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Lesson 33 Volume 39

Novel Surgical Technologies for Symptomatic BPH*

Learning Objective: At the conclusion of this continuing medical education activity, the participant will be able to describe emerging minimally invasive options for the treatment of lower urinary tract symptoms attributed to benign prostatic hyperplasia, including periprocedural considerations and expected outcomes. The participant will also be able to outline the context, limitations and clinical applicability of minimally invasive surgical treatment in benign prostatic hyperplasia.

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***This AUA Update addresses the Core Curriculum topics of BPH and Surgical Energy, and the American Board of Urology Module on Neurogenic Bladder, Voiding Dysfunction, Female Urology, BPH and Urethral Stricture.**

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INTRODUCTION

Benign prostatic hyperplasia increases in prevalence as individuals age. **Nearly 70% of U.S. men between 60 and 69 years old and nearly 80% of men ≥70 years old have some degree of BPH.[1,2]** An autopsy study found a prevalence of histologically confirmed BPH in prostates with gross enlargement of 14%, 37% and 39%, respectively, in men 50–59, 60–69 and older than 70 years old.[3] The prevalence and severity of lower urinary tract symptoms in men increase with advancing age; the prevalence is low in men less than 40 years of age but approaches 80% in men over 80 years. LUTS attributed to BPH (LUTS/BPH) is many times the culprit of these bothersome symptoms.

The Urologic Diseases in America project noted that medication usage increased and surgery decreased over the years 2003–2013.[2] Treatment approaches for LUTS/BPH vary greatly by patient age, with the frequency of surgery and medication use increasing with advancing age. While a minority of men in their 40s and 50s required any treatment, a sharp increase in treatment use was seen between these decades. **Younger men were more likely to use less invasive surgical options.[3]** Despite the increase in prevalence of medical therapy, significant technological advancements have increased the surgical options for men suffering from BPH. **With ejaculation dysfunction representing a significant adverse effect of alpha blockade and growing concerns regarding the long-term impact of 5alpha-reductase medical therapy, much effort has been given to the development of newer, minimally invasive surgical treatments that preserve antegrade ejaculatory and erectile function.**

Prior to proceeding to a surgical intervention the patient should be informed about potential complications of all available procedures, including new onset ejaculatory dysfunction and/or worsening erectile dysfunction. The patient's attitude toward potential sexual dysfunction may influence the choice of procedure. This issue is particularly critical given the emergence of therapies that have little or no impact on sexual function (i.e. convective water vapor therapy and prostatic urethral lift; see below). Data on the sexual side effects of BPH surgery can be difficult to ascertain as many studies are not primarily designed to answer this question. **As such, many studies evaluate sexual side effects by looking at reported adverse events only, rather than specifically assessing sexual function. Doing so will very likely *underestimate* the impact of a given procedure on ED or EjD.** In addition, in some studies patients may be not only undergoing a surgical procedure, but also stopping the previous medical therapy, which can confound interpretation of postoperative sexual function. Given the strong observed relationship between ED and LUTS/BPH, this group of men is at high risk for sexual dysfunction.[4] Patients should be counseled about the sexual side effects of any surgical intervention and should be made aware that surgical treatment can cause ejaculatory dysfunction and may worsen ED.

Interventions for LUTS/BPH have clear sexual side effects. These treatments have a significant rate of EjD. Libido does not appear to be affected significantly by surgical therapy. **Most importantly, sexual side effects from surgical treatments are more likely to be permanent than those from medical treatments, which can often be reversed by stopping medical treatment or switching to an alternative treatment.**

MISTs strive for novel approaches that rival standard methodology, ideally providing effective therapy and fewer side effects. **From the patient standpoint the hallmarks or stipulations of a successful MIST might include 1) tolerability, 2) rapid and durable relief of symptoms, 3) a short recovery time with rapid return to life activities, 4) minimal adverse events and 5) affordability.** In addition to endorsing the patient's concerns, urologists are interested in 1) capacity to be performed in an ambulatory setting under reduced anesthesia, 2) a fast learning curve, 3) generalizability from randomized controlled trials, 4) ease of performance and 5) reasonable start-up costs and payment.[5,6]

The indications for standard surgical intervention include the more advanced presentations of renal insufficiency secondary to BPH, refractory urinary retention, recurrent bladder calculi, recurrent gross hematuria, recurrent urinary tract infections and failure of optimized medical therapy. Other than those who have failed medical therapy there is little information on how many patients with more progressed LUTS/BPH proceed to standard surgical interventions. The clinician should be cautious about extension of the new technologies to such advanced disease as the outcomes are not defined or well understood.

Three newer therapies (2 MISTs and an invasive robotic procedure) have dominated the BPH landscape over the last few years, each with ejaculatory and erectile preservation as a key benefit over traditional transurethral resection. In this Update we will discuss the mechanisms of action, operative indications, surgical technique and outcomes data for each of these novel treatments (PUL, convection water vapor therapy and image guided robot-assisted waterjet ablation of the prostate, the latter of which is not classified as a MIST due to the mandatory anesthetic requirement), while also exploring MIST technologies currently in development.

