NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of transurethral water jet ablation for lower urinary tract symptoms caused by benign prostatic hyperplasia

Benign prostatic hyperplasia is a non-cancerous enlargement of the prostate. It can block or narrow the tube (urethra) that urine passes through to leave the body, causing urination problems. During this procedure, a high-speed jet of water is injected into the prostate using a special probe that is passed up the urethra. This destroys some of the prostate tissue, making it smaller.

Contents

Introduction

The National Institute for Health and Care Excellence (NICE) prepared this interventional procedure overview to help members of the interventional

procedures advisory committee (IPAC) make recommendations about the safety and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and specialist opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This overview was prepared in March and updated in July 2018.

Procedure name

- Transurethral water jet ablation for lower urinary tract symptoms caused by benign prostatic hyperplasia.

Specialist societies

- British Association of Urological Surgeons
- Royal College of Surgeons.

Description of the procedure

Indications and current treatment

Benign prostatic hyperplasia is a common condition that affects older men. Stromal and epithelial cells increase in number, causing the prostate to get bigger. It often happens in the periurethral region of the prostate, with large discrete nodules compressing the urethra. Symptoms include hesitancy during urination, interrupted or decreased urine stream (volume and flow rate), nocturia, incomplete voiding and urinary retention.

Mild symptoms are usually managed conservatively. Drugs may also be used, such as alpha blockers and 5-alpha-reductase inhibitors. If other treatments have not worked, there are a range of surgical options that may be considered including transurethral resection of the prostate (TURP), transurethral vaporisation, holmium laser enucleation, insertion of prostatic urethral lift implants, prostatic artery embolisation or prostatectomy (see NICE's clinical guidance on lower urinary tract symptoms in men). Potential complications of some of these surgical procedures include bleeding, infection, urethral strictures, incontinence and sexual dysfunction.

What the procedure involves

Transurethral water jet ablation for lower urinary tract symptoms caused by benign prostatic hyperplasia uses a specialised system that combines image guidance and robotics for the targeted heat-free removal of prostate tissue. The procedure is usually done with the patient under general or spinal anaesthesia. Transrectal ultrasound is used throughout the procedure. A special handpiece with an integrated cystoscope and ablation probe is inserted through the urethra and into the bladder. Positioning is confirmed by using visual markers on a computer screen, and the surgeon is able to plan the depth and angle of resection using the system software. Once the surgical mapping is complete, a high-speed jet of saline is delivered to the prostate at various flow rates, according to the depth of penetration needed. The ablated tissue is aspirated through ports in the handpiece and can be used for histological analysis. Haemostasis can be achieved by cautery or by inflating a Foley balloon catheter inside the prostatic cavity. The average resection time is typically about 3 to 5 minutes. After the procedure, a 3-way Foley catheter is placed under traction and continuous bladder irrigation is started. Traction is removed the evening after the procedure and irrigation is progressively decreased. The catheter is removed before the patient is discharged from hospital, usually the day after the procedure.

The possible advantages of the procedure include a reduction in resection time compared with other endoscopic methods, and the potential to preserve sexual function. The procedure is heat-free, which removes the risk of complications arising from thermal injury.

Outcome measures

International Prostate Symptom Score

The International Prostate Symptom Score (IPSS) is a validated questionnaire often used to assess symptoms of BPH (it is also referred to as the American Urological Association BPH Symptom Score Index). It includes questions on incomplete bladder emptying, frequency, intermittency and urgency of urination, weak urine stream, straining to urinate and nocturia. Higher scores represent worse symptoms. In general, an IPSS symptom score of 0 to 7 indicates mild symptoms, 8 to 19 indicates moderate symptoms and 20 to 35 indicates severe symptoms. An additional question asks men how they feel about their BPH symptoms and the response yields a score for quality of life (ranging from 0 to 6, with 0 representing ‘delighted’ and 6 representing ‘terrible’).

International Index of Erectile Function

The International Index of Erectile Function (IIEF) is a 15-item questionnaire used to assess men's sexual function in 5 domains: erectile function, orgasmic function, sexual desire, intercourse satisfaction, and overall satisfaction. Each domain has its own score range and lower scores represent greater dysfunction:

- Erectile function score: range 0 to 30 (scores of 24 or less represent increasing dysfunction)
- Orgasmic function score: range 0 to 10 (scores of 8 or less represent increasing dysfunction)
- Sexual desire score: range 0 to 10 (scores of 8 or less represent increasing dysfunction)
- Intercourse satisfaction score: range 0 to 15 (scores of 12 or less represent increasing dysfunction)
- Overall satisfaction score: range 0 to 10 (scores of 8 or less represent increasing dysfunction).

Efficacy summary

International Prostate Symptom Score (IPSS)

In a randomised controlled trial (RCT) of 184 patients treated by water jet ablation or transurethral resection of the prostate (TURP), the mean decrease in IPSS from baseline at 6 month follow-up was 16.9 and 15.1 points respectively ($p<0.0001$ for non-inferiority, $p=0.1346$ for superiority). At 6 months, 100% of patients in the water jet ablation group and 98% of patients in the TURP group showed improvements in IPSS scores. 90% of patients in the water jet ablation group and 79% of patients in the TURP group met the threshold of IPSS change score of at least 50%. Men with prostate size more than 50 ml had greater improvements in IPSS after water jet ablation compared with TURP ($p=0.0099$). [1] In a subanalysis of 93 patients who were included in the RCT of 184 patients, the decrease in IPSS was 14.5 points in the water jet ablation group and 13.8 points in the TURP group at 1 year follow-up ($p=0.7117$).[6] In a case series of 47 patients, there was a statistically significant improvement in IPSS from 24.4 at baseline to 5.0 at 3 month follow-up ($p<0.01$). [2] In a case series of 21 patients, there was a statistically significant improvement in IPSS from 22.8 at baseline to 6.6 at 12 month follow-up ($p<0.0001$). [3] In a case series of 15 patients, there was a statistically significant improvement in IPSS from 23.1 at baseline to 8.6 at 6 month follow-up ($p<0.001$). [4]

Quality of life

In the RCT of 184 patients treated by water jet ablation or TURP, the mean improvement in IPSS quality-of-life score from baseline at 6 month follow-up was similar in the 2 groups (3.5 and 3.3 points respectively; p=0.4706). [1] In the subanalysis of 93 patients who were included in the RCT of 184 patients, mean improvement in IPSS quality-of-life score was also similar in the 2 groups at 1 year follow-up (3.1 and 3.4 points respectively; p=0.5760).[6] In the case series of 47 patients, there was a statistically significant improvement in IPSS quality-of-life score from 4.5 at baseline to 0.3 at 3 month follow-up (p<0.01). [2] In the case series of 21 patients, there was a statistically significant improvement in IPSS quality-of-life score from 5.0 at baseline to 1.7 at 12 month follow-up (p<0.0001). [3] In the case series of 15 patients, there was a statistically significant improvement in IPSS quality-of-life score from 5.0 at baseline to 2.5 at 6 month follow-up (p<0.001). [4]

Sexual function

In the RCT of 184 patients, the proportion of patients with a 2-point drop in Male Sexual Health Questionnaire (MSHQ-EjD) or a 6-point drop in the International Index of Erectile Function (IIEF-5) score was 32% in the water jet ablation group compared with 56% in the TURP group (p=0.0165).[1] In the case series of 21 patients, no patient who was sexually active at baseline and at each study visit reported a reduction in ejaculatory or orgasmic function. In the 11 sexually active patients, measures of sexual function improved but the only statistically significant improvement was for intercourse satisfaction.[2]

