

# Surgical Treatment

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## 1. Overview

Multiple open, laparoscopic/robotic and transurethral options are available for treating lower urinary tract symptoms (LUTS) due to benign prostatic hyperplasia (LUTS/BPH). Transurethral options range from the classic monopolar transurethral resection of the prostate (TURP) to the newer bipolar, laser, and minimally invasive surgical techniques (MISTs). Early interventions were typically performed with open simple prostatectomy or monopolar TURP (mTURP), but newer technology has led to less invasive modalities. BPH represents one of the few conditions in which virtually all men will experience some degree of symptoms as they age. In fact, up to 90% of men report LUTS by the age of 85.

Electrosurgical TURP still represents the gold standard in endoscopic treatment of LUTS/BPH.<sup>2</sup> With the introduction of improved medical therapy and minimally invasive options, the number of TURPs performed yearly in the United States has declined,<sup>3</sup> but the procedure remains one of the most effective treatment options. However, multiple transurethral options are now available for treating LUTS/BPH.

Per AUA guidelines, indications for non-medical treatments for LUTS/BPH include (i) acute urinary retention, (ii) recurrent bladder calculi, (iii) azotemia, (iv) recurrent urinary tract infection, (v) recurrent hematuria, or (vi) worsening LUTS refractory to medical therapy or unwillingness to use or intolerance to other therapies.<sup>2,3</sup>

**AUA Guideline on Non-Medical treatment of BPH**<sup>4,5</sup>

**Algorithm associated with Surgical Management of BPH**

## 2. Monopolar Transurethral Resection of the Prostate (mTURP)

### 2.1 Operative Considerations

Cystoscopic equipment required for a mTURP includes a 24 or 26-french resectoscope, an Iglesias working element with a thin-loop wire electrode, and a 30 or 12-degree lens. The irrigant is either body-temperature hypotonic glycine or water, which allows current to conduct from the working element through tissue and then to the grounding pad (placed on the patient's thigh or lower back). Irrigant should be warmed to body temperature to prevent hypothermia. Video cameras are strongly preferable to traditional direct visualization because of the better visibility, risk of contamination, surgeon fatigue, musculoskeletal injuries (back and neck strain) and for teaching purposes.

**The goal of transurethral resection, no matter which ablative energy used, is to remove adenomatous tissue present in the transition zone of the prostate responsible for the outlet obstruction.** The intra-vesical component of the prostate and bladder neck are first resected, typically with a cutting current. The starting point is usually at the 6 o'clock (posterior) position.<sup>6,7</sup> The bladder neck is resected circumferentially down to muscular fibers and then the posterior aspect (between 5 and 7 o'clock) of the prostate is resected from the bladder neck to verumontanum. Hemostasis is achieved by placing the wire loop on bleeding vessels to temporarily stop bleeding with tamponade and then using coagulation to seal the bleeding vessel. Arterial bleeding should be controlled as it arises during the case with venous bleeding controlled before terminating the procedure, based on visualization requirements.

Alternate techniques exist for starting the mTURP, including one popularized by Nesbit where the resection is commenced at the 12 o'clock position.<sup>7</sup> It is important to be conscious of time resecting during mTURP, as increased operative time increases the risk of **absorption of hypotonic solution with resultant dilutional hyponatremia (TUR Syndrome).** Most authorities recommend limiting the operative time of mTURP to 60-90 minutes.<sup>8</sup>

Each lobe is resected to the surgical capsule before moving to the other lobe – typically the middle lobe is resected first, followed by lateral lobes. For very large glands, due to increased operative duration and risk of complications, mTURP can be performed as a staged procedure. An Ellik evacuator is then used to evacuate resected prostate chips from the bladder through the resectoscope sheath and a final survey of the bladder should ensure no persistent prostate chips and no injury to the bladder or ureteral orifices. **A large 22 to 24 French three-way catheter is usually placed** and bladder irrigation with normal saline begun while the patient is monitored in the recovery area. Complete blood count and serum electrolytes, particularly serum sodium to rule out TUR syndrome may be obtained in the recovery room. The clinical picture of TUR syndrome can vary widely ranging from mild neurologic symptoms to coma. Cardio-respiratory symptoms may also be present from fluid overload if a large volume of fluid was absorbed through the resected bed of the prostate. Treatment for TUR syndrome is mainly supportive with slow correction of serum sodium using hypertonic saline. Correction of hyponatremia should be judicious and at no greater than 1mmol/L/hour to avoid central pontine myelinolysis.

### 2.2 Outcomes

Most patients report immediate improvement in voiding symptoms after transurethral resection. Some may have delayed improvement, particularly those that presented in urinary retention or those with a significant component of bladder dysfunction (detrusor underactivity or acontractility).