CONVECTIVE WATER VAPOR ABLATION: REZŪM® SYSTEM

Mechanism of action. **Convective water vapor energy ablation, the Rezūm System, provides a minimally invasive thermal ablation without a discernible thermal gradient as seen with *conductive* heat transfer, as in transurethral needle ablation and transurethral microwave therapy. This transurethral *convective* thermal therapy uses radio frequency to generate wet thermal energy in the form of water vapor (fig. 1). Convection disperses the water vapor in a uniform manner, intercalating the tissue interstices and rapidly disrupting tissue cell membranes, effecting cell death and necrosis.** The therapy can be targeted to

ABBREVIATIONS: BPH (benign prostatic hyperplasia), ED (erectile dysfunction), EjD (ejaculatory dysfunction), IIEF (International Index of Erectile Function), I-PSS (International Prostate Symptom Score), LUTS (lower urinary tract symptoms), MIST (minimally invasive surgical treatment), MSHQ (Male Sexual Health Questionnaire), PUL (prostatic urethral lift), Qmax (maximum flow rate), QOL (quality of life), RAWAP (robot-assisted waterjet ablation of prostate), TURP (transurethral resection of the prostate)

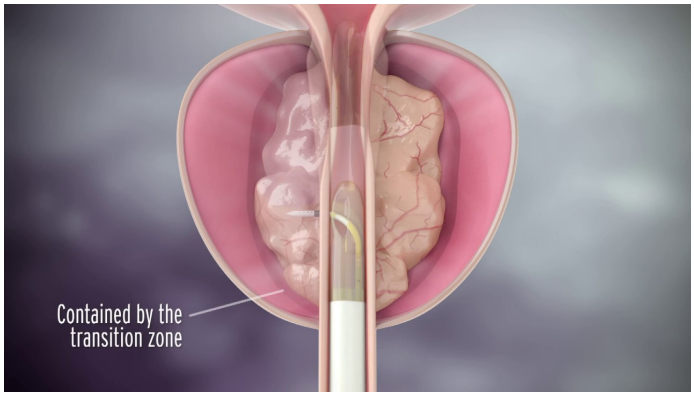

Figure 1. Dispersion of steam ablation zone of prostate with convective water vapor energy ablation (Rezūm). Reproduced with permission of Boston Scientific, Marlborough, Massachusetts.

defined areas, such as the *transition zone*, as steam will travel between cells until it encounters a barrier such as a collagen pseudo-capsule or the planes between prostatic zones**. No thermal effects occur outside the prostate or targeted treatment zone.**

Indications. The American Urological Association Guideline on Surgical Management of Lower Urinary Tract Symptoms Attributed to Benign Prostatic Hyperplasia (amended 2019)[7] supports urologists to offer water vapor thermal therapy to men with LUTS attributed to BPH provided that their *prostate volume is less than 80 gm*, although necessitate a thorough discussion regarding efficacy and re-treatment rates. A second statement in the Guideline speaks to the use of water vapor thermal therapy in qualified patients who express a *desire to preserve erectile and ejaculatory function*.

Surgical technique. This procedure can be performed in an *office based setting* with minimal pain management or anesthetic. To begin, a proprietary single use Rezūm System handpiece is fashioned over a 30-degree cystoscopic lens. The length of the prostatic fossa is measured from the bladder neck to the verumontanum. **Beginning 1 cm distal to the bladder neck, which is measured using the cystoscopic field of view, a retractable needle is positioned at 90 degrees to the area of interest. Once deployed within the prostatic tissue, a 9-second injection of water vapor is delivered (see Water Vapor video).** The total number of injections may vary according to prostate size, conformation and length of the urethra, although in the initial phase III trial the mean number of injections was 5.5 per procedure.[8]

Perioperative considerations. Although there is no standard of practice, commonly employed in-office anesthetic techniques for water vapor thermal therapy include a combination of local urethral anesthetic (e.g. xylocaine lubrication jelly), transrectal prostatic block, oral anxiolytics, inhalation agents (e.g. nitrous oxide) and/or intravenous anesthetics. **Recent data indicate that 88% of Rezūm procedures are performed in-office, supporting that particular component of a MIST**.

It is advised to place an indwelling urethral catheter at the conclusion of the procedure to ensure bladder drainage in the setting of transient prostatic edema and inflammation. The duration of catheterization is subject to surgeon preference. **Within the initial phase III trial the mean duration was 48 hours, although duration tends to be prolonged with enlarging gland volume and the number of steam treatments delivered.**

Perioperative counseling should include the potential for increased LUTS in the immediate postoperative period. As prostatic tissue undergoes cell death and resultant atrophy, men may experience a transient worsening of irritative voiding symptoms, although this tends to resolve beginning 2 to 3 weeks following the procedure.

