

Modern advancements in minimally invasive surgical treatments for benign prostatic obstruction

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Abstract: A wide variety of minimally invasive surgical techniques are now being offered for treating voiding lower urinary tract symptoms (LUTS) secondary to benign prostatic obstruction (BPO). These options offer an alternative to both medical therapy and traditional surgical options. Minimally invasive surgical treatments in LUTS/BPO boast both day case and local anaesthetic options, with a potentially reduced side effect profile compared to traditional surgical interventions matching the needs for a range of patients. We provide a narrative review of minimally invasive surgical treatments available for BPO in terms of the technology, efficacy, safety, institutional recommendations, cost and potential future developments.

Keywords: BPH, BPO, iTIND, LUTS, minimally invasive surgical treatments, PAE, RezumTM, Urolift[®]

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Introduction

Benign prostate hyperplasia (BPH) is a common condition affecting males over the age of 50. BPH is a histological diagnosis characterised by a proliferation of both stromal and epithelial cells within the prostate, mostly within the transitional zone. This can lead to bladder outflow obstruction (BOO) due to benign prostatic obstruction (BPO) resulting in lower urinary tract symptoms (LUTS). In some cases, BPO can be complicated by urinary retention, urinary incontinence, renal impairment and urinary tract infections. These symptoms can have a significant effect on quality of life. As the age of the population increases, the incidence of BPO is expected to increase by as much as 50% by 2025.¹

For many, medical therapy offers a great deal of symptomatic improvement, but for others it proves ineffective or has an unfavourable side effect profile.² In cases of urinary retention, a urinary catheter may be required on either a short- or long-term basis. The physical, social and psychological effect of a catheter may be unacceptable. One study found that patients

considered the insertion of a urethral catheter for acute retention more detrimental to quality of life than surgery.³

Each year, 25,000 BPO operations are performed in the United Kingdom (UK) and over 100,000 in the United States (US), with recent data suggesting transurethral resection of the prostate (TURP) represents 80% of such operations.^{4,5} For many, bipolar TURP still represents the gold standard in the surgical management of BPO.⁶ One meta-analysis, from Ahyai *et al.*⁷ with twenty randomized controlled trials across 5 years demonstrated monopolar TURP was excellent in the relief in BOO in terms of International Prostate Symptom Score (-70%), Quality of life Score (-69%) Flow/ Q_{Max} (+162%) and Post Void Residual (-77%). Whilst further studies in to bipolar TURP compared to monopolar TURP have shown no differences in efficacy, they have demonstrated a favourable safety profile.⁸

In larger prostates, holmium enucleation of prostate (HoLEP) has largely replaced open prostatectomy.⁹

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Both TURP and HoLEP require a general or spinal anaesthetic, as well as an inpatient hospital stay, in the majority of cases. Although these invasive management options are associated with a significant relief of LUTS, for some patients these benefits are outweighed by an unacceptable side effect profile.

For those undergoing a TURP, both The European Association of Urologists (EAU) and The British Association of Urologists (BAUS) quote risks of erectile dysfunction (ED), incontinence and retrograde ejaculation. BAUS state a 2–10% risk of: *de novo* erectile dysfunction, temporary or permanent urinary incontinence and the need for repeat procedures. Whilst the rate of retrograde ejaculation is reported between 65 and 75%.^{10,11}

More recently, the UNBLOCS trial reported a high prevalence of sexual dysfunction before TURP with rates of ED reported at 71% and rates of reduced or anejaculation at 84%. Overall, post operatively there was little change in sexual function. Of note, only 24% of patients without sexual dysfunction at baseline developed sexual dysfunction 12 months post-surgery.¹²

Minimally invasive surgical treatments (MIST's) for the management of LUTS/BPO are now commonplace amongst most urological practices. For the purpose of this review, a MIST is a procedure with the potential to be performed on a day case basis, avoiding general anaesthetic boasting a potentially lower side effect profile than invasive treatments.

In this narrative review, we discuss MIST's in terms of efficacy, safety, institutional recommendations, cost and future developments. Where possible efficacy will be stratified by randomised controlled trials in comparison to TURP.

Table 1 summarises the key attributes from each modality, whilst Tables 2–6 look at the key trials underpinning each treatment.

Urolift®

The Urolift® system has been licenced for use since 2010. It uses nitinol implants to displace prostatic tissue aiming to relieve obstruction and improve LUTS. Throughout the procedure, a urologist uses a single use device to deliver a probe to the prostatic urethra. Here, implants are

placed through the prostatic urethra to the outer prostate capsule.¹³

It is most commonly performed as a day case procedure under local anaesthetic or sedation. A catheter is not routinely placed post-procedure.

The National Institute for Clinical and Health Excellence (NICE), American Association of Urologists (AUA) and the European Association of Urology (EAU) guidelines all recommend Urolift® for men with LUTS who are keen to preserve their sexual function. NICE recommend Urolift® for prostates <100g, AUA state <80g and EAU state <70g. Although these organisations do not recommend Urolift® for prostates with obstructing median lobes, there is now evidence supporting its use in this setting.^{14–17}

There are two randomised controlled trials (RCTs), LIFT and BPH6, comparing the efficacy of Urolift®.