Unlike most newer modalities for LUTS/BPH, initial studies of mTURP did not include patient reported outcome measures of efficacy such as AUA symptom score. Historical studies focused on perioperative mortality and morbidity, both of which have decreased over time with improvements in technique and equipment. Treatment failures were uncommon, reported to be approximately 13.3%. Success as measured by improvement in symptom outcomes (measured by the AUA Symptom Score, AUA-SS) has been reported by these studies. Improvements in post-void residual and maximum urinary flow rate (Qmax) were seen as were reductions in prostate volume.

### 2.3 Complications

(See **Table 1**)

The major risks of mTURP include hematuria, which is typically self-limited and **dilutional hyponatremia (TUR Syndrome)**, occurring in 1-2% of patients. Delayed complications include **urinary tract infections, urethral stricture (up to 10%), urinary incontinence (up to 10%, although usually urgency related and self-limiting), retrograde ejaculation (60-90%), and the need for re-operation (3-8%)**

**Table 1. Morbidity Associated With mTURP**

Author	Date	Patients (n)	Surgical Options			
			Mortality	Morbidity	Transfusion	Reoperation
				TUR Syndrome		
Holtgrewe, et al	1962	2015	2.5%			3.4%
Melchior, et al	1974	2223	1.3%		2.8%	
Mebust, et al	1989	3885	0.2%	2.0%	6.2%	
Horninger, et al	1996	1211	0.0%	2.8%	7.6%	2.5%
Haupt, et al	1997	934	0.1%	0.3%	2.2%	

### **3. Bipolar Transurethral Resection of the Prostate (bTURP)**

Bipolar TURP (bTURP) is performed with the same technique as mTURP however, utilizes an isotonic solution that virtually eliminates TUR syndrome

#### **3.1 Operative Considerations**

Bipolar TURP is performed in similar fashion to mTURP with the major difference in the operative electrode configuration. In bTURP, both electrodes are contained within the operative device (resecting loop), **which allows for the use of isotonic saline** and for increased energy density at the resecting element allowing improved coagulation and reducing bleeding related complications. In mTURP, one electrode is the resecting loop with the return electrode on the exterior of the patient in the form of a grounding pad. A non-conductive irrigation solution is typically required to ensure the current does not dissipate from the cutting loop; this is not necessary in bTURP since the electrodes are both found in the working electrode.<sup>10</sup>

#### **3.2 Outcomes**

Several randomized controlled trials (RCTs) have been performed to compare bTURP vs. mTURP (**Table 2**). The results suggest that bTURP is an efficacious method for prostate resection.<sup>11-12,13,14</sup> More recently, a large meta-analysis including 31 randomized controlled trials demonstrated significantly improved Qmax and decreased episodes of TUR syndrome and clot retention for bTURP.<sup>5</sup> In regards to the use of bTURP in larger prostates (glands > 80 g), post hoc analysis of a large multicenter trial demonstrated similar outcomes for bTURP and mTURP.<sup>16</sup> Additionally, bTURP may prove cost effective as there is not a large additional capital equipment cost as the majority of the equipment needed is similar to that for mTURP. As such, bTURP may represent the next generation "gold standard" for LUTS/BPH. A variant of bTURP is the Plasmakinetic (PK®) Button vaporization that allows for a large surface area on the working element (**Table 3**). Large scale vaporization with concomitant coagulation versus resection with later coagulation of bleeding vessels is a potential advantage of the PK® system.

#### **3.3 Complications**

**Use of bTURP has produced results comparable to that of mTURP but with decreased prevalence of TUR syndrome and potentially bleeding complications in addition to shorter resection times and durations of postoperative catheterization**(**Table 2** and **Table 4**).<sup>17-18,19</sup> It has also been suggested that the use of bTURP decreases postoperative hospitalization stay, which can on average reduce cost by over \$1000 per patient per day if the patient is discharged home the same day as surgery.<sup>20,21</sup>