Maximum urinary flow rate

In the RCT of 184 patients treated by water jet ablation or TURP, the mean maximum urinary flow rate increased from 9.4 ml/sec and 9.1 ml/sec at baseline to 20.3 ml/sec and 18.0 ml/sec respectively at 6 month follow-up (p=0.10 between groups).[1] In the subanalysis of 93 patients who were included in the RCT of 184 patients, maximum urinary flow was 11 ml/sec and 10 ml/sec respectively at 1 year follow-up.[6] In the case series of 47 patients, there was a statistically significant improvement in mean maximum urinary flow rate from 7.1 ml/sec at baseline to 16.5 ml/sec at 3 month follow-up (p<0.01).[2] In the case series of 21 patients, there was a statistically significant improvement in mean maximum urinary flow rate from 8.7 ml/sec at baseline to 18.3 ml/sec at 12 month follow-up (p<0.0001).[3] In the case series of 15 patients, there was a statistically significant improvement in mean maximum urinary flow rate from 8.6 ml/sec at baseline to 18.6 ml/sec at 6 month follow-up (p<0.001).[4]

Post void residual volume

In the RCT of 184 patients treated by water jet ablation or TURP, the mean post void residual volume decreased from 97 ml and 112 ml at baseline to 42 ml and

48 ml respectively at 6 month follow-up (p=not significant between groups).[1] In the subanalysis of 93 patients who were included in the RCT of 184 patients, the decrease in postvoid residual from baseline was 54 ml and 39 ml respectively at 1 year follow-up (p value not reported).[6] In the case series of 47 patients, there was a statistically significant improvement in mean post void residual volume from 119 ml at baseline to 43 ml at 3 month follow-up (p<0.01).[2] In the case series of 21 patients, there was a statistically significant improvement in mean post void residual volume from 136.1 ml at baseline to 53.5 ml at 12 month follow-up (p=0.0007).[3] In the case series of 15 patients, there was a statistically significant improvement in mean maximum urinary flow rate from 91 ml at baseline to 30 ml at 6 month follow-up (p=0.013).[4]

Improvement in incontinence

In the RCT of 184 patients treated by water jet ablation or TURP, the mean incontinence scores improved by 1.2 and 0.6 points respectively at 6 month follow-up (p=0.0786 between groups).[1] In the case series of 47 patients, there was a statistically significant improvement in incontinence severity scores from about 4.5 at baseline to 3 at 3 month follow-up (p<0.01).[2]

Prostate size reduction

In the RCT of 184 patients treated by water jet ablation or TURP, the mean reduction in prostate size (measured on transrectal ultrasound) was 31% and 44% respectively at 3 month follow-up (p=0.0072 between groups).[1] In the case series of 21 patients, there was a statistically significant decrease in mean prostate volume from 53 ml at baseline to 35 ml at 6 month follow-up (p<0.01; n=16).[3] In the case series of 15 patients, there was a 31% reduction in mean prostate size from baseline at 6 month follow-up (p<0.001).[4]

Reduction in medication

In the RCT of 184 patients treated by water jet ablation or TURP, 71% and 90% of the 85 patients who were taking alpha blockers at baseline had stopped taking them by month 6 (p=0.06 between groups). Of the 41 patients taking 5 alpha-reductase inhibitors at baseline, 67% of patients in the water jet ablation group and 82% of patients in the TURP group (p=0.3092) had stopped taking them by month 6. No patients who were not taking alpha blockers or 5 alpha-reductase inhibitors had started them by month 6.[1]

Safety summary

Bleeding

Bleeding (Clavien-Dindo grade 2 or higher) was reported in 3.4% (4/116) of patients in the water jet ablation group and 4.6% (3/65) of patients in the TURP group (p=not significant), in an RCT of 184 patients. Clavien-Dindo grade 1 bleeding was reported in 9.5% (11/116) and 10.8% (7/65) of patients respectively (p=0.7995).[1] Haematuria needing transfusion was reported in 1 patient in a case series of 47 patients.[2] Haematuria, which resolved spontaneously, was reported in 1 patient in a case series of 21 patients and in 20% (3/15) of patients in a case series of 15 patients.[3,4] Clavien-Dindo grade 2, 3 and 4 bleeding was reported in 5.9% (6/101), 5.9% (6/101) and 2.0% (2/101) of patients respectively in a case series of 101 patients with large volume BPH. There were 6 perioperative blood transfusions and 6 patients needed transfusion or cystoscopic fulguration for delayed bleeding.[8]

Retrograde ejaculation

Retrograde ejaculation was reported in 7.0% (8/116) of patients in the water jet ablation group and 24.6% (16/65) of patients in the TURP group (p=0.0012), in the RCT of 184 patients.[1]

Urinary retention

Clavien-Dindo grade 3b urinary retention was reported in 1 patient who had water jet ablation and no patients who had TURP in the RCT of 184 patients. Grade 1 urinary retention was reported in 7.8% (9/116) and 6.2% (4/65) of patients respectively (p=0.7730).[1] Clavien-Dindo grade 3 and grade 1 urinary retention were each reported in 6.4% (3/47) of patients in the case series of 47 patients.[2] Urinary retention was reported in 14.3% (3/21) of patients in the case series of 21 patients.[3] The need for recatheterisation was reported in 33.3% (5/15) of patients in the case series of 15 patients; all patients had subsequent successful trials of void.[4]

Urethral stricture or adhesions or other damage

Clavien-Dindo grade 3a urethral stricture or adhesions was reported in 2.6% (3/116) of patients who had water jet ablation and 1.5% (1/65) of patients who had TURP (p=1.00) in the RCT of 184 patients.[1] Urethral stricture was reported in 4.3% (2/47) of patients in the case series of 47 patients.[2] Meatal stenosis was reported in 1 patient in the case series of 21 patients.[3] Clavien-Dindo grade 3 meatal stenosis and urethral stricture were reported in 2 patients and 1 patient respectively in the case series of 101 patients.[8]

Urethral damage (Clavien-dindo grade 1) was reported in 1 patient who had water jet ablation and 1 patient who had TURP in the RCT of 184 patients (p=1.00).[1]

Bladder spasm

Clavien-Dindo grade 2 bladder spasm was reported in 3.4% (4/116) of patients who had water jet ablation and 3.1% (2/65) of patients who had TURP (p=1.00) in the RCT of 184 patients. Grade 1 bladder spasm was reported in 2.6% (3/116) and 1.5% (1/65) of patients respectively (p=1.00).[1] Bladder spasm was reported in 1 patient in the case series of 15 patients.[4]

Urinary tract infection

Clavien-Dindo grade 2 urinary tract infection was reported in 7.0% (8/116) of patients who had water jet ablation and 7.7% (5/65) of patients who had TURP (p=1.00) in the RCT of 184 patients. Grade 1 urinary tract infection was reported in 1.7% (2/116) of patients who had water jet ablation and no patients who had TURP (p=0.5371).[1] Infection was reported in 1 patient in the case series of 47 patients.[2] Urinary tract infection with 30-day treatment was reported in 1 patient in the case series of 21 patients.[3] Urinary tract infection was reported in 4.0% (4/101) of patients in the case series of 101 patients.[8]

Dysuria

Dysuria (Clavien-Dindo grade 1) was reported in 10.3% (12/116) of patients who had water jet ablation and 7.7% (5/65) of patients who had TURP in the RCT of 184 patients.[1] Dysuria, which resolved spontaneously, was reported in 1 patient in the case series of 21 patients and in 20% (3/15) of patients in the case series of 15 patients.[3,4] Clavien-Dindo grade 2 or 3 dysuria were each reported in 1 patient in the case series of 101 patients.[8]

Urinary urgency, frequency, difficulty or leakage

Clavien-Dindo grade 2 urinary urgency, frequency, difficulty or leakage was reported in 1.7% (2/116) of patients who had water jet ablation and 3.1% (2/65) of patients who had TURP (p=0.6191) in the RCT of 184 patients. Grade 1 urinary urgency, frequency, difficulty or leakage was reported in 3.4% (4/116) and 1.5% (1/65) of patients respectively (p=1.00).[1] Clavien-Dindo grade 3 urinary incontinence was reported in 1 patient in the case series of 101 patients. In the same study, Clavien-Dindo grade 2 urinary frequency or urgency were each reported in 1 patient.[8]

Pain

Clavien-Dindo grade 2 pain was reported in 0.9% (1/116) of patients who had water jet ablation and 3.1% (2/65) of patients who had TURP (p=0.2932) in the RCT of 184 patients. Clavien-Dindo grade 1 pain was reported in 4.3% (5/116)

and 4.6% (3/65) of patients respectively (p=1.00).[1] Pelvic pain or discomfort was reported in 20% (3/15) of patients in the case series of 15 patients.[4]

Other

Arrhythmia (Clavien-Dindo grade 4) was reported in 1 patient who had water jet ablation and no patients who had TURP in the RCT of 184 patients.[1] Postoperative cardiac arrhythmia was reported in 1 patient in the case series of 15 patients.[4] A Clavien-Dindo grade 4b complication was reported in 1 patient in the case series of 101 patients: the patient had a cerebrovascular accident the day after surgery that evolved into multiorgan failure.[8] In the same study, 2 Clavien-Dindo grade 4 cardiac complications were reported (not further described).