LIFT randomised patients to either sham or Urolift® and were followed up for 5 years. At 3 months, Urolift® showed statistically significant improvements in IPSS score, flow rate and quality of life. This improvement was maintained for 5 years.¹⁸

In BPH6, at 12 months, Urolift® demonstrated non-inferiority compared to TURP. This was based on specific BPH6 endpoints. Of note, recovery was deemed faster and rates of retrograde ejaculation were lower in the Urolift® group. IPSS was not significantly different until 12 months, where TURP proved superior.¹⁹

The LIFT study demonstrated that 80% of patients experienced an adverse side effect in the first 3 months. These complications however remained minor, including dysuria, haematuria, pelvic pain or storage LUTS. There were no cases of ejaculatory or ED.

At 5 years 13 implants had been removed with 10 being encrusted and 3 being prophylactically removed due to incorrect positioning. The authors state that correctly sited implants showed no signs of encrustation. Endoscopic review at 1 year however identified that 2.1% of implants were incorrectly sited

Overall, the BPH6 study demonstrated a numerically higher rate of adverse effects in those

Table 1. Comparisons of four minimally invasive surgical treatments used in the management of LUTS in BPO.

	Urolift®	Rezum™	Prostate artery embolization	Aquablation	iTind
Description	Mechanical displacement of prostate lobes using implants	Water vapour uses convective heating to ablate prostate tissue	Under X ray guidance – vascular catheters are used to embolize prostate arteries	High pressure saline hydrodissects the prostate under robotic control	A nitinol frame is inserted using a cystoscope for a short period of time to remodel the prostate
Anaesthetic	Local ± sedation	Local ± sedation ± regional block	Local ± sedation	General anaesthetic or spinal	Local ± sedation
Urinary catheter	Not required	Required for 3–5 days	Removed post procedure	Removed 1 day post procedure	Not required
Cost analysis	Available	Available	Available	Not available	Not available
Professional approval					
NICE	X	X	X	In specific circumstances	X
EAU	X		X	X	
AUA	X	X		X	

AUA, American Urological Association; BPO, benign prostatic obstruction; EAU, The European Association of Urology; NICE, The National Institute for Health and Care Excellence; LUTS, lower urinary tract symptoms.

randomised to TURP opposed to Urolift®. However, only the rates of urinary incontinence and ejaculatory dysfunction were found to be statistically higher in the TURP group ($p < 0.05$).

The ability to perform Urolift® under local anaesthetic in a day-case environment has obvious financial benefits. A cost effectiveness study from NICE suggested savings of £981, £1242 and £1230 compared to an inpatient bipolar TURP, monopolar TURP and HoLEP respectively.¹⁰

NICE also stated that costs were related to the number of implants used with each implant costing £329. Therefore, using the lowest number of implants necessary would keep costs low. This cost analysis does not take in to account the long term need for re-intervention, pre-operative investigations to rule out an obstructing median lobe or using day case TURP as a comparator.

The Medlift study, a non-randomised prospective study, shows promising results the use of Urolift® in those patients with a median lobe.¹⁷ There is also now limited data on the use of Urolift® in patients with a history of urinary retention. Early

work from the PULSAR study demonstrated that 79% of patients with a history of urinary retention were catheter free 3 months post Urolift®. The current data available is limited by 6 months of follow up is awaiting formal publication.²⁰

A RCT is required to fully assess the efficacy and safety of Urolift® in these specific sub-groups.

Rezum™

Rezum™ is another minimally invasive surgical option used in LUTS/BPO managements gaining Federal Drug Agency (FDA) approval in the US in 2015. The Rezum™ delivery system uses radiofrequency energy to convert water droplets to steam. Cystoscopically, this steam is delivered into the transition zone of the prostate *via* 9s injections destroying prostate tissue by convective heating.²¹ Magnetic resonance imaging (MRI) imaging before and post-procedure suggested Rezum™ decreased the volume of the transition zone by as much as 38% by 6 months.²²

It is most commonly performed as a daycase procedure under varying levels of anaesthetic,

Table 2. Key papers in Urolift®.

Urolift®			
Trial, authors, country	Methods	Participants	Outcomes at 5 years
L.I.F.T, Roehrborn et al., ¹⁸ North America, Australia	Prospective	N=206	Urolift®
	Randomized controlled trial	Inclusion criteria	Improvement in IPSS (%)
	Urolift® versus Sham procedure	LUTS	-7.9 (35)
	Unblinded at 3 months	>50 years old Prostate size 30–80 cc	Improvement in IPSS QOL score (%)
		Active UTI	-2.1 (44.4)
		Obstructing median lobe	Improvement in Q _{max} (%)
		Exclusion criteria	3.2 ml/s (49.9)
			0 (0)
			0 (0)
			0 (0)
			0 (0)
Outcomes at 2 years			
BPH6, Gratzke et al., ¹⁹ Europe	Prospective	N=80	Urolift®
	Randomized controlled trial	Inclusion criteria	TURP
	Urolift® versus TURP	LUTS	Urolift®
	Unblinded	>50 years old	Improvement in IPSS (%)
	Two years follow up	Suitable for TURP	-9.2 (43.0)
		IPSS ≥ 12	Improvement in IPSS QOL score (%)
		Q _{max} ≤ 15 ml/s	-2.5 (54.3)
		Prostate size ≤ 60 cc	Improvement in IPSS QOL score (%)
		Sexually active until 6 months prior to procedure	-3.3 (71.7)
			5.0 ml/s (53.8)
			15.8 ml/s (164.6)
			-42.5 ml (43.0)
			2 (5.7)
			36 (94)
			37 (100)
			20 (66.7)
BPH6, benign prostatic hyperplasia 6; IPSS, International prostate symptom score; LUTS, lower urinary tract symptoms; Qmax, maximum flow rate; QOL, quality of life; UTI, urinary tract infection.			

Table 3. Key papers in Rezum™.