**Table 2. Outcomes and Complications with bTURP**

Authors	Trial Size	Follow-up	Operative Time	Catheterization Time	TUR Syndrome	Postop Change in Hemoglobin	Hospital Stay	Change in Qmax (ml/s)	Change in PVR
Xie et all (2012) <sup>22</sup>	110 mTURP	60 months	60.01 min	3.61 days	2 pts	1.58 g/dl	5.19 days	15.29 ml/s	81.91 ml
	110 bTURP	60 months	55.03 min	2.70 days	0 pts	1.22 g/dl	4.18 days	16.55 ml/s	82.79 ml
			(p = 0.033)		(p < 0.001)	(p = 0.014)	(p < 0.001)	(p = 0.176)	(p = 0.176)
Chen et all (2010) <sup>23</sup>	50 mTURP	24 months	60 min	n/a	0 pts	1.6 g/dl	n/a	16.9 ml/s	n/a
	50 bTURP	24 months	59 min	n/a	0 pts	1.1 g/dl	n/a	18.4 ml/s	n/a
			(p = 0.82)			(p = 0.008)		(p = 0.72)	
Michielsen et all (2007) <sup>24</sup>	120 mTURP	18 months	44 min	4.5 days	1 pts	1.3 mg/dl	5.1 days	n/a	n/a
	120 mTURP	18 months	56 min	4.0 days	0 pts	1.4 mg/dl	4.9 days	n/a	n/a
			(p = 0.201)	(p = 0.201)	(p = 1.00)		(p = 0.591)		
Autorino et al (2009) <sup>14</sup>	35 mTURP	48 months	53 min	n/a	n/a	1.0 g/dl	n/a	15 ml/s	30 ml
	35 mTURP	48 months	49 min	n/a	n/a	0.8 g/dl	n/a	2.7 ml/s	38 ml
			(p = 0.07)					(p = 0.44)	(p = 0.3)
Kong et al (2009) <sup>11</sup>	51 mTURP	12 months	NS (no values given)	57.7 hr	n/a	1.8 g/dl	2.6 days	11.91 ml/s	81.63 ml
	51 mTURP	12 months	NS (no values given)	37.2 hr	n/a	0.6 g/dl	1.5 days	12.63 ml/s	82.79 ml
						(p = 0.01)	(p = 0.02)		
Ho et al (2007) <sup>25</sup>	52 mTURP	12 months	58 min	n/a	2 pts	1.8 mg/dl	n/a	At 12 months	n/a
	48 bTURP	12 months	59 min	n/a	0 pts	1.2 mg/dl	n/a	NS difference (no exact values given)	n/a
			(p = NS)		(p < 0.05)	(p = NS)			
	53 mTURP	12 months	72.6 min	3.12 days	n/a	0.62 g/dl	4.27 days	10.2 ml/s	n/a

Yoon et al (2006) <sup>26</sup>	49 bTURP	12 months	74.2 min	2.28 days	n/a	0.67 g/dl	3.52 days	10.1 ml/s	n/a
			(p = 0.451)			(p = 0.278)	(p = 0.11)	(p = NS)	
Starkman et al (2005) <sup>27</sup>	18 mTURP	18 months	n/a	3.2 days	n/a	n/a	2.1 days	n/a	n/a
	18 mTURP	18 months	n/a	1.8 days	n/a	n/a	1.2 days	n/a	n/a
				(p = 0.12)			(p = 0.11)		

n/a – not available

**Table 3. Outcomes of Plasmakinetic (PK®) Button Vaporization**

Authors	Trial Size	Follow-up	Mean Operative Time	Mean Catheterization Duration	Hospital Stay	Change in IPSS	Change in Qmax (ml/s)	Change in PVR (mL)	Change in PSA (ng/mL)
Geavlete et al (2011) <sup>28</sup>	170 mTURP	18 months	55.6min	72.8 hours	4.2 days	24.2 preop to 8.3 at 18mos postop	6.4 preop to 20.2 at 18mos postop	88 mls preop to 33 mls at 18mos postop	2.06 preop to 0.91 at 18mos postop
	170bTURP	18 months	39.7min	23.5 hours	1.9 days	24.3 preop to 5 at 18mos	6.6 preop to 23.7 at 18mos	91 mls preop to 29 mls at 18mos	1.95 preop to 0.87 at 18mos
			(p = 0.001)	(p = 0.001)	(p = 0.001)	(p = 0.671 pre & 0.0001 post)	(p = 0.053 pre and 0.0001 post)	(p = 0.528 pre & 0.107 post)	(p = 0.369 pre & 0.651 post)
Geavlete et al (2010) <sup>29</sup>	80 mTURP	6 months	50.4min	71.2 hours	93.1 hours	24.4 preop to 9.1 at 6mos postop	6.3 preop to 19.3 at 6mos postop	85.3 mls preop to 26 mls at 6 mos postop	1.85 preop to 0.8 at 6 mos postop
	75 PKVP	6 months	35.1min	23.8 hours	47.6 hours	24.2 preop to 5 at 6most	6.2 preop to 21.8 at 6 mos	84.8 mls preop to 16 mls at 6mos post	1.82 preop to 0.74 at 6mos
			(p = 0.002)	(p = 0.002)	(p = 0.018)	(p = 0.595 pre & 0.020 post)	(p = 0.878 pre and 0.018 post)	(p = 0.712 pre & 0.281 post)	(p = 0.501 pre & 0.499 post)
Reich et al. (2010) <sup>30</sup>	30 PKVP	6 months	61 ± 26min	41 ± 35 hours	n/a	20.8 preop to 8.1 at 6mos	6.6 preop to 18.1 at 6most	165 mls preop to 38 mls at 6mos post	n/a
Karament et al. (2005) <sup>31</sup>	37 mTURP	12 months	55min	68 hours	68 hours	22 preop to 12 at 12mos postop	6 preop to 15 at 12most postop	n/a	n/a
	38 PKVP	12 months	40.3min	35 hours	35 hours	21 preop to 7 at 12mos	6 preop to 16 at 12mos	n/a	n/a
			(p = 0.001)	(p = 0.001)	(p = 0.001)	(p < 0.001)	(p > 0.05)		