Outcomes. A multicenter, randomized, controlled trial enrolled 197 men who were then randomized to convective water vapor therapy vs sham procedure.[9] The men in the study group exhibited a 50% improvement in their I-PSS compared to a 20% improvement in the control arm (11.4 vs 4.2 points, p <0.0001), while maximum flow rates improved by 67% (from 9.9 ml per second to 16.1 ml per second) compared to no change within the control group at 3 months following the procedure. Subsequent reporting of 2 and 4-year data has displayed durability of voiding improvement.[10] Meanwhile, longer term data have also confirmed preservation of erectile and ejaculatory function. At 1 year postoperatively no significant difference in IIEF responses were noted, while only 3% of men (4 of 136) reported EjD.[8] Long-term durability data continue to be accrued, although they have not yet been reported for year 5. However, re-treatment rates through 4 years are favorable (table 1).

Comparison of water vapor thermal therapy vs medical therapies or TURP. Many clinicians may wonder how the new MISTs compare to medical therapy or traditional transurethral surgery. Unfortunately data to address this relevant question are sparse. However, Gupta et al conducted an ad hoc evaluation of the long-term treatment outcomes for LUTS/BPH,[11] comparing the onetime application of the water vapor thermal therapy procedure to daily medical therapy in the treatment cohorts of the MTOPS study.[12] The risk of clinical progression of BPH and objective and subjective outcomes were assessed for a 3-year period after each of the treatments. Propensity scores were used to adjust for potential confounders by weighting the MTOPS cohorts such that baseline characteristics (I-PSS, QOL, prostate volume and other variables) were balanced between the water vapor thermal therapy group and each weighted MTOPS group. **They noted that water vapor thermal therapy provides clinically meaningful, rapid and durable relief**

Table 1. Re-treatment rates following convection water vapor thermal therapy

	Follow-up			
	1 Yr[8]	2 Yrs[9]	3 Yrs	4 Yrs[10]
No. pts/total No.	121/135	109/135	99/135	90/135
No. TURP/laser	1	3	3	3
No. repeat or other interventional procedure (%)	2 (2.2)	2 (3.7)	3 (4.4)	3 (4.4)
No. BPH medication	1	3	5	7
Total No. additional procedures or medication (%)	4 (3.0)	8 (5.9)	11 (8.1)	13 (9.6)

of LUTS in both storage and voiding functions when compared to the medically treated cohort. Thermal therapy demonstrated lower observed clinical BPH progression compared to medical therapy and showed greater improvement in LUTS compared to medical monotherapy (i.e. alpha blockers or 5alpha-reductase inhibitors). Interestingly using this same type of comparison technique, these same authors noted that water vapor thermal therapy had a significantly improved profile on erectile and ejaculation function compared to the weighted MTOPS group.[13] Early intervention with thermal therapy prior to use of pharmaceutical agents or invasive surgery or as an alternative to these modalities may be an ideal option for men with moderate to severe LUTS at risk for BPH progression.

PROSTATIC URETHRAL LIFT: UROLIFT® SYSTEM

Mechanism of action. PUL represents a unique, non-ablative technique for treating men with LUTS/BPH. Nitinol capsular anchor implants are deployed to achieve transprostatic tissue compression, thus mechanically opening the prostatic lumen to relieve obstruction. The anchor implants consist of a stainless steel end piece attached to a nitinol capsular anchor via a monofilament polyethylene terephthalate suture (fig. 2).[14] The nitinol capsular tabs of PUL are not perceived by MRI, while the stainless steel urethral end pieces create a "lucent halo." Whether such prostate metal will induce sufficient scatter or shadowing on MRI done for prostate cancer detection is controversial.

Indications. **The AUA Guideline on Surgical Management of Lower Urinary Tract Symptoms Attributed to Benign Prostatic Hyperplasia (amended 2019) states that urologists may offer PUL to men with LUTS/BPH provided they have a prostate volume less than 80 gm and verified absence of an obstructive median prostatic lobe.**[7] The Guideline obliges a thorough discussion regarding efficacy and re-treatment rates of PUL. Specifically symptom reduction and flow rate improvement have been shown to be less significant compared to conventional TURP. **A second Guideline statement speaks to the use of PUL in such patients who express a desire to preserve erectile and ejaculatory function.**

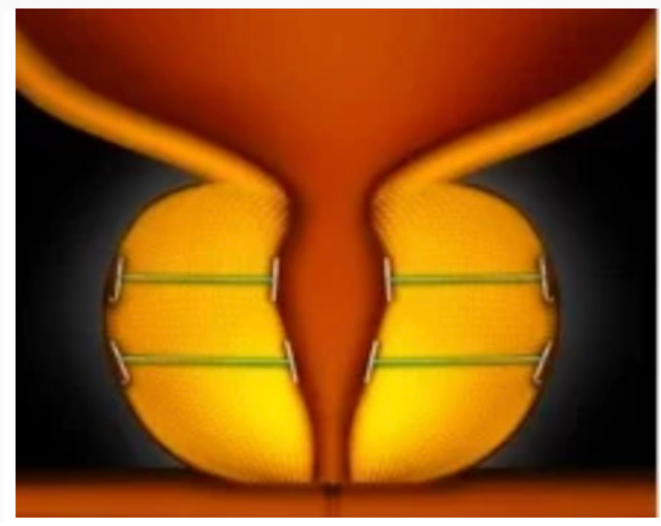

Figure 2. Prostatic urethral lift (UroLift). Expansion of prostatic urethra after treatment. Reproduced with permission of Neotract Inc., Pleasanton, California.