Rezum™							
Trial, authors, country	Methods	Participants		Comparison		Outcomes at 4 years	
	Prospective	N=188		2:1 Randomisation		Rezum™	
McVary <i>et al.</i> , ²³ North America	Randomized controlled trial	Inclusion criteria	Exclusion criteria	Rezum™ N=135	Sham N=61	Improvement in IPSS (%)	-10.1 (46.7)
	Rezum™ versus Sham procedure	LUTS	Obstructing median lobe	Crossover Rezum™ at 3 months N=53	Rigid cystoscopy	Improvement in IPSS QOL score (%)	-2.0 (42.9)
	Unblinded at 3 months	>50 years old	Active UTI		Blinded to patient	Improvement in Q _{max} (%)	4.2 ml/s (49.5)
	Four years follow up	IPSS ≥ 13	Post void residual ≥ 250 ml	Rezum™ device used to deliver water vapour to prostatic tissue		Improvement in post void residual (%)	-8.2 ml (38)
		Q _{max} ≤ 15 ml/s Prostate size 30–80 cc	Prostate cancer PSA ≥ 2.5 (unless benign on biopsy)	Local anaesthetic	Local anaesthetic	Surgical re-treatment (%) Restarted on BPH medication (%) De Novo erectile dysfunction (%) Improvement in Male Sexual Health Questionnaire – ejaculatory dysfunction bother score (%)	6 (4.4) 7 (5.2) 0 (0) -0.1 (5.7)

BPH, benign prostatic hyperplasia; IPSS, International prostate symptom score; LUTS, lower urinary tract symptoms; Q_{max}, maximum flow rate; QOL, quality of life; UTI, urinary tract infection; PSA, prostate specific antigen.

including local anaesthetic transperineal block or oral/intravenous sedation.²³ A urethral catheter is inserted for 5–7 days following the procedure whilst the swelling of the prostate settles.

NICE states that Rezum™ can be considered for men with moderate to severe LUTS with a prostate volume between 30 and 80 ml as an alternative to TURP or HoLEP.²⁴ AUA similarly approves the use of Rezum™ for prostates less than 80 g.¹⁵ At present, EAU makes no recommendation for the use of Rezum™ stating the need for RCT against a reference technique.¹⁴

At the time of writing, there is one RCT assessing Rezum™ in which patients were randomised to Rezum™ or a sham treatment. 197 patients were

randomised over 3 months and followed up for 4 years. Of note, patients with prostates larger than 80 ml, post-void residual volumes >250 ml and prostate specific antigen values >2.5 ng/ml were excluded from the study.²³

Results noted statistically significant improvements in urinary flow, IPSS and quality of life that remained stable across a 4-year follow up period. In particular, there was a 50% reduction in IPSS score in the Rezum™ arm. There was no change in erectile or ejaculatory function reported at 4 years.

Most adverse events were minor, including haematuria, storage LUTS and urinary tract infections. They did resolve 3 weeks post procedure. At 4 years,

Table 4. Key papers in PAE.

PAE	Trial, authors, country	Methods	Participants	Exclusion criteria	Comparison	Outcomes at 2 year
		Prospective	N = 114		1:1 Randomisation	
	Gao et al., ²⁸ China	Randomized controlled trial	Inclusion criteria	Exclusion criteria	PAE=57 TURP=57	Improvement in IPSS (%) -15.6 (64.2)
		PAE versus TURP	IPSS ≥ 7	Detrusor hyperactivity on urodynamics	Embolization performed using polyvinyl alcohol microspheres (Ivalon, Cook)	Bipolar TURP Improvement in IPSS QOL score (%) -3.2 (69.6)
		Two years follow up	Failed medical therapy Prostate size 20–100 cc Q _{max} ≤ 15 ml/s	Urethral stricture Prostate/bladder cancer PSA ≥ 4 (unless benign on biopsy) Previous prostate or bladder neck surgery Diabetes	Local anaesthetic Spinal anaesthetic	Improvement in Q _{max} (%) 13.7 ml/s (175.6) 14.8 ml/s (202.7) Improvement in post void residual (%) 107.5 ml (84.7) 100.2 ml (86.8) Surgical re-treatment (%) 5 (8.8) 2 (3.5) Sexual function Not reported
	Insausti et al., ³¹ Spain	Non-inferiority	N=45		1:1 Randomisation	
		Randomized controlled trial	Inclusion criteria	Exclusion criteria	PAE=23 TURP=22	Improvement in IPSS (%) -21.0 (78.9)
		PAE versus TURP	LUTS refractory to 6 months of medical therapy	Estimated glomerular filtration rate <30 ml/min	Embolization performed using polyvinyl alcohol microspheres (Bead Block, BTG PLC)	Bipolar TURP Improvement in IPSS QOL score (%) -3.09 (65.3)
		One years follow up	>60 years old Suitable for TURP IPSS ≥ 8 IPSS QOL score ≥ 3 Q _{max} ≤ 10 ml/s or urinary retention	Prostate cancer Detrusor failure or neurogenic bladder Urethral stenosis Advanced atherosclerosis or tortuosity of iliac arteries Non-visualisation of prostatic arteries	Local anaesthetic Spinal or general anaesthetic	Improvement in Q _{max} (%) 6.14 ml/s (80.1) 9.65 ml/s (137.7) Improvement in post void residual (%) -20.2 ml (24.5) -44.7 ml (35.9) Erectile dysfunction – baseline not reported (%) 1 (4.3) 5 (22.7) Ejaculatory dysfunction – baseline not reported (%) 1 (4.3) 9 (40.9)
	Abt et al., ²⁹ Switzerland	Non-inferiority	N=99		1:1 Randomisation	
						Improvement in IPSS (%) -16.3 (66.0) TURP -3.2 (69.6) PAE -15.6 (64.2) TURP -3.2 (69.6)