n/a – not available

**Table 4. Complications of Plasmakinetic (PK<sup>®</sup>) Button Vaporization**

Authors	Hemoglobin change (dL)	Clot Retention	UTI	Urge Incontinence	Urethral Stricture	TUR Syndrome	Hematuria	Re-hospitalization for hemorrhage
Geavlete et al (2011) <sup>28</sup>	1.6g mTURP	7 (4.1%) pts	6 (3.5%) pts	4 (2.4%) pts	9 (5.3%) pts	3 (1.8%) pts	26 (15.3%) pts	6 (3.5%) pts
	0.5g PKVP	1 (0.6%) pts	4 (2.4%) pts	1 (0.6%) pts	8 (4.7%) pts	0 (0%) pts	5 (2.9%) pts	1 (0.6%) pts
	(p = 0.0001)	(p = 0.042)	(p = 0.841)	(p = 0.363)	(p = 0.768)	(p = 0.049)	(p = 0.0001)	(p = 0.04)
Geavlete et al (2010) <sup>29</sup>	1.5g mTURP	4 (5.0%) pts	9 (11.3%) pts	n/a	n/a	n/a	13 (16.3%) pts	2 (2.5%) pts
	0.6g PKVP	0 (0%) pts	6 (8.0%) pts	n/a	n/a	n/a	3 (4.0%) pts	0 (0%) pts
	(p = 0.002)	(p = 0.029)	(p = 0.561)				(p = 0.012)	(p = 0.167)
Reich et al. (2010) <sup>30</sup>	n/a	0 (0%) pts	3 (10%) pts PKVP	1 (3.3%) pts PKVP	0 (0%) pts PKVP	0 (0%) pts PKVP	0 (0%) pts PKVP	0 (0%) pts PKVP
Karament et al. (2005) <sup>31</sup>	n/a	n/a	n/a	n/a	2 (5.4%) pts mTURP	0 (0%) pts mTURP	0 (0%) pts mTURP	n/a
	n/a	n/a	n/a	n/a	2 (5.3%) pts PKVP	0 (0%) pts PKVP	0 (0%) pts PKVP	n/a

n/a – not available

## 4. Laser Prostatectomy

Laser prostatectomy has demonstrated several advantages over mTURP, including technical simplicity, a forgiving learning curve and the absence or minimization of complications such as intraoperative fluid absorption, bleeding, ED, and incontinence.

### 4.1 Operative Considerations

Laser light consists of a beam of a single wavelength with all electromagnetic waves in phase. These properties of laser light determine how the laser interacts with target tissue. Tissue is heated rapidly after absorbing laser energy. At temperatures above 60°C, protein is denatured, and the tissue is coagulated resulting in tissue sloughing and potentially prolonged dysuria postoperatively. At temperatures around the boiling point of water (100 °C), vaporization (transformation of liquid or solid into gas) occurs. Temperatures above 150 °C result in tissue carbonization (charring of prostatic tissue).<sup>32</sup> For prostate ablative surgery, vaporization is the goal, as target tissue is quickly removed from the operative field.

There are multiple laser systems in use for ablative prostate surgery. They can be divided by wavelength into two groups: those in the **visible spectrum (390-700nm)**, and those in the **infrared spectrum (>700nm)**. The **Nd:YAG system (wavelength of 1064nm)**, was the first laser system to be introduced into regular clinical practice in the 1990's. This was used in various prostate procedures from transurethral ultrasound guided laser induced prostatic coagulation (TULIP) to visual laser ablation of the prostate (VLAP). Early enthusiasm for this laser modality waned after the clinical effect of extensive coagulative necrosis became apparent; patients often experienced acute urinary retention with prolonged irritative voiding symptoms and need for prolonged catheter drainage.<sup>33</sup> Given the difficulties with the postoperative course, these lasers are no longer used for prostate surgery. The **diode laser** possesses similar properties to the Nd:YAG laser, with a wavelength of 980nm and potentially high power levels of up to 200W. The diode laser has excellent hemostatic properties, although deep tissue coagulation remains a postoperative challenge, contributing to dysuria and sloughing requiring re-operation<sup>34-35</sup>.