Anecdotal and theoretical adverse events

In addition to safety outcomes reported in the literature, specialist advisers are asked about anecdotal adverse events (events which they have heard about) and about theoretical adverse events (events which they think might possibly occur, even if they have never happened). For this procedure, specialist advisers listed the following anecdotal adverse events: bleeding, urosepsis and anejaculation. They considered that the following were theoretical adverse events: massive bleeding, injury to surrounding structures if targeting not accurate (distal urinary sphincter would be main concern, although rectal or ureteric injuries also theoretically possible), and bladder neck stenosis.

The evidence assessed

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to transurethral water jet ablation for lower urinary tract symptoms caused by benign prostatic hyperplasia. The following databases were searched, covering the period from their start to 30 May 2018: MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and other databases. Trial registries and the Internet were also searched. No language restriction was applied to the searches (see the literature search strategy). Relevant published studies identified during consultation or resolution that are published after this date may also be considered for inclusion.

The following selection criteria (table 1) were applied to the abstracts identified by the literature search. Where selection criteria could not be determined from the abstracts the full paper was retrieved.

Table 1 Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	Clinical studies were included. Emphasis was placed on identifying good quality studies. Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, or a laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising study methodology, unless they reported specific adverse events that were not available in the published literature.
Patient	Patients with lower urinary tract symptoms caused by benign prostatic hyperplasia.
Intervention/test	Transurethral water jet ablation.
Outcome	Articles were retrieved if the abstract contained information relevant to the safety and/or efficacy.
Language	Non-English-language articles were excluded unless they were thought to add substantively to the English-language evidence base.

List of studies included in the IP overview

This IP overview is based on 368 patients from 1 randomised controlled trial (reported in 3 separate studies), 1 prospective single arm trial and 3 case series. In addition, 1 study reported pooled results from the randomised controlled trial and the single arm trial.[1–8]

Other studies that were considered to be relevant to the procedure but were not included in the main extraction table (table 2) have been listed in the appendix.

Table 2 Summary of key efficacy and safety findings on transurethral water jet ablation for lower urinary tract symptoms caused by benign prostatic hyperplasia

Study 1 Gilling P (2018)

Details

Study type	**Randomised controlled trial (WATER; NCT02505919)**
Country	Australia, New Zealand, UK, US (17 sites)
Recruitment period	2015 to 2016
Study population and number	**n=184 (117 water jet ablation, 67 transurethral resection of the prostate [TURP])** Patients with moderate-to-severe lower urinary tract symptoms related to benign prostatic hyperplasia
Age	Mean 66 years
Patient selection criteria	Men aged 45 to 80 years, prostate size between 30 and 80 g, moderate-to-severe symptoms as indicated by International Prostate Symptom Score (IPSS) of 12 or higher, maximum urinary flow rate (Q_{max}) less than 15 ml/s. Exclusion criteria: history of prostate or bladder cancer, neurogenic bladder, bladder calculus or clinically significant bladder diverticulum, active infection, treatment for chronic prostatitis, diagnosis of urethral stricture, meatal stenosis or bladder neck contracture, damaged external urinary sphincter, stress urinary incontinence, post void residual greater than 300 ml or urinary retention, use of self-catheterisation, or prior prostate surgery. Men taking anticoagulants or on bladder anticholinergics or with severe cardiovascular disease were also excluded.
Technique	Water jet ablation was done using the Aquabeam system (PROCEPT BioRobotics, US). Haemostasis was achieved using either focal, non-resective electrocautery or low-pressure inflation of a Foley balloon catheter in the prostatic fossa.
Follow-up	**6 months**
Conflict of interest/source of funding	Not reported

Analysis

Follow-up issues: Three patients (1 water jet ablation and 2 TURP) voluntarily withdrew from the study before treatment, leaving 181 in the intent-to-treat population. 98% (178/181) of patients completed the 3-month follow-up and 97% (175/181) completed the 6-month follow-up.

Study design issues: Prospective, double-blind, multicentre randomised controlled trial. Randomisation was done through a web-based system and was stratified by study site and baseline IPSS score category with random block sizes. Baseline evaluation and study treatment were provided by an unblinded research team who did not reveal treatment assignment to the patient. A separate blinded team did the follow-up visits. All adverse events were adjudicated by an independent clinical events committee blinded to treatment assignment. Blinding was assessed at each visit and was deemed to be adequate throughout the study. The primary efficacy endpoint was the change in IPSS from baseline to 6 months. Non-inferiority was declared if the lower 95% confidence limit of the difference in score change at 6 months exceeded -4.7 points. The primary safety endpoint was the proportion of patients with adverse events rated by the clinical events committee as possibly, probably or definitely related to the study procedure classified as Clavien-Dindo Grade 2 or higher or any Grade 1 event resulting in persistent disability (ejaculatory or erectile dysfunction or incontinence). A sample size of 177 randomised patients had >80% power to detect non-inferior change scores with a non-inferiority margin of 4.7 points assuming a 16-point improvement in IPSS, an effect size of 1.5 points worse in the water ablation group and a standard deviation of 6 points.

Study population issues: Baseline characteristics were similar between the 2 groups. The mean prostate size was 53 ml and 81% of patients were sexually active.

Other issues: Most of the study sites (14/17) had no previous experience of transurethral water jet ablation.

Key efficacy and safety findings

Efficacy

Number of patients analysed: **181 (116 versus 65)**

Operative characteristics (mean values)

Characteristic	Water jet ablation	TURP	p value
Operative time (minutes)	32.8	35.5	0.2752
Instrument in/out time (minutes)	23.3	34.2	<0.0001
Resection time (minutes)	3.9	27.4	<0.0001
Intraoperative fluid use (litres)	5.2	13.1	<0.0001
Hospital length of stay	1.4	1.4	0.3357

The urinary catheter was removed a median of 1 day after surgery in both groups.

Decrease in IPSS from baseline at 6 month follow-up

- Water jet ablation=16.9 points
- TURP=15.1 points

p<0.0001 for non-inferiority, p=0.1346 for superiority

At 6 months, 100% of patients in the water jet ablation group and 98% of patients in the TURP group showed improvements in IPSS scores. 90% of patients in the water jet ablation group and 79% of patients in the TURP group met the threshold of IPSS change score of at least 50%.

Men with prostate size >50 ml had superior improvements in IPSS after water jet ablation compared with TURP (p=0.0099).