(Continued)

Table 4. (Continued)

PAE		Participants		Comparison		Outcomes at 2 year	
Trial, authors, country	Methods	Inclusion criteria	Exclusion criteria	PAE N=48	TURP N=51	Improvement in IPSS (%)	-10.77 (61.2)
Randomized controlled trial							
PAE <i>versus</i> TURP	LUTS refractory or unsuitable to medical therapy	Detrusor failure or neurogenic bladder	Embolization performed using Embosphere microspheres (Boston Scientific)	Monopolar TURP	Improvement in IPSS QOL score (%)	-2.33 (58.3)	-2.69 (63.4)
Twelve weeks follow up	>40 years old Suitable for TURP IPSS ≥ 8 Q _{max} ≤ 12 ml/s or urinary retention	Estimated glomerular filtration rate < 60 ml/min Urethral stenosis Bladder stones Prostate cancer	Local anaesthetic	Spinal or general anaesthetic	Improvement in Q _{max} (%)	5.5 ml/s (42.5)	15.3 ml/s (67.8)
	Prostate size 25–80 cc	Advanced atherosclerosis or tortuosity of iliac arteries Contraindication to MRI or CT contrast			Improvement in post void residual (%) <i>De novo</i> ejaculatory dysfunction (%) <i>De novo</i> erectile dysfunction (%)	-98.2 ml (58.3) 14 (56) Not reported	-197 ml (85.4) 21 (84)
Outcomes at 1 year							
PERFECTED, Carnevale <i>et al.</i> , ³⁰ Brazil	Randomized controlled trial	N=30	1:1 Randomisation				
Original PAE (oPAE) <i>versus</i> TURP	Inclusion criteria	Exclusion criteria	PAE N=15	TURP N=15	Improvement in IPSS (%)	-12.5 (49.4)	21.5 (77.9)
One year follow up	LUTS refractory to 6 months of medical therapy	Renal failure	Embolization performed using tris-acryl gelatin microspheres (Embosphere Microspheres, Merit Medical)	Not specified if bipolar or monopolar	Improvement in IPSS QOL score (%)	-2.5 (53.2)	-3.7 (80.4)
	>45 years old IPSS ≥ 19 Prostate size 30–90 cc Urodynamic proven obstruction	Bladder stones Prostate cancer Urethral stenosis Detrusor failure or neurogenic bladder	Local anaesthetic	Spinal anaesthetic	Improvement in Q _{max} (%)	3.1 ml/s (44.3)	17.4 ml/s (179.4)
					Improvement in post void residual (%) <i>De novo</i> ejaculatory dysfunction (%) <i>De novo</i> erectile dysfunction (%)	64.7 ml (50.9) 2 (13.3) Not reported	70 ml (89.4) 15 (100)

IPSS, International prostate symptom score; LUTS, low urinary tract symptoms; PAE, prostate artery embolization; PSA, prostate specific antigen; Q_{max}, maximum flow rate; QOL, quality of life; TURP, transurethral resection of the prostate.

Table 5. Key papers in aquablation.

Aquablation		Comparison		Outcomes at 1 year		
Trial, authors, country	Methods	Participants	Comparison	Outcomes at 1 year	Outcomes at 1 year	
WATER 1, Gilling <i>et al.</i> , ³⁷ North America, UK, Australia, New Zealand	Prospective	N= 181	2:1 Randomisation	Aquablation	TURP	
Randomized control trial		Inclusion criteria	Aquablation N= 110	TURP =59	Improvement in IPSS (%)	-14.7 (61.1) -14.9 (22.3)
Double blinded	LUTS	Exclusion criteria	Destruction of prostatic tissue using Procept Aquabeam system	Either monopolar or bipolar TURP	Improvement in IPSS QoL score (%)	-3.2 (67.7) -3.3 (68.8)
Two years follow up	IPSS \geq 12	Neurogenic Bladder	Haemostasis with foley catheter \pm resectoscope and rollerball electrocautery	Anaesthetic not specified	Improvement in Q_{max} (% not available as baseline not clear)	11.2 ml/s 8.6 ml/s
	$Q_{max} \leq$ 15 ml/s	Bladder stones or large diverticula	Anaesthetic not specified		Improvement in post void residual (% not available as baseline not clear)	57 ml 101 ml
		Chronic prostatitis			<i>De novo</i> erectile dysfunction (%)	0 0
		Meatal stenosis			<i>De novo</i> ejaculatory dysfunction (%)	10 36
		Urethral stricture				
	Prostate size 30–80 cc	Active infection				
		Post void residual \geq 300 ml/urinary retention				
		Previous prostate surgery				

IPSS, International prostate symptom score; LUTS, low urinary tract symptoms; TURP, transurethral resection of the prostate; Q_{max} , maximum flow rate; QoL, quality of life.