The **Holmium:Yttrium Aluminum Garnet (Ho:YAG) laser (2140nm)** was originally used in treating stones but has since been adapted to BPH therapy. Laser energy is absorbed by aqueous irrigant adjacent to the laser fiber tip, resulting in a vaporization bubble, leading to "micro-explosions". This results in tissue destruction, although its ability to vaporize is inefficient as minimal energy penetrates the tissue surface. Holmium laser ablation of the prostate (HoLAP) utilizing a side-firing fiber is an example of the ablative use of this laser.<sup>36</sup> The holmium laser has also been used extensively in enucleation of the prostate, described as **HoLEP**. Multiple patient series have described how large glands have been successfully treated by HoLEP.<sup>37</sup> Critics note a difficult learning curve, as well as the need for morcellation to extract large lobes that have been pushed into the bladder.<sup>38</sup> Similar to holmium technology, the **thulium laser** has wavelengths that can be tuned from 1750nm to 2200nm in both pulsed and continuous modes. The physical effect is similar to the holmium laser, but a more continuous beam may result in more rapid tissue ablation and improved hemostasis.<sup>39</sup> It should be noted that other energy sources (Greenlight, thulium fiber laser, holmium with pulse modulation and even bipolar energy) have been found to have similar outcomes.<sup>39-41,42</sup>

In contrast to the holmium and thulium lasers, the **532nm Greenlight™ laser** possesses a low absorption coefficient for water but high affinity for hemoglobin, leading to selective absorption by the oxyhemoglobin chromophore in a process called photoselective vaporization (PVP). Depending on the system, laser energy is created through a potassium titanyl phosphate (KTP) crystal addition to an Nd:YAG laser (KTP laser) or a lithium triborate crystal (LiB<sub>3</sub>O<sub>5</sub> or LBO) added to a diode pumped Nd:YAG laser. Initial generations used 80 or 120W power however the most recent update is able to generate up to 180W allowing for more efficient tissue vaporization.<sup>43</sup> The improved hemostatic properties of the Greenlight™ laser has allowed for use in patients on oral anti-coagulants and anti-platelet medications.<sup>44-46</sup>

### 4.2 Outcomes

RCTs between laser treatments are lacking. However, several RCTs comparing individual laser techniques to TURP exist. The earliest RCTs compared HoLEP to TURP<sup>47-48,49-50,51-52</sup> Voiding parameters and symptoms similarly improved between the HoLEP and TURP group at one year. However, those treated with HoLEP had shorter catheterization and hospitalization times. TURP was a faster operation and complications were minimal, and similar, between both groups.

Contrary to TURP, HoLEP is a size independent procedure which may represent an advantage in treating larger glands where previously open simple prostatectomy or multiple procedures may have been recommended. Retrospective review of 507 patients stratified based on preoperative prostate volume found no significant difference in AUA-SS, Qmax, catheterization time, hospital stay, and complications regardless of prostate size.<sup>53</sup> In 2008, Kuntz et al. conducted a RCT comparing HoLEP to open prostatectomy in patients with glands >100ml. They found similar improvements in AUA-SS and Qmax at five-year follow up. The HoLEP cohort had significantly decreased length of stay, catheterization time, blood loss and transfusion rates. Neither group required re-operation and overall complication rates in the HoLEP group were low.<sup>44</sup> These findings have been echoed in several smaller RCTs as well as retrospective analyses.<sup>55-56</sup> HoLEP is limited however by a challenging learning curve (>50 cases before reproducible results with many experts suggesting over 100 cases) which is attributed to the end-firing laser, difficulty in identifying tissue planes and the need for blind morcellation in the bladder. Despite this limitation, HoLEP, in the experienced surgeon's hands, represents an efficacious and durable endourological alternative to non-transurethral options like open or robotically assisted simple prostatectomy or requiring patients to undergo multiple staged TURP procedures.