Surgical technique. This procedure can putatively be performed in an office based setting. To begin, a proprietary single use, spring activated implant delivery handpiece is fashioned over a 30-degree cystoscopic lens. The length of the prostatic fossa is measured from the bladder neck to the verumontanum. **The implants in PUL are placed anterolateral to avoid the neurovascular bundles (posterolateral) and the prostate veins (anterior). Beginning 1.5 cm distal to the bladder neck, the tip of the delivery system is positioned at 90 degrees to the area of interest, and gentle lateral compression is performed.** The handpiece trigger is then pulled to deploy a 19 gauge needle through the lobe, and as the needle is retracted, the capsular anchor is set. The implant is then tensioned by slowly moving the handpiece proximally until a white line becomes visible within a suture window visible near the end of the device. At this point a second pull of the handpiece trigger deploys the implant, thereby allowing for customized length and location to achieve adequate tension. A mirroring implant is deployed in an identical procedure similarly positioned on the contralateral side (see PUL video). The total number of implants may vary according to prostate size and length of the urethra, with the goal being to create a continuously open anterior channel. The mean number of implants from the phase III trial was 4.9 (range 2 to 11).[14]

Perioperative considerations. Similar to other MIST procedures, there is no standard of practice. Commonly employed anesthetic techniques for prostatic urethral lift include a combination of local urethral anesthetic (e.g. xylocaine lubrication jelly), transrectal prostatic block, oral anxiolytics, inhalation agents (e.g. nitrous oxide) and/or intravenous anesthetics. Interestingly a review of 2018 proprietary all payers dataset claims data suggests that the majority of PULs are delivered in the ambulatory surgery center (35%) or hospital outpatient setting (49%) rather than in-office, a previously mentioned ideal MIST stipulation (unpublished data).

In contrast to ablative techniques, prostatic implants hold the prostatic fossa open during the immediate postoperative period when post-procedural prostatic edema would be anticipated. **As such, use of urinary catheterization has been shown to be as low 20%, with a mean duration of less than 24 hours.**[15] In the phase III trial 32% of PUL patients required catheterization for failed voiding trial, resulting in mean catheter duration of 0.9 days.

Similar to convective water vapor therapy, PUL may be associated with transient worsening of urinary symptoms. Mild to moderate periprocedural effects, including dysuria, hematuria, urinary urgency and pelvic pain, have been shown to commonly resolve within 2 to 3 weeks postoperatively.[14, 15]

Outcomes. **At 3 months PUL was associated with a mean±SD improvement of -11.1±7.7 in I-PSS and increase of 4.28±5.16 ml per second in Qmax. These results proved durable with the published 5-year outcomes data, with men maintaining a mean 35% improvement in I-PSS and 50% improvement in Qmax.**[16] At 5 years surgical re-treatment for recalcitrant symptoms was 13.6% (6 patients undergoing placement of additional implants, 13 undergoing traditional TURP or laser ablation), while an additional 10.7% of patients were taking either a 5alpha-reductase inhibitor or an alpha blocker. **Overall, the re-treatment rate, which included those returning to the operating room for additional implants, implant removals and/or starting medication, was 33.4% at 5 years (table 2).** At 5 years no PUL patients

Table 2. Re-treatment rates following PUL

	Follow-up				
	1 Yr[14]	2 Yrs[29]	3 Yrs[30]	4 Yrs[31]	5 Yrs[16]
No. pts/total No.	123/140	109/135	99/135	90/135	72/140
No. TURP/laser	2	5	9	13	13
No. repeat PUL (%)	5 (5.0)	5 (7.1)	6 (10.7)	6 (13.6)	6 (13.6)
No. BPH medication	7	11	13	13	13
No. PUL removed	0	6	10	10	13
Total No. procedures or medication (%)	14 (10.0)	27 (19.2)	38 (27.1)	42 (30.0)	47 (33.6)

reported significant changes in either erectile or ejaculatory function as measured by the IIEF-5 and the MSHQ-EjD questionnaires.

Comparison of PUL vs medical therapies or TURP. As mentioned, many patients and clinicians wonder how PUL will compare to medical therapy or traditional transurethral surgery. Unfortunately data to address this relevant question with regard to medications are absent. Importantly there is a single study comparing PUL vs TURP.[17, 18] This study revealed that a lower proportion of men in the PUL group responded to treatment at 12 months of follow-up compared to TURP as measured by I-PSS reduction goal of ≥30% (73% vs 91%; p=0.05). At 24 months of follow-up the mean difference between PUL and TURP was 6.1 points (CI 2.2, 10.0), favoring TURP. Additionally flow rate was significantly lower in men allocated to PUL at all follow-up intervals.

ROBOT-ASSISTED WATERJET ABLATION OF PROSTATE: AQUABLATION

It is important to remember that even though this Update is intended to address new developments in MIST, robot-assisted waterjet ablation is actually not in this MIST category. Its absolute dependence on significant anesthesia, need for postoperative continuous bladder irrigation with a large bore catheter, and need for an overnight stay in a hospital setting for hematuria observation and care contravenes most stipulations of the MIST categorization.