Table 6. Key papers in iTind.

iTind	Trial, authors, country	Methods	Participants	Comparison	Outcomes at 1 year	
	Porpiglia <i>et al.</i> , ⁴¹ Italy, Switzerland, UK, Belgium, Spain	Prospective	N=81	Single arm study	iTIND	
		Single arm	Inclusion criteria	iTind N = 81	Improvement in IPSS (%)	15.3 (6.0)
		One year follow up	LUTS IPSS ≥ 10 $Q_{max} \leq 12$ ml/s Prostate size 75 cc	Haemostatic disorders Post void residual ≥ 250 ml Obstructing median lobe Previous prostate surgery	Improvement in Q_{max} (%) Improvement in post void residual (%) Surgical re-treatment (%) <i>De novo</i> sexual dysfunction (Erectile or ejaculatory) (%)	7.3 ml/s (96.1) 39.5 ml (53.7) 2 (2.5) 0 (0)
	Chughtai <i>et al.</i> , ⁴² North America, Canada	Prospective	N=175	2:1 Randomisation	iTIND	
		Randomized controlled trial	Inclusion criteria	iTind N=118	Improvement in IPSS (%)	-9.3 (42.7)
		iTind versus Sham Procedure	LUTS	The iTind device is cystoscopically inserted within the prostatic urethra	Improvement in IPSS QOL score (%)	-1.9 (42.1)
		Unblinded at 3 months	IPSS ≥ 10	The device is subsequently removed after 5-7 days	Improvement in Q_{max} (%)	3.5 ml/s (41.8)
		One year follow up	$Q_{max} \leq 12$ ml/s Prostate size 25-75 cc	Obstructing median lobe Abnormal urinalysis/UTI Previous prostate surgery Prostate/bladder cancer Post void residual ≥ 250 ml Bladder stones Significant renal, cardiac or pulmonary disease	Improvement in post void residual (%) Surgical re-treatment (%) Restarted on BPH medication (%) <i>De novo</i> sexual dysfunction (Erectile or ejaculatory dysfunction) (%)	-0.16 ml (0.27) 6 (4.7) 6 (4.7) 0 (0)

IPSS, International prostate symptom score; iTIND, minimally invasive treatment for BPH; IV, intravenous; LUTS, low urinary tract symptoms; TURP, transurethral resection of the prostate; PSA, prostate specific antigen; Q_{max} , maximum flow rate; QOL, quality of life; UTI, urinary tract infection

re-treatment rate remained low at 4.4% as did initiation of medication (alpha-blockers) at 5.2%.

A small retrospective analysis of 38 catheter-dependent patients who underwent Rezum™ demonstrated that 70% were able to spontaneously void post-procedure. Follow up data remained sparse but promising.²⁵

A NICE cost analysis suggests a saving of £550 per person over 4 years compared to TURP or HoLEP; at present, this cannot account for the long-term cost of potential re-intervention.²⁴

Prostate artery embolization

Prostate artery embolization (PAE) is another MIST performed for LUTS/BPO, usually by uro-radiologists. A computed tomography (CT) angiogram is performed prior to the procedure in order to delineate prostate arterial vasculature and assess patient suitability. Vascular catheters are introduced into the femoral or radial artery and use various agents to selectively embolize branches of prostatic arteries. This causes ischaemia and necrosis of the prostate, resulting in a decrease in prostate size, reduction in bladder outlet obstruction and improvement in LUTS.²⁶

Whilst PAE is also performed under local anaesthetic and on a daycase basis unlike the other MIST's discussed PAE is performed by an interventional radiologist under x-ray guidance. The use of contrast in the planning CT angiogram means that poor renal function may make PAE inappropriate.

NICE supports the use of PAE for LUTS/BPO when performed by an interventional radiologist with a special interest and training in PAE.²⁷ The EAU state that PAE can be considered in men with moderate to severe LUTS if they are willing to accept less optimal objective outcomes compared to TURP. Both NICE and the EAU state patient selection should be multidisciplinary between a urologist and interventional radiologist.¹⁴ Conversely, AUA does not recommend PAE outside of clinical trials stating clear benefit over risk has not yet been demonstrated by current data and adequate trial designs.¹⁵

There are four RCT's comparing PAE to TURP with follow up ranging from 3 months to 2 years. All cases of PAE were performed under local anaesthetic. In terms of inclusion criteria, definitions of

bladder outlet obstruction and outcome measurements, there was significant heterogeneity. In particular, prostate size varied from 20 to 100 cm³ and the control measure is bipolar TURP in two studies whilst monopolar TURP in the other two.²⁸⁻³¹

Across all four RCT's, patients in the TURP arm of each study had superior outcomes in terms of IPSS score and flow rate. Despite this, the most recent RCT from Insausti *et al.*³¹ demonstrates a narrowing gap in outcomes.

In the RCTs that reported an objective measure of erectile dysfunction, PAE proved superior. All RCTs report a radiological measure of difference in prostate volume using either MRI or TRUS. The largest RCT with the longest follow up period, by Gao *et al.*,²⁸ reported a 46% decrease in prostate volume on MRI at 2 years following PAE *versus* 58% with TURP.

Overall, the rates of reported adverse events remained low and overall remained minor including pain/discomfort, haematuria, voiding LUTS and retention. Rates of reported pain varied significantly between RCT and treatment option with different methods of recording pain being utilised. Most pelvic pain resolved shortly post procedure. No RCT reported lower limb claudication post PAE.

All four RCT's specifically reported major adverse events categorised as Clavien Dindo ≥ 3 . In three of the four studies, the incidence of serious adverse events was higher in the TURP arm. However, in the largest of the trials, Gao *et al.*,²⁸ the rate of adverse events was higher in the PAE group. In particular, the rate of post procedural acute urinary retention was significantly higher in the PAE group (25.9% *versus* 5.5%).