Improvement in IPSS quality of life score from baseline at 6 month follow-up

- Water jet ablation=-3.5 points
- TURP=-3.3 points, p=0.4706

Reoperation

- Water jet ablation, n=0
- TURP, n=1

Proportion of patients with 2-point drop in Male Sexual Health Questionnaire (MSHQ-EjD) or 6-point drop in the International Index of Erectile Function (IIEF-5) score

- Water jet ablation=32%
- TURP=56%, p=0.0165

Safety

Safety outcomes (all patients)

	Water jet ablation	TURP	p value
Primary safety endpoint	25.9%	41.5%	<0.02
Persistent Clavien-Dindo (C-D) Grade I events at month 3	6.9%	24.6%	0.0004
C-D Grade 2 or higher	19.8%	23.1%	0.3038

Distribution of events at month 3 categorised by Clavien-Dindo grades

	Water jet ablation No. of events	Water jet ablation No. of patients (%)	TURP No. of events	TURP No. of patients (%)	p value
C-D Grade 1	**63**	**39 (33.6%)**	**41**	**27 (41.5%)**	**0.3350**
Bladder spasm	3	3	1	1	1.00
Bleeding	12	11	7	7	0.7995
Dysuria	12	12	5	5	0.7912
Pain	5	5	3	3	1.00
Retrograde ejaculation	8	8	16	16	0.0012
Urethral damage	1	1	1	1	1.00
Urinary retention	11	9	4	4	0.7730
Urinary tract infection	2	2	0	0	0.5371
Urinary urgency /frequency/ difficulty/leakage	4	4	1	1	1.00
Other	5	5	3	3	1.00
C-D Grade 2	**20**	**19 (16.4%)**	**15**	**11 (16.9%)**	**1.00**
Bladder spasm	4	4	2	2	1.00
Bleeding	1	1	0	0	1.00
Dysuria	0	0*	1	1	0.3591
Pain	1	1	2	2	0.2932
Urinary tract infection	9	8	5	5	1.00
Urinary urgency /frequency/ difficulty/leakage	2	2	3	2	0.6191
Other	3	3	2	5	1.00
C-D Grade 3a	**4**	**4 (3.4%)**	**2**	**2 (3.1%)**	**1.00**
Bleeding	1	1	1	1	1.00
Urethral stricture or adhesions	3	3	1	1	1.00
C-D Grade 3b	**3**	**3 (2.6%)**	**3**	**3 (4.6%)**	**0.6684**
Bleeding	2	2	2	2	0.6191
Urethral stricture or adhesions	0	0	1	1	0.3591
Urinary retention	1	1	0	0	1.00
C-D Grade 4	**1**	**1 (0.9%)**	**0**	**0 (0%)**	**1.00**
Arrhythmia	1	1	0	0	1.00

* reported as 9 in the paper

In sexually active men, mean erectile function scores (IIEF-15) were stable after water jet ablation and decreased slightly after TURP except for overall sexual satisfaction where water jet ablation was statistically significantly better (p=0.0492).
Ejaculatory function scores (MSHQ-EjD) were stable after water jet ablation but worsened significantly after TURP (p=0.0254).

Maximum urinary flow rate (ml/sec)

	Baseline	6 months	p value (between groups)
Water jet ablation	9.4±3.0	20.3±10.9	0.10
TURP	9.1±2.7	18±7.5	

Post void residual (ml)

	Baseline	6 months	p value (between groups)
Water jet ablation	97±79	42±50	Not significant
TURP	112±93	48±57	

Prostate size reduction at 3 months (assessed on transrectal ultrasound)

- Water jet ablation=17.3 ml (mean 31% reduction)
- TURP=24.0 ml (mean 44% reduction), p=0.0072

Reduction in PSA at 6 months

- Water jet ablation=1.2 ng/ml (median 30% reduction)
- TURP=1.1 ng/ml (median 36% reduction), p=0.7205

Improvement in mean incontinence scores at 6 months

- Water jet ablation=1.2 points
- TURP=0.6 points (p=0.0786)

Reduction in medication
Of the 85 patients taking alpha blockers at baseline, 71% of patients in the water jet ablation group and 90% of patients in the TURP group (p=0.06) had stopped taking them by month 6.

Of the 41 patients taking 5 alpha-reductase inhibitors at baseline, 67% of patients in the water jet ablation group and 82% of patients in the TURP group (p=0.3092) had stopped taking them by month 6.

No patients not taking alpha blockers or 5 alpha-reductase inhibitors had started them by month 6.

Safety outcomes (patients with prostate size >50 ml)

	Water jet ablation	TURP	p value
Primary safety endpoint	20%	46%	0.0082
Persistent Clavien-Dindo (C-D) Grade I events at month 3	2%	26%	0.0003
C-D Grade 2 or higher	19%	29%	0.1911
Anejaculation among sexually active men without the condition at baseline	2%	41%	0.0001

Abbreviations used: C-D, Clavien-Dindo; IIEF, International Index of Erectile Function; IPSS, International Prostate Symptom Score; MSHQ-EjD , Male Sexual Health Questionnaire; PSA, prostate specific antigen; TURP, transurethral resection of the prostate.	

Study 2 Desai M (2018)

Details

Study type	**Case series**
Country	India
Recruitment period	Not reported
Study population and number	**n=47** Men with lower urinary tract symptoms attributable to benign prostatic hyperplasia
Age	Mean 66 years (range 50 to 79)
Patient selection criteria	Men aged 50 to 80 years with lower urinary tract symptoms; International Prostate Symptom Score (IPSS) greater than 12; prostate size 20 to 120 ml; maximum urinary flow rate (Q_{max}) 15 ml/s or less; history of inadequate response, contraindication or refusal of medical therapy. Exclusion criteria: history of prostate or bladder cancer, elevated prostate specific antigen (PSA) level, neurogenic bladder, prostatitis within the last year, urethral stricture, meatal stenosis or bladder neck contracture, previous prostate surgery, active infection, use of anticoagulants, gross haematuria, allergy to device materials, use of immune suppressants or corticosteroids, and serious medical or mental illness.
Technique	A second-generation Aquabeam system (PROCEPT BioRobotics) was used. The procedures were done with the patient under general or spinal anaesthesia. Haemostasis was achieved by Foley catheter traction or by focal non-resective electrocautery coagulation.
Follow-up	**3 months**
Conflict of interest/source of funding	The first author is a consultant for PROCEPT Biorobotics.

Analysis

Follow-up issues: At 3 months, 2 patients were lost to follow-up and 1 patient withdrew consent.

Study design issues: Single-centre, prospective study with consecutive patients. Seven surgeons from 4 institutions used the device in the study. The primary endpoint was completion of the intended surgical procedure and the primary safety endpoint was the perioperative complication rate. Secondary outcomes included change in IPSS, maximum urinary flow rate and post-void residual urine volume.

Study population issues: The mean prostate volume was 48 ml (range 20 to 118). 53% (25/47) of patients had a median lobe and 8 patients had urinary retention before the procedure.

Other issues: Several parameters and treatment settings were improved throughout the study. For cultural reasons, the study did not include questions about sexual function.

Key efficacy and safety findings

Efficacy

Number of patients analysed: **47**

All procedures were technically successful.

Mean total procedure time (defined as pre-procedure cystoscopy to post-procedure catheter insertion)=35 minutes
Mean resection time=4 minutes

Haemostasis was achieved adequately in 57% (27/47) of patients by Foley catheter traction and by focal non-resective electrocautery in 43% (20/47) of patients. The mean time to achieve haemostasis was 9 minutes (range 1 to 70).

Length of hospital stay
Mean length of hospital stay=3.1 days (range 1 to 8) (1 patient stayed in hospital for 8 days, primarily for social/travel reasons)

Catheterisation
Mean duration of urethral catheterisation=1.9 days (range 1 to 11) (1 patient with preoperative chronic urinary retention had prolonged [11 day] catheter use)

Subsequent treatment
1 patient had a transurethral resection of the prostate (TURP) 3 weeks after the procedure because of inability to void, dribbling and haematuria.

2 patients, who had urinary retention at baseline, did not void after catheter removal on day 3. Approximately 3 weeks later, they had TURP for inability to urinate after catheter removal.

Symptom improvement

Outcome	Baseline	3-month follow-up	p value
International Prostate Symptom Score (IPSS)	24.4	5.0	<0.01
IPSS quality of life score	4.5	0.3	<0.01
Mean Q_{max} (ml/s)	7.1	16.5	<0.01
Post-void residual volume (ml)	119	43	<0.01

Incontinence severity scores improved after treatment from approximately 4.5 at baseline to 3 at 3 month follow-up (p<0.01; results presented graphically).
Pelvic pain scores were low postoperatively and decreased rapidly.
Dysuria intensity and frequency scores were low throughout follow-up and improved by 3 months.