Several RCTs comparing thulium laser prostatectomy to mTURP, bTURP and HoLEP have demonstrated non-inferior data in terms of safety and efficacy. These studies suggest thulium lasers may provide better hemostasis, less overall morbidity and shorter hospital and catheterization times as compared to traditional TURP.<sup>57-58,59-60,61-62</sup>

Multiple RCTs have compared PVP to TURP. Thangasamy, et al compiled all RCTs comparing the 80W KTP laser or 120W LBO laser with mTURP between 2002-2012.<sup>63</sup> Overall data analysis showed that length of stay and catheterization times were significantly shorter in the laser group, by 2.1 and 1.9 days respectively. Operative time was shorter in the TURP group by 19.6 minutes, with fewer blood transfusions in the laser group. The GOLIATH trial compared the latest XPS system with 180 W laser and TURP which echoes the results of the Thangasamy analysis, at 2 year follow up, which demonstrated sustained non-inferiority on International Prostate Symptom Score (IPSS/AUA-SS), Qmax and freedom of complications.<sup>64</sup>

PVP has been shown to be favorable in cost when compared to TURP.<sup>21</sup> In a cost comparison at two institutions in the United States, Goh and Gonzalez reported that the actual costs of PVP were lower than those associated with mTURP due to the higher likelihood of PVP being performed on an outpatient basis and fewer significant complications.<sup>65-66</sup> Durability of PVP Greenlight has been demonstrated by Ajib et al. with a 5-year surgical retreatment rate of 2.6%.<sup>67</sup>

Further safety outcomes in men with cardiovascular disease and those on anti-thrombotic anticoagulation medications have been well demonstrated by Meskawi et al.<sup>68</sup>

### 4.3 Complications

The Nd:YAG laser is typically no longer used for transurethral resection of the prostate due to acute urinary retention and irritative voiding that occurred postoperatively in the setting of extensive tissue coagulative necrosis.<sup>33</sup> The diode laser also suffers from deep tissue coagulation, resulting in extensive dysuria and sloughing postoperatively.<sup>35</sup> The holmium and Greenlight lasers demonstrate reduced bleeding complications compared to traditional mTURP. All laser modalities also utilize normal saline irrigation, thus removing the risk of dilutional hyponatremia.

## 5. Aquablation

Aquablation, robotic-guided hydrodissection which ablates prostatic parenchyma while sparing collagenous structures such as blood vessels and the surgical capsule, has shown comparable improvements in efficacy and safety compared to TURP in men with <80 cc prostates (50% with median lobes) with significant decrease in risk of anejaculation at 12 months.<sup>70</sup> Based on recent publications, Aquablation is now FDA approved for the treatment of men with LUTS interested in preserving ejaculatory function, with prostates <80 cc, with or without middle lobe. Recent 5 and 3 year data from the Water and Water II trials respectively have become available. At 5 years, the

Water trial demonstrated that for prostate glands <80 grams the function outcomes and safety were comparable to TURP. At 3 years, the Water II trial demonstrated a 17 point reduction in IPSS and an 8cc/sec increase in Q max in patients with prostates between 80-150 cc with an acceptable complication rate.<sup>72</sup>

## 6. Simple Prostatectomy

Simple prostatectomy is an appropriate alternative for patients in whom transurethral options are not feasible due to prostate size or in limited resource environments where lasers are not available. Generally, simple prostatectomy is reserved for prostates larger than 80ml or in patients with large bladder diverticula or bladder stones who may benefit from concomitant procedures. Simple prostatectomy involves enucleation of the gland within the surgical capsule. The open procedure can be performed via a suprapubic or retropubic approach. Both a laparoscopic and robotically assisted laparoscopic approach have also been described.<sup>3</sup>

Recent advances in endoscopic technology including bipolar current (allowing for longer resection time), and laser techniques have largely replaced the need to perform open simple prostatectomy. According to American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP), between 2011-2015, HoLEP accounted for 4-5% of total BPH procedures, whereas open simple prostatectomy accounted for 3%.<sup>73</sup> The ability to vaporize or enucleate with laser energy has reliably been shown to effectively treat glands >100mL.<sup>74-75-76</sup>

### 6.1 Outcomes

The largest series investigating outcomes in open prostatectomy was conducted in 2004. Vakkarakis et al evaluated long term efficacy in 232 patients with prostates larger than 75g. IPSS/AUA-SS, post void residual, and Qmax were all significantly improved ( $p<0.001$ ) at one year as well as at last follow up visit.<sup>77</sup> In a smaller (n=56) but similar cohort, Helfand et al demonstrated substantial decrease in AUA-SS from 18.5 to 4 at one month follow up. These differences were maintained over the course of 11 year follow up.<sup>78</sup>

A large multi-institutional study including 1330 robotic and laparoscopic prostatectomies in men with prostate volume >100ml demonstrated significantly improved Qmax and IPSS/AUA-SS with no change in SHIM score.<sup>79</sup>

### 6.2 Complications:

Significant blood loss and transfusion requirements are the most commonly cited complications following prostatectomy. Other complications include bladder neck contracture and urethral stricture.<sup>77-78</sup> Additionally, prostatectomy generally requires a longer hospital stay than transurethral procedures. These complications appear to be reduced with the use of minimally invasive techniques.<sup>76-80</sup>

## 7. Minimally Invasive Surgical Therapies (MISTS)

MISTS exploit technological advancement to offer new treatment strategies for LUTS/BPH. These generally involve minimal to no anesthesia and provide the convenience of performing the procedure in an office-based environment.