Mechanism of action. **Robot-assisted waterjet ablation of prostate uses a robotic, image guided, highly engineered platform to ablate the prostate using a concentrated, high velocity waterjet (AquaBeam®). The waterjet is a high velocity hydrodissection tool that ablates prostatic parenchyma while sparing major blood vessels and the prostatic capsule.** The urologist performs surgical mapping of the prostate using transrectal ultrasound images. **By eliminating the use of thermal energy, RAWAP bolsters a low adverse effect profile.** Current critiques include the continued requirement of general anesthesia and significant setup time and effort; however, once set up, the procedure is performed with efficiency. After the hydrodissection is complete the urologist is required to introduce a standard resectoscope or cystoscope for sometimes extensive fulguration.

Indications. **The AUA Guideline on Surgical Management of Lower Urinary Tract Symptoms Attributed to Benign Prostatic Hyperplasia (amended 2019)[7] contains a conditional recommendation for RAWAP in patients with LUTS attributed to BPH, provided their prostate volume falls within the confines of the WATER I trial (>30 gm but <80 gm), with the caveat that the patient be thoroughly counseled regarding the limited long-term efficacy data and unclear re-treatment rates.**

Surgical technique. **This procedure is performed in a standard operative room setting.** The patient is placed in the dorsal

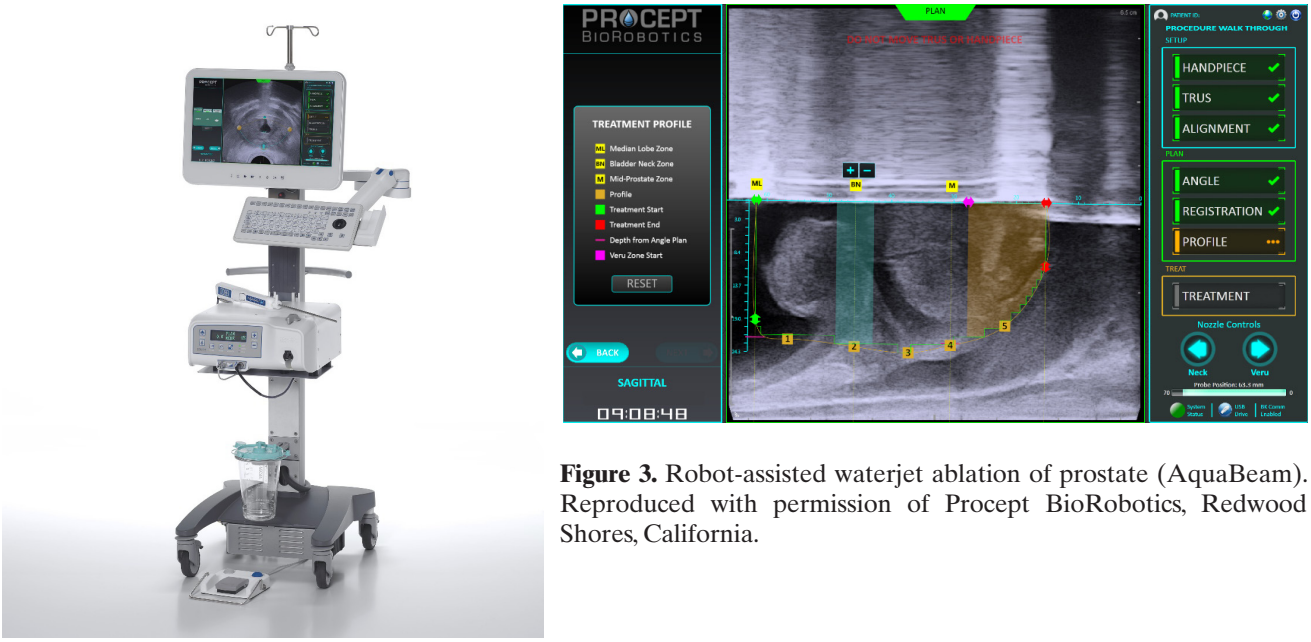

Figure 3. Robot-assisted waterjet ablation of prostate (AquaBeam). Reproduced with permission of Procept BioRobotics, Redwood Shores, California.

lithotomy position after induction of anesthesia. The platform consists of a robotic handpiece, control console and conformal planning unit (fig. 3). The handpiece, which includes both a cystoscope and transrectal ultrasound, is used to map out the area of interest from the bladder neck to the verumontanum, with specific attention turned toward limiting treatment distally. Once the area of interest is mapped, the control console is used to activate the automated high velocity waterjet to ablate the designated treatment area. The transrectal ultrasound allows observation of this ablation in real time (see RAWAP video). This automated portion of the procedure is performed efficiently. After conclusion of the ablative treatment hemostasis is generally achieved with use of the standard cystoscopic electrocautery, resectoscope or catheter traction. Continuous bladder irrigation is used postoperatively.