Residual apical adenoma was found in 2 patients – the authors noted that subsequent revisions of the system have incorporated a feature to target apical tissue around and distal to the verumontanum.

Safety

Complications
There were 10 complications in 8 patients by day 90.

Adverse event	Number of events
Clavien-Dindo I	
Acute urinary retention	3
Clavien-Dindo II	
Haematuria needing transfusion	1
Infection	1
Clavien-Dindo III	
Urinary retention	3
Urethral stricture	2

Of the 6 patients with acute urinary retention, 1 needed cystoscopy to remove bladder clots, 3 needed TURP, and 2 started voiding after temporary recatheterisation.

Abbreviations used: IPSS, International Prostate Symptom Score; Q_{max}, maximum urinary flow rate

Study 3 Gilling P (2017)

Details

Study type	**Case series**
Country	Australia, New Zealand
Recruitment period	November 2013 to July 2014
Study population and number	**n=21** Men with moderate to severe symptomatic benign prostatic hyperplasia
Age	Mean 70 years (range 62 to 78)
Patient selection criteria	Men aged between 50 and 80 years with moderate to severe symptomatic benign prostatic hyperplasia; International Prostate Symptom Score (IPSS) greater than 12; maximum urinary flow 12 ml per second or less; Schafer scale 2 or greater; prostate volume 25 to 80 ml as determined by transrectal ultrasound. Exclusion criteria included active urinary tract infection, urinary retention or post void residual 400 ml or greater, abnormal renal function, elevated PSA, history of current or suspected prostate or bladder cancer, neurogenic bladder or external urinary sphincter abnormalities, previous prostate surgery, current therapy affecting prostate physiology or another medical condition that would pose an unacceptable patient risk.
Technique	Water jet ablation was done using an updated version of the Aquabeam system (PROCEPT BioRobotics, US). General anaesthesia was used for all patients. Focal cautery was applied for haemostasis at surgeon discretion using standard monopolar or bipolar techniques.
Follow-up	**1 year**
Conflict of interest/source of funding	The study was supported by PROCEPT BioRobotics. All 3 authors have a financial interest or other relationship with PROCEPT BioRobotics.

Analysis

Follow-up issues: 1 patient voluntarily withdrew from the study after 3 months.

Study design issues: Small, prospective, multicentre, single arm trial. The primary performance endpoint of the study was completion of the target procedure. The primary safety endpoint was the perioperative complication rate. Secondary endpoints included the change from baseline in IPSS, International Index of Erectile Function (IIEF), peak urinary flow rate, post void residual and detrusor pressure at maximum urinary flow.

Study population issues: Mean prostate volume was 57.2 ml (range 30 to 102). All patients met the eligibility criteria except 1, who had a larger prostate (102 ml).

Key efficacy and safety findings

Efficacy

Number of patients analysed: **21**

All procedures were technically successful.

Mean procedure time (pretreatment to posttreatment cystoscopy)=38 minutes

Mean total procedure time=45 minutes (range 28 to 69)
Mean ablation time=5 minutes (range 2 to 13)
Mean cautery time=7.5 minutes (range 3 to 15)

The urinary catheter was removed on day 1 in 95% (20/21) of patients.

91% (19/21) of patients were discharged the day after the procedure.

Functional outcomes (mean values)

Outcome	Baseline	3 month follow-up	6 month follow-up	12 month follow-up	p value
IPSS	22.8	7.0	7.1	6.6	<0.0001
Quality of life score	5.0	1.8	1.7	1.7	<0.0001
Q_{max}, ml/sec	8.7	16.5	18.9	18.3	<0.0001
Post void residual, ml	136.1	52.2	39.4	53.5	0.0007

Urodynamics
In the 14 patients in whom urodynamics were done at both baseline and follow-up, detrusor pressure at maximum urinary flow improved from 64 cmH_2O at baseline to 39 cmH_2O at 6 month follow-up ($p<0.01$). The bladder outlet obstruction index decreased from 48 at baseline to 13 at 6 month follow-up ($p<0.01$).

Prostate volume
Mean prostate volume, measured by transrectal ultrasound, decreased from 53 ml at baseline to 35 ml at 6 month follow-up ($p<0.01$; n=16).

Prostate specific antigen (PSA)
Mean PSA showed no statistically significant change from 3.15 ng/ml at baseline to 2.56 ng/ml at 12 month follow-up (p=0.72; n=20).

Sexual function
No patient who was sexually active at baseline and at each study visit reported a reduction in ejaculatory or orgasmic function. In the 11 sexually active patients, measures of sexual function improved but the only statistically significant improvement was for intercourse satisfaction.

Reoperation
There were no reoperations.

Safety

There were no serious device-related adverse events.

No patients needed a transfusion or intravenous electrolyte treatment.

28.6% (6/21) of patients had at least 1 adverse event, including grade 1 complications (self-resolving dysuria and haematuria, and catheter reinsertion for retention) and grade 2 complications (medically treated urinary tract infections).

Adverse events occurring within 30 days of procedure

Adverse event	Number of events
Dysuria	1
Haematuria	1
Urinary retention	3
Urinary tract infection with 30-day treatment	1
Bladder spasm	1
Meatal stenosis	1

Abbreviations used: IPSS, International Prostate Symptom Score; PSA, prostate specific antigen; Q_{max}, maximum urinary flow rate

Study 4 Gilling P (2016)

Details

Study type	**Case series**
Country	New Zealand
Recruitment period	January 2013 to February 2014
Study population and number	**n=15** Men with moderate to severe lower urinary tract symptoms secondary to benign prostatic hyperplasia
Age	Mean 73 years (range 59 to 86)
Patient selection criteria	Men aged 50 to 80 years with moderate to severe lower urinary tract symptoms secondary to benign prostatic hyperplasia that have not responded adequately to standard medical therapy, International Prostate Symptom Score (IPSS) higher than 12, maximum urinary flow (Q_{max}) of 12 ml/s or less, Schaffer scale of 2 or higher, and a prostate size between 25 and 80 ml (as determined by transrectal ultrasound). Exclusion criteria included an active urinary tract infection, urinary retention or post-void residual urine volume (PVR) or more than 400 ml, abnormal renal function, elevated prostate specific antigen (PSA), history of current or suspected prostate or bladder cancer, neurogenic bladder or sphincter abnormalities, previous nonpharmacological prostate treatment, current therapy affecting prostate physiology or another medical condition that would pose an unacceptable patient risk.
Technique	Water jet ablation was done using 2 different versions of the Aquabeam system (PROCEPT BioRobotics, US). The first system was used in the first 7 patients and the second system was used in the final 8 patients. The second system had 3 modifications: integration of the transrectal ultrasound image directly into the system's console screen, addition of an integrated pump for active aspiration, and elimination of a laser for cautery. All procedures were done with the patient under general anaesthesia.
Follow-up	**6 months**
Conflict of interest/source of funding	The study was supported by Procept BioRobotics (US). The first author received payment for research costs and support for investigator meetings for this work from Procept BioRobotics.

Analysis

Follow-up issues: One patient withdrew from the study at 3 months; he was satisfied with the results at his last follow-up.

Study design issues: Small, prospective single-centre trial. Consecutive patients were invited to participate and 15 met the inclusion/exclusion criteria. The primary outcome for the study was safety, as measured by the reporting of adverse events. Secondary endpoints included catheterisation time, IPSS, IIEF, Incontinence Severity Index (ISI), Q_{max}, PVR, detrusor pressure at maximum flow and changes in prostatic volume as determined by transrectal ultrasound at 6 months.

Study population issues: Mean prostate size was 54 ml (range 27 to 85). 40% (6/15) of patients had a substantial median lobe.

Other issues: This study is the first to report the use of this procedure in man.