Overall procedural time was noted to be longer in PAE overall compared to TURP in three of the four RCTs ranging between 89 and 147 min.²⁸⁻³¹

Three of the RCTs include patients with a history of urinary retention as part of their inclusion criteria. However, a sub-analysis of retention patients is only present in the work of Carnevale, with 91% of patients with a history of retention being catheter free at 1 year.³⁰ More recently, a retrospective multi-centre study compared different surgical techniques in catheter dependent patients with 15 undergoing PAE and 47% being catheter free at 1 year.³²

NICE do not provide a cost analysis comparing TURP and PAE. A sub-analysis of the Swiss Abt *et al.* RCT specifically looked at an in-hospital cost analysis comparing TURP and PAE. This demonstrated that, whilst costs per patient were numerically higher in the TURP group, it was not statistically significant.³³

Aquablation

The Aquabeam® system has also attracted appeal as another MIST. Using a transrectal ultrasound probe and a cystoscopic hand piece, the prostate is assessed by the surgeon. After a treatment plan is established and mapped using specialist software, high pressure normal saline is used to dissect the prostate parenchyma under robotic control. Following dissection, haemostasis is performed using a resectoscope and rollerball. A three-way catheter is inserted on traction and removed the next day. Unlike the other MIST's discussed, aquablation requires a general or spinal anaesthetic and is rarely a day case procedure. However, it does come with the advantageous procedural time of approximately 4 min.^{34,35}

NICE state the paucity of long term evidence for aquablation and state it should only be used with special arrangements for clinical governance, consent, audit and research.³⁶ The EUA and AUA recommend the use of aquablation in prostates of 30–80 g, with the EUA also encouraging clinicians to advise patients on the risk of bleeding and absence of long term data.^{14,15}

The key RCT is the WATER trial, by Gilling *et al.*, a prospective double-blinded international trial assessing the safety and efficacy of aquablation relative to TURP in the management of LUTS. 181 patients were randomised 2:1 in aquablation (n=116) and TURP (n=65). There is now 2 years of follow up data available. Exclusion criteria included a post void residual of >300 ml, bladder or prostate cancer, prostates >80 g, neurogenic bladder, active infection or prior urinary retention.³⁷

Improvements in IPSS, quality of life scores, flow rate and post void residual were seen in both groups at 2 years and seemed to favour aquablation in terms of IPSS and flow rate.

The rates of Clavien Dindo 3 complications remained low, at 6.9% for aquablation and 7.7% for TURP. In men with no sexual dysfunction before surgery, rates of anejaculation remained lower in the

aquablation arm (10%) than in the TURP arm (36%). Neither arm reported *de novo* ED.

Although the initial WATER trial was limited to patients with prostates <80 g, the WATER II study compared results to prostates 80–150 g showing similar and sustained outcomes at 2 years.³⁸

Evidence for aquablation in patients with urinary retention, although promising, is still strictly limited to small case series and requires further research.³⁹

At present there is no cost analysis evidence for aquablation.

iTind

iTind is the second generation of a temporarily implanted nitinol device used to re-model the bladder neck and prostatic urethra. iTIND is comprised of three elongated struts configured at the 12, 5 and 7 o'clock position held together with nitinol wires.

Under local anaesthetic, with or without mild sedation, the device is placed in the patient under cystoscopic guidance. The insertion is said to take approximately 10 min. Five to seven days later, the device is removed using a flexible cystoscope. The device causes a degree of ischaemic necrosis where the struts have compressed prostatic tissue, resulting in longitudinal channels. These channels and the overall remodelling process reduces bladder outflow obstruction and subsequent LUTS.⁴⁰

At present, neither NICE, the AUA or EAU offer any specific guidance on the use of iTIND, other than the EAU suggesting the need for RCT level evidence to a reference technique.¹⁴

At present, there is no RCT comparing iTIND with TURP. Porpiglia *et al.* present a single armed, multi-centre prospective study of 32 patients assessing the safety and feasibility of iTIND with a 3 year follow up period. It demonstrated statistically significant improvements in IPSS, quality of life score and flow at 12 months, with the former two variables being maintained at 3 years.⁴¹ In 2020, Chugthai *et al.* published data on a RCT comparing iTIND to sham with 118 undergoing treatment with iTIND. At 12 months the iTIND group demonstrated a decrease in IPSS score of 9.25 points, 3.25 ml/s improvement in flow and 1.9 point improvement in quality of life score.⁴²

Across both studies adverse events remained rare and no cases of *de novo* ejaculatory or erectile function were reported. Neither study looked at the role of iTIND in patients with retention.

Whilst an outpatient local anaesthetic procedure has potential to be a cost saving alternative to LUTS/BPO management, there is no cost analysis study published on iTIND at present.

Conclusion

At present, for many, TURP remains the gold standard for the management of BPO. The drive to avoid the potential sexual side effects, general anaesthetic and hospital admission has led to a rapidly evolving number of options for clinicians and patients alike. Nonetheless, at present, the RCTs discussed in this review suggest that the outcomes are more modest compared to traditional surgical treatments. As the long-term benefits from MISTs become apparent, as well as surgeon and patient experience the role for such procedures may become clearer.

At present, MISTs may be most appropriate in men who are keen to avoid the risk of sexual dysfunction or a general anaesthetic at the expense of potentially inferior outcomes compared to traditional BPH surgery. Shared patient-clinician decision making, and patient selection is therefore paramount.

