treatment, or cardiac disease including arrhythmias and uncontrolled diabetes mellitus. The intervention consisted of the implantation of the iTind system which was then removed after five to seven days. Sham served as the comparator which consisted of the insertion and removal of an 18F silicon Foley catheter to simulate insertion and removal of the iTind system. The primary outcome measured was the percentage of patients achieving a three-point reduction in IPSS at three months. Quality of life (QoL), PFR, PVR, and sexual function served as secondary outcomes. Follow-up occurred at 6 weeks, three months, and twelve months. At least a three-point significant reduction in IPSS at three months was observed in 78.6% of participants who received the iTind procedure compared to 60% of participants in the control arm (p=0.029). Overall, non-significant improvement of IPSS was observed in the iTind group by an average of 9 points compared to 6.6 points in the sham group (p=0.63). Non-significant improvement in QoL, PFR, and PVR scores were observed in the intervention group compared to the control group (p=0.264, p=0.230, p=0.781, respectively). There was no change in sexual function according to questionnaires. Significant improvement in IPSS in the intervention group was maintained at 12 months. Adverse events in the intervention group included: urinary retention (n=2), UTI (n=2), and sepsis (n=1). These adverse events did not occur in the control group. Author noted limitations included: loss to follow-up of 29% of patients in the intervention group and 30% in the control group and an inability to generalize the results to all men with LUTS due to BPH due to specific inclusion criteria. Additional limitations of the study include the small patient population and short-term follow-up.

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 two 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.

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.

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).

Currently 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.

Medicare Coverage Determinations

	Contractor	Determination Name/Number	Revision Effective Date
NCD	National	No National Coverage Determination found	
LCD	CGS	Fluid Jet System in the Treatment of Benign Prostatic Hyperplasia (BPH) (L38378)	10/22/2023
LCD	CGS	Laser Ablation of the Prostate (L34090)	3/23/2023
LCD	NGS	Fluid Jet System in the Treatment of Benign Prostatic Hyperplasia (BPH) (L38367)	11/1/2020
LCD	NGS	WATER VAPOR Thermal Therapy for LUTS/BPH (L37808)	4/1/2023
LCD	First Coast	Transurethral Waterjet Ablation of the PROSTATE (L38726)	12/27/2020
LCD	Noridian	Transurethral Waterjet Ablation of the PROSTATE (L38705)	12/27/2020
LCD	Novitas	Transurethral Waterjet Ablation of the PROSTATE (L38712)	12/27/2020
LCD	Palmetto	Transurethral Waterjet Ablation of the PROSTATE (L38549)	1/29/2023
LCD	Wisconsin Physicians Service	Transurethral Waterjet Ablation of the PROSTATE (L38682)	10/15/2023

Note: Please review the current Medicare Policy for the most up-to-date information.
(NCD = National Coverage Determination; LCD = Local Coverage Determination)

Coding Information

Notes:

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:

CPT®* Codes	Description
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)
53854	Transurethral destruction of prostate tissue; by radiofrequency generated water vapor thermotherapy

CPT®* Codes	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).

HCPCS Codes	Description
C2596	Probe, image-guided, robotic, waterjet ablation
C9739	Cystourethroscopy, with insertion of transprostatic implant; 1 to 3 implants
C9740	Cystourethroscopy, with insertion of transprostatic implant; 4 or more implants

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):

CPT®* Codes	Description
37242	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)
53899	Unlisted procedure, urinary system
55880	Ablation of malignant prostate tissue, transrectal, with high intensity-focused ultrasound (HIFU), including ultrasound guidance
55899	Unlisted procedure, male genital system
76999	Unlisted ultrasound procedure (eg, diagnostic, interventional)

HCPCS Codes	Description
C9769	Cystourethroscopy, with insertion of temporary prostatic implant/stent with fixation/anchor and incisional struts

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Revision Details

Type of Revision	Summary of Changes	Date
Annual Review	• Title change. • Removed policy statement for: cryosurgical ablation, interstitial laser coagulation (ILC), plasma kinetic vaporization (e.g., PlasmaKinetic™ Tissue Management System), transperineal laser ablation (TPLA) (e.g., SoracteLite), and transurethral ultrasound-guided laser incision of the prostate (TULIP).	12/15/2023