Key efficacy and safety findings

<table>
<tr><th>Efficacy</th><th>Safety</th></tr>
<tr><td>
Number of patients analysed: 15
All procedures were technically successful.
Mean procedure time=48.3 minutes (range 30 to 94)
Mean ablation time=8.2 minutes (range 2 to 22)
Mean time to catheter removal=1.4 days (range 1 to 7)
Mean time to hospital discharge=1.8 days (range 1 to 7)

Repeat treatment
One patient needed a repeat water jet ablation procedure within 90 days of the first procedure because of a conservative contour profile during the first procedure. There were no further clinical sequelae at the 6 month follow-up.

Functional outcomes (n=14); mean (standard deviation, range)
<table>
<tr><th>Variable</th><th>Baseline</th><th>1 month</th><th>3 months</th><th>6 months</th></tr>
<tr><td>IPSS</td><td>23.1 (4.9, 16 to 33)</td><td>11.8 (6.8, 3 to 27)
p=0.002</td><td>9.1 (5.7, 2 to 20)
p<0.001</td><td>8.6 (5.1, 2 to 20)
p<0.001</td></tr>
<tr><td>IPSS QoL score</td><td>5.0 (0.9, 4 to 6)</td><td>2.6 (1.9, 0 to 6)
p<0.001</td><td>2.2 (1.9, 0 to 6)
p<0.001</td><td>2.5 (1.8, 0 to 6)
p<0.001</td></tr>
<tr><td>Q_{max}, ml/sec</td><td>8.6 (2.0, 4.8 to 12.1)</td><td>13.8 (6.1, 7.5 to 27.9)
p=0.027</td><td>15.5 (7.3, 6.5 to 31.1)
p=0.004</td><td>18.6 (7.9, 7.0 to 31.5)
p<0.001</td></tr>
<tr><td>PVR, ml</td><td>91 (77, 7 to 294)</td><td>38 (34, 0 to 120)
p=0.022</td><td>60 (63, 1 to 219)
p=0.190</td><td>30 (1.8, 6 to 65)
p=0.013</td></tr>
</table>
Detrusor pressure at maximum flow decreased from 66 cmH_2O at baseline to 45 cmH_2O ($p<0.05$).

Prostate specific antigen (PSA)
Serum PSA decreased from 3.2 to 2.6 ng/ml.

Prostate size
Mean prostate size (measured by transrectal ultrasound) at 6 months=36 ml, a 31% reduction in size from baseline ($p<0.001$).
</td><td>
At least 1 adverse event was reported in 53.3% (8/15) of patients.

30-day adverse events

Dysuria, n=3 (resolved spontaneously)
Haematuria, n=3 (no intervention needed)
Pelvic pain or discomfort, n=3
Need for recatheterisation, n=5 (all patients had subsequent successful trials of void)
Urgency/incontinence, n=0
Postoperative cardiac arrhythmia, n=1
Bladder spasm, n=1

There was no retrograde ejaculation or erectile dysfunction reported in any patient.
</td></tr>
<tr><td colspan="2">Abbreviations used: IPSS, International Prostate Symptom Score; PSA, prostate-specific antigen; PVR, post-void residual; Q_{max}, maximum urinary flow rate; QoL, quality of life</td></tr>
</table>

Study 5 Plante M (*in press)*

Details

Study type	**Randomised controlled trial (WATER)**
Country	Australia, New Zealand, UK, US (17 sites)
Recruitment period	2015 to 2016
Study population and number	**n=184 (116 water jet ablation, 65 transurethral resection of the prostate [TURP]; 3 patients withdrew before treatment)** Patients with moderate-to-severe lower urinary tract symptoms related to benign prostatic hyperplasia
Age	Mean 66 years
Patient selection criteria	Men aged 45 to 80 years, prostate size between 30 and 80 g, moderate-to-severe symptoms as indicated by International Prostate Symptom Score (IPSS) of 12 or higher, maximum urinary flow rate (Q_{max}) less than 15 ml/s. Exclusion criteria: history of prostate or bladder cancer, neurogenic bladder, bladder calculus or clinically significant bladder diverticulum, active infection, treatment for chronic prostatitis, diagnosis of urethral stricture, meatal stenosis or bladder neck contracture, damaged external urinary sphincter, stress urinary incontinence, post void residual greater than 300 ml or urinary retention, use of self-catheterisation, or prior prostate surgery. Men taking anticoagulants or on bladder anticholinergics or with severe cardiovascular disease were also excluded.
Technique	Water jet ablation was done using the Aquabeam system (PROCEPT BioRobotics, US). Haemostasis was achieved using either focal, non-resective electrocautery or low-pressure inflation of a Foley balloon catheter in the prostatic fossa.
Follow-up	**6 months**
Conflict of interest/source of funding	Not reported

Analysis

Follow-up issues: Three patients (1 water jet ablation and 2 TURP) voluntarily withdrew from the study before treatment, leaving 181 in the intent-to-treat population. 98% (178/181) of patients completed the 3-month follow-up and 97% (175/181) completed the 6-month follow-up.

Study design issues: Prospective, double-blind, multicentre randomised controlled trial. Randomisation was done through a web-based system and was stratified by study site and baseline IPSS score category with random block sizes. Baseline evaluation and study treatment were provided by an unblinded research team who did not reveal treatment assignment to the patient. A separate blinded team did the follow-up visits. All adverse events were adjudicated by an independent clinical events committee blinded to treatment assignment. Blinding was assessed at each visit and was deemed to be adequate throughout the study. The primary efficacy endpoint was the change in IPSS from baseline to 6 months. Non-inferiority was declared if the lower 95% confidence limit of the difference in score change at 6 months exceeded -4.7 points. The primary safety endpoint was the proportion of patients with adverse events rated by the clinical events committee as possibly, probably or definitely related to the study procedure classified as Clavien-Dindo Grade 2 or higher or any Grade 1 event resulting in persistent disability (ejaculatory or erectile dysfunction or incontinence). This article reported results from prespecified and post-hoc exploratory subgroup analysis from the original RCT. The prespecified subgroups were prostate size, age and baseline IPSS. The other subgroup analyses were exploratory.

Study population issues: Baseline characteristics were similar between the 2 groups. The mean prostate size was 53 ml.

Other issues: this is a subgroup analysis from the same RCT that is reported in study 1 of the overview (Gilling P et al, 2018).

Key efficacy and safety findings

Efficacy

Number of patients analysed: **181 (116 versus 65)**

Improvements in IPSS by subgroup

Prostate size

For men with larger prostates (>50 g), IPSS change scores were 4 points larger after water jet ablation compared with TURP (p=0.0197)

Men with larger prostates had better improvements after water jet ablation for both IPSS voiding and storage subscores.

Baseline IPSS

IPSS improvements were larger in both treatment groups for men with higher (≥20) versus lower (<20) baseline IPSS. In the group with baseline IPSS <20, slightly larger responses were seen after water jet ablation compared with TURP (p=0.0491).

Age

There were no statistically significant differences in IPSS improvements by treatment group with regard to age.

Exploratory analysis showed larger 6-month IPSS improvements in men with a middle lobe (p=0.005), men with severe middle lobe obstruction (p=0.0767), men with baseline maximum urinary flow rate <9 ml/second (p=0.0289), men without bladder obstruction at baseline (p=0.0321) and men with an elevated post-void residual (p=0.0058). Both voiding and storage score improvements were larger after water jet ablation compared to TURP within these subgroups.

Maximum urinary flow rates

There were no statistically significant differences in improvement in maximum urinary flow rates in the pre-planned subgroups across treatments. In patients with a middle lobe, maximum urinary flow rate improvement was 4.4 points larger in the water jet ablation group compared to TURP (p=0.0482).

Post void residual

In men with elevated post void residual at baseline, there were no statistically significant differences between the groups.

Prostate-specific antigen

There were no statistically significant differences across treatment arms within individual subgroup levels.