For some clinicians, the evidence supporting MIST's is not yet there to replace the gold standard TURP. Speakman *et al.* warn of past endeavours in BPO/LUTS treatment calling for set standards in evidence and certainty for BPO/LUTS treatments. Quoting the absence in longer term data, widespread marketing and unsatisfactory results in prior MIST's now deemed obsolete.⁴³

Given the wide variety of options in the surgical management of BPH a well-designed RCT comparing each option in various patient settings with common outcome measures and long term follow up would help define both the role of MISTs. It may also help provide a tailored option for individual patients. In particular, exploring MISTs in patients with prostates >80ml, obstructing median lobes, a history of retention, those who have undergone previous prostate surgery and perhaps even those with low-risk prostate cancer would prove beneficial.

Overall, it could be surmised that centres should be able to offer a variety of different surgical treatment options appropriate for the specific patient and prostate. As clinician experience increases and evidence continues to amass MISTs is highly likely to become an essential resource in the management of BPO/LUTS.

Conflict of interest statement

The author(s) declare that there is no conflict of interest.

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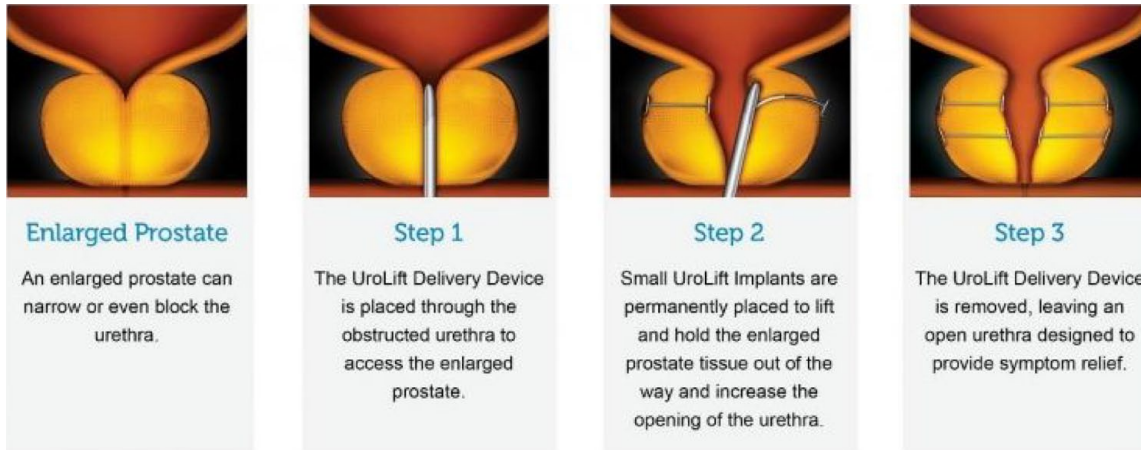
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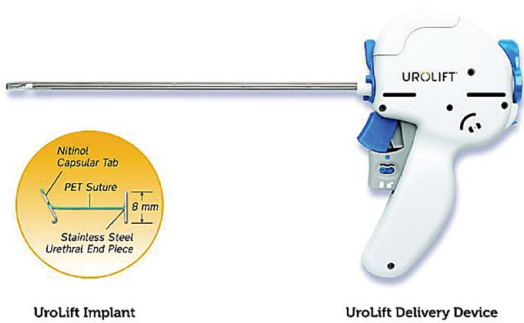
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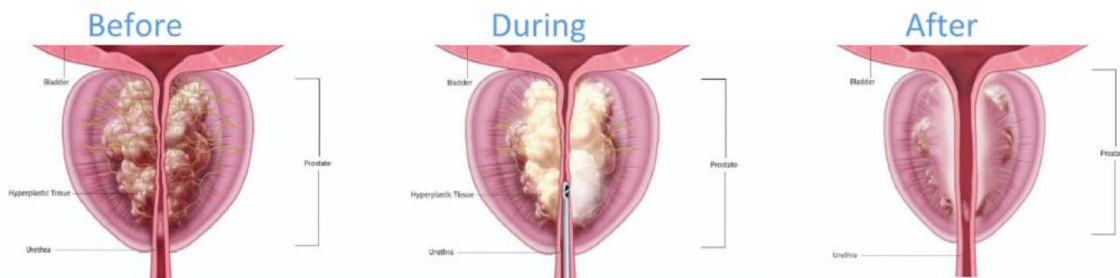
Appendix



Appendix Figure 1. A diagram illustrating the insertion of the UroLift® system for BPO.
Source: UroLift.com/what-is-uroLift.¹³



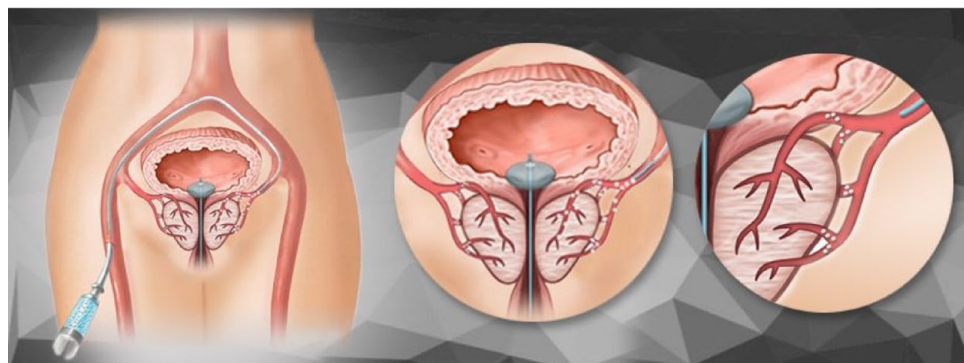
Appendix Figure 2. The UroLift® device.
Source: MEQnordic/products/urology/UroLift.⁴⁴