### 7.1 Transurethral Needle Ablation (TUNA) of the Prostate

Under direct visualization through a device similar to a cystoscope, two needles at a fixed lateral angle are inserted into the prostate parenchyma. Each needle emits radiofrequency energy, heating the prostate with the goal of focal tissue necrosis. Depending on prostate size/length multiple rounds can be completed. The proposed advantage is heating of the prostatic tissue with urethral mucosal preservation aiding in patient tolerance. Several studies comparing TUNA with TURP have demonstrated improvement in symptoms in the TUNA group however improvements were greater in TURP groups. Re-treatment rates were prohibitively higher in TUNA groups. Compared to TURP however, side effects are infrequent, mild, and self-limiting.<sup>81-82</sup> According to the 2019 AUA guidelines, TUNA is no longer recommended for the treatment of LUTS/BPH?

### 7.2 Transurethral Microwave Thermotherapy (TUMT)

Using microwave antennae mounted on a urethral catheter, TUMT radially heats the prostate leading to tissue necrosis without unintended thermal spread to the sphincter, rectum and bladder neck. A wide variety of TUMT systems were once available however due to decreasing use in preceding years only a few are still commercially available. TUMT enthusiasm has waned as there are significant concerns about efficacy and durability.<sup>3</sup> The advent of higher energy systems seemed to improve durability without increasing complications, but a lack of efficacy has moved this technology towards obsolescence. Serious complications are infrequent.<sup>83-84-85-86-87</sup>

### 7.3 Prostatic Urethral Lift (UroLift®)

The prostatic urethral lift (UroLift®) involves placement of tissue retracting implants under cystoscopic guidance using the UroLift® delivery system. Appropriate patient selection based on prostate anatomy is critical for the success of this operation. An obstructive middle lobe has traditionally been a contraindication due to the inability to treat this portion of the gland, however further data is emerging that has expanded this option. Typically, 4-6 implants are placed in an anterolateral position that avoids the dorsal venous complex and neurovascular bundles

The first multicenter, prospective randomized controlled study known as the L.I.F.T study randomly assigned 206 patients in a 2:1 fashion to either UroLift® or sham control. Statistically significant improvements in AUA-SS as well as Qmax were noted at 12-month follow up. No benefits were observed in post-void residual although there was no ejaculatory or erectile dysfunction noted with treatment. Adverse effects were few and self-limited including dysuria and hematuria.<sup>88</sup> In regard to durability, Roehrborn et al. found a sustained improvement of IPSS/AUA-SS at 4 and 5 year follow up when compared to sham procedure. IPSS/AUA-SS improvement after UroLift® was 88% greater than that of sham at 3 months. Improvement in IPSS, QOL, BPHII, and Qmax were durable through 5 years with improvements of 36%, 50%, 52%, and 44% respectively. The surgical retreatment was 13.6% over 5 years. Adverse events were mild to moderate. **Sexual function was stable over 5 years with no de novo, sustained erectile or ejaculatory dysfunction.**<sup>89</sup> Further studies are needed to define the role UroLift® will play in the treatment of LUTS/BPH.<sup>88-90-89-91</sup>

### 7.4 Convective Water Vapor Therapy (Rezum®)

Convective water vapor therapy, or the Rezum® system, delivers targeted and controlled doses of thermal energy directly into the prostate causing transitional zone cell death. Under direct vision, a narrow sheath, similar in size and shape to a cystoscope, is inserted via the urethra. A thin needle is deployed near the tip of the scope through the urethral urothelium into the prostate parenchyma. Water is heated externally and injected via the needle (over 9 seconds) as steam to supply convective heat into the hyperplastic prostate tissue. When the water vapor contacts the prostatic tissue, it releases the stored thermal energy leading to cell death and tissue volume contraction.

In 2015, McVary et al conducted a multicenter randomized controlled trial included 197 men randomized in 2:1 fashion to Rezum® vs sham procedure. IPSS/AUA-SS in the Rezum and control group was reduced by 11.2 plusmn; 7.6 and 4.3 ± 6.9 respectively. Peak flow rate increased by 6.2 ml/s and was sustained throughout 12 months. In 2017, Roehrborn et al reported durable 2-year results. They found that Rezum® therapy improved urinary symptoms significantly over controls at 3 months and provided a sustained 51% reduction from baseline at 24 months ( $p <0.0001$ ). Rezum® produced a 5 and 8-point or greater score decrease in 84% and 74% of subjects, respectively, at 24 months.<sup>92</sup> **No new ejaculatory or erectile dysfunction was noted, and adverse effects were mild to moderate and resolved rapidly.**<sup>93</sup> Early results for Rezum are promising, however, as with all new MISTS follow up data centering on durability/need for retreatment will need to be carefully examined.<sup>77-80</sup>

Most recently, 5-year data was published demonstrating a surgical retreatment rate of 4.4% over 5 years.<sup>94-95</sup> No disturbances in sexual function were reported.