Safety

Primary safety endpoint by treatment and subgroups
(defined as Clavien-Dindo 2 or higher and persistent Clavien-Dindo 1 events)

	N with event (%)		
	Water jet ablation	**TURP**	**p value**
Baseline IPSS			
<20	6/36 (17%)	9/23 (39%)	0.0530
≥20	24/80 (30%)	18/42 (43%)	0.1118
Age, years			
<65	10/50 (20%)	11/27 (41%)	0.0578
≥65	20/66 (30%)	16/38 (42%)	0.1159
Prostate volume, ml			
<50	17/52 (33%)	11/30 (37%)	0.4481
≥50	13/64 (20%)	16/35 (46%)	0.0082

Anejaculation by treatment and subgroups

	N with event (%)		
	Water jet ablation	**TURP**	**p value**
Baseline IPSS			
<20	2/30 (7%)	7/16 (44%)	0.0049
≥20	6/48 (12%)	9/29 (31%)	0.0467
Age, years			
<65	3/37 (8%)	8/24 (33%)	0.0159
≥65	5/41 (12%)	8/21 (38%)	0.0224
Prostate volume, ml			
<50	7/34 (21%)	7/23 (30%)	0.2947
≥50	1/44 (2%)	9/22 (41%)	0.0001

Abbreviations used: IPSS, International Prostate Symptom Score; TURP, transurethral resection of the prostate.

Study 6 Kasivisvanathan V (2018)

Details

Study type	**Randomised controlled trial (WATER)**
Country	US (12 sites)
Recruitment period	2015 to 2016
Study population and number	**n=93 (61 water jet ablation, 32 transurethral resection of the prostate)** Patients with moderate-to-severe lower urinary tract symptoms related to benign prostatic hyperplasia
Age	Mean 65 years
Patient selection criteria	Men aged 45 to 80 years, prostate size between 30 and 80 g, moderate-to-severe symptoms as indicated by International Prostate Symptom Score (IPSS) of 12 or higher, maximum urinary flow rate (Qmax) less than 15 ml/s. Exclusion criteria: history of prostate or bladder cancer, neurogenic bladder, bladder calculus or clinically significant bladder diverticulum, active infection, treatment for chronic prostatitis, diagnosis of urethral stricture, meatal stenosis or bladder neck contracture, damaged external urinary sphincter, stress urinary incontinence, post void residual greater than 300 ml or urinary retention, use of self-catheterisation, or prior prostate surgery. Men taking anticoagulants or on bladder anticholinergics or with severe cardiovascular disease were also excluded. Only patients who were enrolled in the US were included in this analysis.
Technique	Water jet ablation was done using the Aquabeam system (PROCEPT BioRobotics, US). Haemostasis was achieved using either focal, non-resective electrocautery or low-pressure inflation of a Foley balloon catheter in the prostatic fossa. General anaesthesia was used in 96% of patients and spinal anaesthesia in 4%.
Follow-up	**1 year**
Conflict of interest/source of funding	The study was funded by PROCEPT Biorobotics.

Analysis

Follow-up issues: Three patients withdrew before treatment, leaving 90 patients in the intent to treat population. 97% (n=87) of patients completed 1 year follow-up.

Study design issues: Prospective, double-blind, multicentre randomised controlled trial (previously described). This study only included patients who were enrolled in the US sites of the trial. The primary efficacy was the change in IPSS from baseline to 1 year. The primary safety outcome was the proportion of patients with adverse events up to 1 year.

Study population issues: Mean prostate size was 53 ml and 88% (82/93) were sexually active. Baseline characteristics were similar between the 2 groups. This is a subgroup analysis from the same RCT that is reported in study 1 of the overview (Gilling P et al, 2018), including only patients who were enrolled in the US but at longer follow-up.

Key efficacy and safety findings

<table>
<tr><th>Efficacy</th><th>Safety</th></tr>
<tr><td>

Number of patients analysed: 87 (59 versus 28)

Decrease in IPSS from baseline at 1 year follow-up
- Water jet ablation=14.5 points
- TURP=13.8 points, p=0.7117

Improvement in IPSS quality of life score from baseline at 1 year follow-up
- Water jet ablation=-3.1 points
- TURP=-3.4 points, p=0.5760

Increase in maximum urinary flow rate from baseline at 1 year follow-up
- Water jet ablation=11 ml/second
- TURP=10 ml/second

Decrease in postvoid residual from baseline at 1 year follow-up
- Water jet ablation=54 ml
- TURP=39 ml

Reduction in prostate specific antigen level from baseline at 1 year follow-up
- Water jet ablation=-1.0 ng/ml
- TURP=-0.7 ng/ml

Reoperation
1 patient in each treatment group had surgical retreatment for benign prostatic hyperplasia within 1 year of the study procedure.

</td><td>

Complications

Safety outcomes at 1 year follow-up

	Water jet ablation	TURP	p value
Primary safety endpoint	20%	47%	0.0132
Persistent Clavien-Dindo (C-D) Grade I events	6.7%	30.0%	Not reported
C-D Grade 2 or higher	13.3%	30.0%	0.3038

Amongst sexually active patients, the rate of anejaculation was lower in those who had water jet ablation compared with transurethral resection of the prostate (9% versus 45% respectively, p=0.0006).

</td></tr>
<tr><td colspan="2">Abbreviations used: C-D, Clavien Dindo; IPSS, International Prostate Symptom Score</td></tr>
</table>

Study 7 Chughtai B (2018)

Details

Study type	**Pooled analysis from 2 trials (WATER and WATER II)**
Country	US
Recruitment period	2016 to 2017
Study population and number	**n=107** Men with lower urinary tract symptoms secondary to benign prostatic hyperplasia treated with water jet ablation
Age	Mean 67 years
Patient selection criteria	Men aged 45 to 80 years with lower urinary tract symptoms secondary to benign prostatic hyperplasia, baseline International Prostate Symptoms Score (IPSS) ≥12 and a maximum urinary flow rate <15 ml/second. For this pooled analysis, patients with 60 to 150 ml prostates were the target population and only patients who were treated at the US centres were included.
Technique	Water jet ablation was done using the Aquabeam system (PROCEPT BioRobotics, US). General anaesthesia or spinal anaesthesia was used.
Follow-up	**3 months**
Conflict of interest/source of funding	WATER and WATER II and article processing fees were funded by PROCEPT BioRobotics. The 2 authors declared no conflicts of interest.

Analysis

Follow-up issues: 97% (104/107) of patients completed the 3 month follow-up visit. Of the 3 missed visits, 1 patient withdrew consent, 1 missed the visit because they were on holiday and 1 patient was recovering from an adverse event.

Study design issues: Pooled analysis of patients treated by water jet ablation from a single-arm trial (WATER II) and a randomised controlled trial (WATER).

Study population issues: Mean prostate size was 99.4 ml (range 61 to 150) and mean IPSS at baseline was 23.4. A middle lobe was present in 77.6% of patients.

Key efficacy and safety findings

Efficacy	Safety
Number of patients analysed: **104** Mean water jet resection time=7±3.3 minutes Mean length of stay=1.6±1 days 62% of patients were discharged home with a catheter. **Improvement in IPSS at 3 months** The mean IPSS at baseline was 23.4±6.5 points and this improved to 6.7±4.9 points (p<0.0001). The baseline IPSS quality of life was 4.7±1 points and improved by 3±2 points. **Mean maximum urinary flow rate** • Baseline=8.9±3.1 ml/second • 3 month follow-up=19.6±12.4 ml/second **Mean post void residual** • Baseline=114.5±111.2 ml • 3 month follow-up=49.7±57.3 ml Mean prostate volume reduction based on transrectal ultrasound at 3 months = 38.3±24.2 ml	The Clavien-Dindo grade 2 or higher event rate at 3 months was 29%. Grade 2 events=18%, comprised primarily of haematuria or clot retention needing catheterisation, and urinary tract infections. Grade 3 or higher events=19%, comprised primarily haematuria or clot retention needing intervention and meatal stenosis needing intervention. 1 patient had a Clavien-Dindo grade 4b event: cerebrovascular accident the day after the procedure that evolved into multiorgan failure. The Grade 1 persistent events consisted of ejaculatory dysfunction (n=7), incontinence (n=3) and erectile dysfunction with incontinence (n=2). Transfusion rate before discharge=5.6% (mean 2.2 units per transfusion).
Abbreviations used: IPSS, International Prostate Symptom Score	