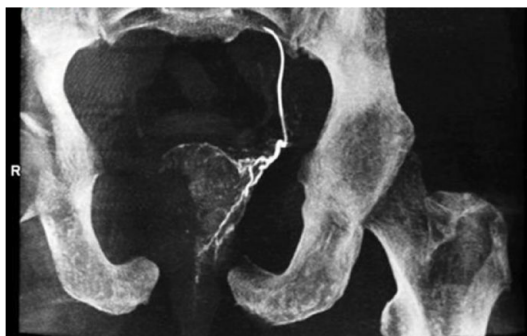
Appendix Figure 3. A diagram illustrating the action of Rezum™ in BPO.
Source: Chestercountyroboticsurgery.com.⁴⁵



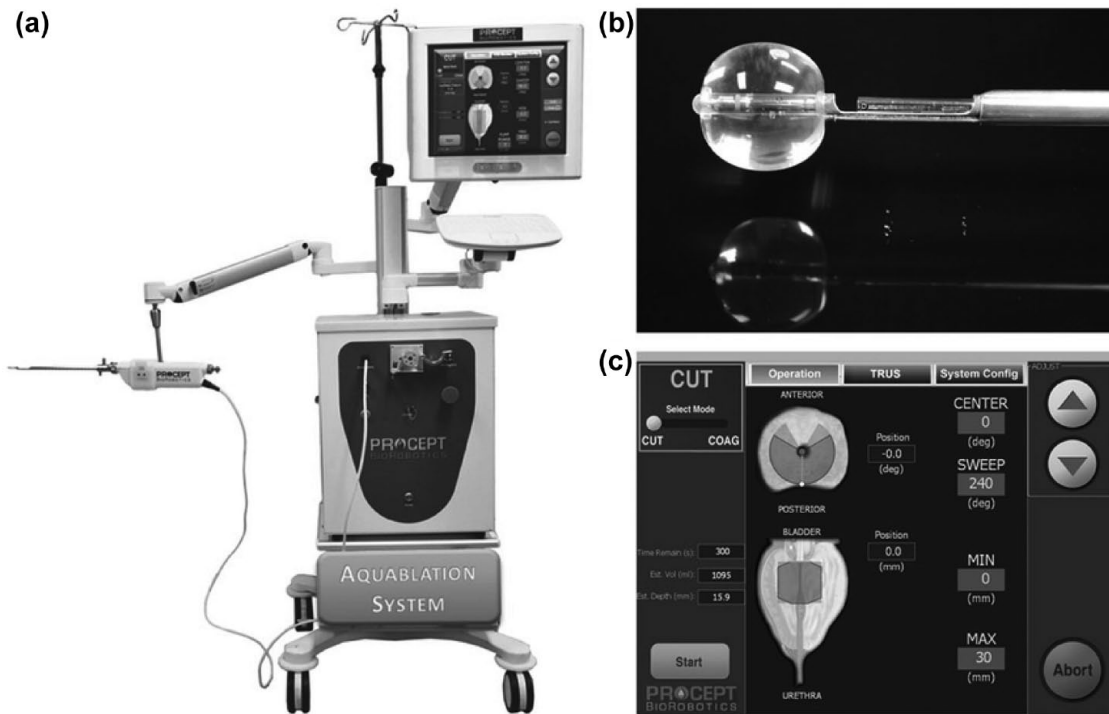
Appendix Figure 4. The Rezum™ device.
Source: Bostonscientific.com.⁴⁶



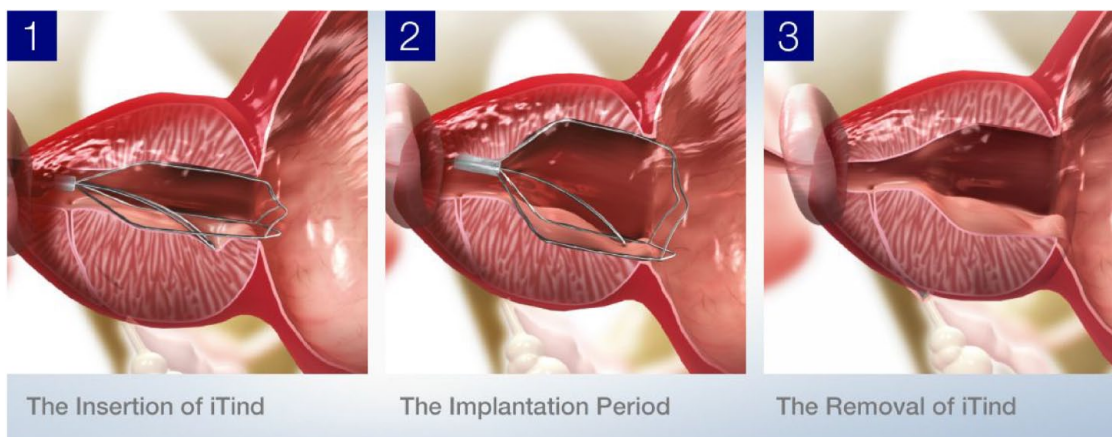
Appendix Figure 5. A diagram illustrating the action PAE in BPO.
Source: Desertveinandvascular.com.⁴⁷



Appendix Figure 6. Contrast injected in the prostatic arteries during PAE.
Source: Kumar and Ravi⁴⁸ via Urology News.



Appendix Figure 7. The aquablation equipment.
Source: Faber *et al.*⁴⁹ via Journal of Endourology.



Appendix Figure 8. A diagram displaying the action of iTIND in BPO.
Source: Olympus-europa.com.⁵⁰