Perioperative considerations. RAWAP requires general or spinal anesthesia, thus giving a robust rationale to disqualify it as a MIST. **Given the automated nature of the platform, it is imperative that the patient remain still during the treatment phase to ensure appropriate application of the high velocity waterjet. Should the patient move during this portion, the entire setup needs to be revisited.** Furthermore, as the waterjet ablation spares prostatic blood vessels and the prostatic capsule, hemostasis by other means is necessitated. Use of transurethral electrocautery and catheter traction has aided surgeons who also commonly use continuous bladder irrigation in the postoperative period. Given these additional measures required, patients are admitted for observation.

In the WATER I trial (prostatic volume <80 gm) the mean length of stay was 1.4 days,[19] while mean length of stay in WATER II (prostatic volume >80 gm) was 1.6 days.[20] **Encouragingly between these 2 studies it appeared that prostatic volume had minimal effect on mean operative time (31 minutes for a 50 ml prostate vs 38 minutes for a 100 ml prostate by general linear modeling).[20] Duration of catheter indwelling time exhibited a significant range in both WATER I and WATER II, although mean catheter time was comparable to both convective water vapor therapy and PUL studies at 2 (range 0.25–19) and 3.9 (range 0.7–30) days, respectively.**

WATER I compared RAWAP to TURP, noting a significantly decreased rate of Clavien-Dindo events within the RAWAP group at 3 months, with 26% of RAWAP subjects reporting a persistent Clavien-Dindo grade I event or a Clavien-Dindo grade II or higher event vs 42% in the TURP group. The WATER II cohort was examined at 6 months, with 22% of subjects experiencing a Clavien-Dindo grade II event, 14% a grade III event and 5% a grade IV event. It should be noted that 10 of the 101 patients within the WATER II trial did require transfusion within 1 month of the procedure.[21, 22]

Outcomes. In a single arm, multicenter, pilot study 21 men were enrolled and treated under general anesthesia. **After 12 months AUA-Symptom Index/I-PSS was reduced from 23.0 points at baseline to 6.8 points (p <0.001). An increase from 8.7 to 18.3 ml per second in Qmax was also demonstrated (p <0.0001).** No cases of urinary incontinence, erectile dysfunction or retrograde ejaculation were reported. However, it is important to remember that data on the sexual side effects of such BPH surgery can be difficult to ascertain as the study is not primarily designed to answer ED or EjD questions. As such, the evaluation of sexual side effects by looking at reported adverse events only, rather than specifically assessing sexual function prospectively using validated questionnaires, is problematic.

In 2019 Gilling et al reported 1-year follow-up data from the WATER I cohort.[23] The trial used standard inclusion/exclusion criteria, limiting participants to prostate sizes of 30–80 gm. Treatment response through 12 months was defined as ≥5-point improvement in I-PSS. The mean improvement in LUTS based on the I-PSS through 12 months was similar for RAWAP and TURP.[19, 23] Mean improvement in QOL based on the I-PSS–QOL through 12 months was similar for RAWAP and TURP. Needs for blood transfusion and reoperation were similar for RAWAP and TURP, with blood transfusion reported for 1 RAWAP participant and none undergoing TURP (RR 1.69, 95% CI 0.70 to 41.0). At follow-up (12 months) maximum flow rates increased similarly in the RAWAP group vs TURP group, at 10.3 vs 10.6 ml per second (p=0.86).

The RAWAP group had a 2.6% re-treatment rate, **while TURP had a 1.5% rate, although this was not statistically significant. Subgroup analysis of men with prostate volumes >50 gm found that RAWAP was superior to TURP in both the primary safety and efficacy end points.** Recent reporting of 6-month outcomes data from WATER II with Qmax increased from a mean of 8.7 to 18.8 cc per second;[22] post-void residual volumes improved from 131 ml to 47 ml, and QOL responses improved from 4.6 at baseline to 1.4 at 6 months.[24]

Among a non-random subset of sexually active men the proportion of subjects who reported worsening sexual function through 6 months on the IIEF-5 (6-point decrease) or MSHQ-EjD (2-point decrease) was 33% in the RAWAP group compared with 56% in the TURP group (p=0.03).[23] However, when followed longer, Gilling et al noted no differences in sexual side effects as measured by MSHQ-EjD and IIEF-ED between RAWAP and TURP. This suggests that the advantages of RAWAP over TURP in sexual side effects are only transient.

Comparison of RAWAP vs medical therapies or TURP. As mentioned above, several clinical trials have compared RAWAP to TURP. On balance, RAWAP appears equivalent to TURP in terms of most outcomes yet has only a transient advantage over TURP in terms of sexual side effects. There are no published studies comparing RAWAP to medications.

EMERGING TECHNOLOGY AND TECHNIQUES

Temporary implantable nitinol device. TIND (Medi-Tate®) is an emerging device that is used to refashion the prostatic urethra, including the bladder outlet (fig. 4). TIND is a set of connected nitinol struts that are delivered cystoscopically and expanded within the prostatic fossa, then left in place for 5 days, after which the device is removed in a second cystoscopic procedure. **The mechanism of action is to compress prostatic transition zone tissue to the point of ischemic necrosis along each strut.** After removal it is intended that a pattern similar to transurethral incision of the prostate remains, in the hope of creating durable relief of bladder outlet obstruction.