## 7.5 Temporarily Implanted Nitinol Device (iTind®)

A new temporary prostatic implant, called the iTind (temporarily implantable nitinol device) has been approved by the FDA and in Europe. The device is placed under direct vision within the prostatic urethra cystoscopically under local anesthesia. Over the subsequent 5 days the nitinol struts exert a radial outward force causing ischemic necrosis and remodeling of the bladder neck and prostatic urethra.<sup>96</sup> The device is removed using a tether through an open-ended catheter in an office setting. Three-year results have shown a 41% rise in Qmax (mean 10.1 mL/s), median (IQR) IPSS of 12 (6-24) and an IPSS/AUA-SS QoL of 2 (1-4).<sup>97</sup> The recently published prospective, randomized, pivotal study, demonstrated a 9.25 point decrease in IPSS ( $p<0.001$ ) and improved Qmax of 3.52 mL/s ( $p<0.001$ ). Additionally, there is no de novo erectile or ejaculatory dysfunction noted.<sup>98</sup>

## 7.6 Prostatic Stents

Intra-prostatic stents have also been proposed in the management of LUTS/BPH. Various types and materials are available and can be placed under local or regional anesthesia. Overall, data on efficacy and tolerability of prostatic stents is poor. Additionally, older stents have been shown to migrate, encrust and exacerbate LUTS. Most of the published data on prostatic stent outcomes featured the Urolume<sup>TM</sup> stent which is no longer commercially available.

There are a number of newly developed, next-generation stents currently under study. They are designed to contain less material thus reducing the risk of encrustation as well as reduced migration. On-going clinical trials should elucidate their safety and efficacy over the coming years.

## 7.7 Intra-prostatic Injection

Several injectables have been studied in the treatment of LUTS/BPH including botulinum toxin, NX-1207, and PRX302. These substances can be injected into the prostate parenchyma via a transurethral, transrectal or perineal approach. In theory, the agent leads to focal changes in the prostate reducing volume and alleviating obstructive LUTS/BPH.

A large placebo-controlled trial of intra-prostatic botulinum toxin versus placebo found no statistical differences in IPSS/AUA-SS, QOL, Qmax and prostate volume changes between placebo and active drug.<sup>78</sup> The sponsoring company has subsequently ended study for botulinum toxin in LUTS/BPH.

Another agent NX-1207 (Fexapotide trifluate, FT), causing apoptotic cell death, has been shown in phase 1 and 2 trials to cause significant clinical improvement with minimal adverse effects. Two large phase 3 studies were recently published, where 995 BPH patients at 72 sites treated 3:2 FT:placebo. Long term IPSS change from baseline was higher in FT treated patients compared to placebo (median FT group improvement - 5.2 versus placebo - 3.0,  $p < 0.0001$ ). Long term incidence of intervention for BPH was reduced in the FT group versus oral BPH medications (8.08% versus 27.85% at 3 years,  $p < 0.0001$ ).<sup>79,99</sup>

PRX302, is a genetically modified bacterial toxin that is activated by PSA and has demonstrated some improvement in IPSS/AUA-SS, QOL, and prostate volume with minimal adverse effects.<sup>100</sup> As with other minimally invasive therapies, the efficacy and safety of this modality require further study before consideration as a treatment alternative.

## Videos

Surgical Guide to Holmium Laser Enucleation of the Prostate (HoLEP)

Holmium Laser Enucleation of the Prostate for Massive Benign Prostatic Hyperplasia: Technique for a 200g Prostate

Robotic simple suprapubic prostatectomy for benign prostatic hyperplasia

Robotic-Assisted Laparoscopic Suprapubic Simple Prostatectomy Step by Step Approach

Extraperitoneal Laparoscopic Simple Prostatectomy – Step by Step Demonstration

Techique and Results of Prostate Waterjet Ablation by Aquablation®

Rezum™ Prostate Vapor Ablation

UroLift Procedure for Treating BPH

Performing Aquablation Therapy for BPH with AQUABEAM Robotic System

Surgical Guide to En-block Holmium Laser Enucleation of the Prostate

Tips & Tricks of Morcellation

iTind Placement

Insertion and Placement of Temporarily Implanted Nitinol Device (iTind).mov

## Presentations

Surgical BPH 1

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