Three-year follow-up data were recently published concerning treatment of men with benign prostatic obstruction with the iTIND (Medi-Tate).[25] All men were treated in the outpatient setting under light sedation. **After 12 months mean changes relative to baseline values were 45% for AUA-Symptom Index and 67% for Qmax.** There were 4 postoperative complications in 32 patients (12.5%), including prostatic abscess in 1, urinary retention in 1, urinary tract infection in 1 and temporary incon-

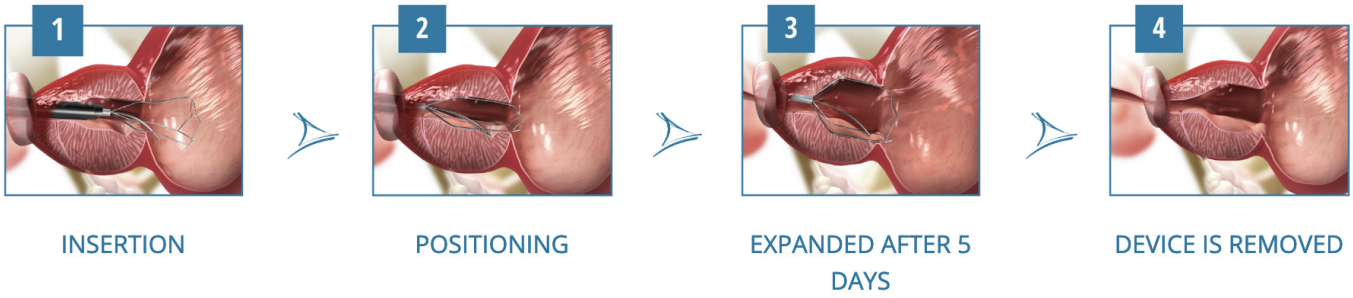

Figure 4. Use of TIND. Illustration courtesy of Medi-Tate.

tinence in 1. This phase I trial demonstrated that implantation is a feasible procedure and, although encouraging, more mature and larger studies are required to assess this technology and are ongoing (NCT02145208, clinicaltrials.gov).

Zenflow Spring® System (Zenflow, Inc, South San Francisco, California). **Spring is a permanent helical nitinol implant delivered through a flexible cystoscope. The nitinol composition creates internal tension that imbeds it into the wall of the prostatic urethra with a minimal footprint in the urethra, thereby resisting incrustation.** It is a single wire, facilitating easy adjustment or removal. The procedure is designed to be atraumatic, allowing a quick and catheter-free recovery. First in man studies are underway in New Zealand and Europe.

SPECIAL CLINICAL CONSIDERATIONS FOR MIST

As mentioned, the indications for standard surgical intervention include the more advanced presentations of BPH progression, including renal insufficiency secondary to BPH, refractory urinary retention, recurrent bladder calculi, recurrent gross hematuria, recurrent urinary tract infections and failure of optimized medical therapy. The clinician should be cautious about the extension of these new technologies to such advanced disease cases as the outcomes are not well studied, defined or understood.

Urinary retention. Acute urinary retention can often be indicative of an end stage bladder. **While the presence of painful urinary retention at a low volume (<500 ml) may be considered a potentially positive sign for a non-atonic bladder, definitive assessment of bladder function can only be made by pressure-flow studies.** A recent multicenter, retrospective, registry based investigation of the impact of convective water vapor therapy on men in recalcitrant urinary retention was published.[26] Among 38 treated patients 26 of 37 (70.3%) voided spontaneously and were catheter-free a median of 26 days (range 4–65) after the procedure, 18 (69%) of whom discontinued BPH medications. No significant differences in age, prostate volume, number of water vapor injections or presence of the median lobe were associated with predicting a successful treatment outcome. Median duration of follow-up for 20 catheter-free patients was 475 days, or 15.8 months (range 140–804 days), and 6 patients were followed for a median of 31.5 days (0–60). In a similar retrospective multicenter report of PUL for men with a wide duration of acute urinary retention (43%, <30 days) Eure et al reported a successful trial without catheter in 87% by the end of the study.[27] There are no data concerning RAWAP in acute urinary retention. **Although encouraging at first glance, it is important that clinicians remember that such uncontrolled reports are subject to bias of many types, and thus a cautious approach regarding MIST in men with acute urinary retention is advised.**

Obstructing middle lobe. PUL is unique in the current MIST and novel technologies realm to have an AUA Guideline statement warning that men with obstructing middle lobes and other such prostatic conformations may not be good candidates for this method. In fact, the Guidelines explicitly state that in men undergoing consideration for PUL the "*verified absence of an obstructive middle lobe*" needs to confirmed.[7] This was an intentional formal statement in the 2018 BPH Clinical Guidelines and was reaffirmed in the 2019 supplement. There is a report of a non-randomized, non-controlled, unblinded study of treatment of the middle lobe using PUL.[28] It is important for the clinician to understand that this particular article was rejected for inclusion as part of the AUA Guidelines because it was a non-randomized cohort study rather than a randomized controlled trial and thus introduced multiple types of bias. At this point the Guidelines are very clear concerning treatment of the middle lobe with PUL and compel clinicians to verify the absence of an obstructive middle lobe in candidates for PUL. There are no such restrictions on RAWAP or convective water vapor therapy.

Upper tract hydronephrosis of renal insufficiency from bladder neck obstruction. In men with hydronephrosis from BPH the clinician needs to provide relief of the obstruction with the paramount goal of preserving the upper tracts and renal function. **Given the consequences of incompletely treated bladder neck obstruction from BPH, it appears unwise to subject such patients to the novel surgical technologies until evidence is presented to their utility therein**.

Anticoagulation. **Similar to the discussion above, there are no peer-reviewed data to support the use of these newer technologies in patients who are medically complicated by antiplatelet and anticoagulant medications.** The recent AUA BPH Clinical Guidelines clearly state that *holmium laser enucleation of the prostate, photoselective vaporization of the prostate and thulium laser enucleation of the prostate should be considered in patients who are at higher risk for bleeding, such as those on anticoagulation drugs*.[7] Given the consequences of multiple transfusions in such a setting, it appears unwise to subject such patients to the novel surgical technologies until evidence is presented of their utility therein.

Post-radiation LUTS. Men with LUTS following radiation therapy are particularly problematic as the prostatic urethra is notoriously a "hostile territory." Many such men suffer from extraprostatic factors contributing to LUTS (i.e. loss of blad-

der compliance), making a prostate centric approach ill advised as the manipulated urethra is prone to contracture formation, non-healing, calcification and recalcitrant bleeding. In such men a comprehensive evaluation with cystoscopy, cytology and pressure flow studies seems warranted. There is no information on the use of convective water vapor therapy in this setting. Whether steam would have a normal intercalation within the tissue interstices of the fibrotic transition zone is unexplored. There is very low level evidence reported on post-radiated men treated with PUL. Using a retrospective ad hoc data set, Eure et al reported on the fate of 48 men (out of 1413 total subjects) who received non-uniform radiation for prostate cancer and were later treated with PUL.[27] The investigators state that prostate cancer therapy subjects did not experience any serious bleeding or painful urination events or significant increases in incontinence, urinary tract infection, urosepsis or urethral stricture compared to subjects without cancer. **Similar to the warnings with acute urinary retention, it is important that clinicians remember that such uncontrolled reports are subject to bias of many types, and thus a cautious approach of MIST in men with pelvic radiation is advised.**

DID YOU KNOW?

- Convective water vapor therapy, prostatic urethral lift and image guided robot-assisted waterjet ablation of the prostate have entered the market with the goal of quickly and effectively treating men with LUTS attributed to BPH with a particular focus on limiting any potential erectile or ejaculatory adverse outcomes. Two of these appear to qualify as MISTs.
- The impact of convective water vapor therapy and PUL on sexual function is likely low and constitutes a major advantage of these to men with LUTS/BPH who harbor concern about maintenance therein. The impact of RAWAP on sexual function may not be different than what is reported with TURP.
- Emerging technologies and treatments are focused on shifting treatment of LUTS attributed to BPH from the operative theater to the office. Factors diverting activity away from this stipulation of MIST are likely multifactorial.
- Men are interested in pursuing efficacious interventions with shortened recovery periods, and new technologies have been designed to meet this need.

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Study Questions Volume 39 Lesson 33

1. A man with LUTS/BPH, a 55 gm prostate, an obstructing middle lobe and bilateral hydronephrosis attributed to bladder neck obstruction is interested in preservation of sexual function. The best surgical treatment is
   a. insertion of a spring device
   b. prostatic urethral lift
   c. convective water vapor therapy
   d. bipolar TURP

2. When using a prostatic urethral lift for treatment of LUTS due to BPH, the implants are placed anatomically in the prostate
   a. anterolateral
   b. posterolateral
   c. anterior
   d. posterior

3. When using convective water vapor therapy for treatment of LUTS due to BPH, ablative energy is transmitted throughout the target zone by
   a. heat transmitted by conduction delivered in the form of steam
   b. heat transmitted by convection delivered in the form of steam
   c. kinetic energy dispersed by a high velocity waterjet
   d. destruction of relevant arterial supply

4. While performing a robot-assisted waterjet ablation of prostate, the anesthesia wears off and the patient begins to cough and buck on the operating table. After stopping the treatment, removing the device and giving the anesthesiologist time to deepen the anesthetic the next step is
   a. restart waterjet ablation using the prearranged treatment plan
   b. repeat the surgical mapping of the prostate using transrectal ultrasound
   c. request a bipolar resectoscope to complete the surgery and control the eventual bleeding
   d. place a Foley catheter on traction and terminate the procedure

5. When using iTIND for treatment of LUTS due to BPH, the implants are placed in the prostate anatomically to
   a. create a transurethral defect similar to a TURP
   b. compress prostatic transition zone tissue to create a defect similar to transurethral incision of the prostate
   c. reduce outlet resistance short-term providing temporary relief to the bladder from high voiding pressures
   d. restructure the soft tissues of the urethra into a more open position

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