Study 8 Desai M (2018)

Details

Study type	**Prospective single arm trial (WATER II)**
Country	Canada and US
Recruitment period	September to December 2017
Study population and number	**n=101** Men with moderate to severe benign prostatic hyperplasia symptoms and prostate volume of 80 to 150 ml
Age	Mean 68 years
Patient selection criteria	Lower urinary tract symptoms attributable to benign prostatic hyperplasia in men aged 45 to 80 years with a prostate volume between 80 and 150 ml (as measured by transrectal ultrasound); baseline International Prostate Symptoms Score (IPSS) ≥12, maximum urinary flow rate <15 ml/second, serum creatinine <2 mg/dl, a history of inadequate or failed response to medical therapy and mental capability and willingness to participate in the study. Exclusion criteria included BMI ≥42 kg/m^2, history of prostate or bladder cancer, clinically significant bladder calculus or bladder diverticulum, active infection, previous urinary tract surgery, urinary catheter use daily for ≥90 days consecutively, chronic pelvic pain, diagnosis of urethral stricture, meatal stenosis or bladder neck contracture, use of anticholinergic agents specifically for bladder problems, and other general problems that could prevent adequate study follow-up.
Technique	Water jet ablation was done using the Aquabeam system (Procept Biorobotics, US). General (18%) or spinal (82%) anaesthesia was used. Haemostasis was achieved using tissue tamponade with a low-pressure Foley balloon catheter inflated with saline, either at the bladder neck or within the prostatic fossa, with adequate traction using transrectal ultrasound guidance. A 'catheter tensioning device' was developed for the trial and used to maintain and hold calibrated tension on the urinary catheter using the pubic area as support.
Follow-up	**1 month**
Conflict of interest/source of funding	The first author is a consultant for Procept BioRobotics, US and Auris Surgical.

Analysis

Follow-up issues: All patients completed the 1 month follow-up visit.

Study design issues: Prospective multicentre single-arm trial. The primary efficacy endpoint was the change in total IPSS at 3 months. The primary safety endpoint was the proportion of patients with adverse events, rated as possibly, probably or definitely related to the study procedure and classified as Clavien-Dindo grade 2 or higher or any grade 1 event resulting in persistent disability during the 3 months after treatment. The study's sample size was based on showing non-inferiority to an IPSS change of 16 points with a non-inferiority margin of 5 points, as well as showing that the primary safety endpoint rate was <65%. The planned sample size was 100 patients.

Study population issues: Mean prostate size was 107 ml (range 80 to 150). A middle lobe was present in 83% of patients, with a mean protrusion distance of 1.8 cm (range 0.7 to 6.8).

Key efficacy and safety findings

<table>
<tr><th>Efficacy</th><th>Safety</th></tr>
<tr><td>Number of patients analysed: 101

Mean procedure time=37 minutes (range 15 to 97)
Mean water jet resection time=7.8 minutes (range 3 to 15)
Mean time to catheter removal=4 days, 68% of patients were discharged home with a catheter.
Mean time to hospital discharge=1.6 days (range <1 to 6), 59% of patients were discharged within 1 day of the procedure.</td><td>Complications

112 adverse events were reported in 55 patients (54.5%) at 1 month follow-up.

Clavien-Dindo grade 2 or higher=29.7%

<table>
<tr><th>Complication</th><th>Events</th><th>Patients, n</th><th>Rate, %</th></tr>
<tr><td>Clavien-Dindo grade 1</td><td></td><td></td><td></td></tr>
<tr><td>Bleeding</td><td>6</td><td>6</td><td>5.9</td></tr>
<tr><td>Cardiac</td><td>1</td><td>1</td><td>1.0</td></tr>
<tr><td>Dysuria</td><td>8</td><td>8</td><td>7.9</td></tr>
<tr><td>Gastrointestinal symptoms</td><td>6</td><td>4</td><td>4.0</td></tr>
<tr><td>Meatal stenosis</td><td>1</td><td>1</td><td>1.0</td></tr>
<tr><td>Other</td><td>11</td><td>7</td><td>6.9</td></tr>
<tr><td>Pain</td><td>7</td><td>5</td><td>5.0</td></tr>
<tr><td>Scrotal oedema</td><td>3</td><td>3</td><td>3.0</td></tr>
<tr><td>Sexual</td><td>1</td><td>1</td><td>1.0</td></tr>
<tr><td>Urinary frequency</td><td>1</td><td>1</td><td>1.0</td></tr>
<tr><td>Urinary incontinence</td><td>7</td><td>7</td><td>6.9</td></tr>
<tr><td>Urinary retention</td><td>2</td><td>2</td><td>2.0</td></tr>
<tr><td>Urinary urgency</td><td>3</td><td>2</td><td>2.0</td></tr>
<tr><td>Total</td><td>57</td><td>31</td><td>30.7</td></tr>
<tr><td>Clavien-Dindo grade 2</td><td></td><td></td><td></td></tr>
<tr><td>Bleeding</td><td>8</td><td>6</td><td>5.9</td></tr>
<tr><td>Cardiac</td><td>1</td><td>1</td><td>1.0</td></tr>
<tr><td>Dysuria</td><td>1</td><td>1</td><td>1.0</td></tr>
<tr><td>Infection</td><td>2</td><td>2</td><td>2.0</td></tr>
<tr><td>Other</td><td>2</td><td>2</td><td>2.0</td></tr>
<tr><td>Pain</td><td>1</td><td>1</td><td>1.0</td></tr>
<tr><td>Urinary frequency</td><td>1</td><td>1</td><td>1.0</td></tr>
<tr><td>Urinary tract infection</td><td>4</td><td>4</td><td>4.0</td></tr>
<tr><td>Urinary urgency</td><td>1</td><td>1</td><td>1.0</td></tr>
<tr><td>Total</td><td>21</td><td>19</td><td>18.8</td></tr>
<tr><td>Clavien-Dindo grade 3</td><td></td><td></td><td></td></tr>
<tr><td>Bleeding</td><td>7</td><td>6</td><td>5.9</td></tr>
<tr><td>Dysuria</td><td>1</td><td>1</td><td>1.0</td></tr>
<tr><td>Meatal stenosis</td><td>2</td><td>2</td><td>2.0</td></tr>
<tr><td>Urethral stricture</td><td>1</td><td>1</td><td>1.0</td></tr>
<tr><td>Urinary incontinence</td><td>1</td><td>1</td><td>1.0</td></tr>
<tr><td>Total</td><td>12</td><td>11</td><td>10.9</td></tr>
<tr><td>Clavien-Dindo grade 4</td><td></td><td></td><td></td></tr>
<tr><td>Bleeding</td><td>2</td><td>2</td><td>2.0</td></tr>
<tr><td>Cardiac</td><td>2</td><td>2</td><td>2.0</td></tr>
<tr><td>Cerebrovascular accident</td><td>1</td><td>1</td><td>1.0</td></tr>
<tr><td>Multisystem organ failure</td><td>1</td><td>1</td><td>1.0</td></tr>
<tr><td>Total</td><td>6</td><td>5</td><td>5.0</td></tr>
</table>

There were 6 perioperative blood transfusions. In addition, 6 patients needed transfusion or cystoscopic fulguration for delayed bleeding.</td></tr>
</table>

Validity and generalisability of the studies

- The randomised controlled trial included some patients from the UK.
- The original device used for the procedure was modified and there are published results for both the first and second generation versions. Safety and efficacy outcomes may differ according to which system was used.
- These results include the first patients to be treated by the procedure.
- There is a lack of long term data.

Existing assessments of this procedure

There were no published assessments from other organisations identified at the time of the literature search.

Related NICE guidance

Below is a list of NICE guidance related to this procedure.

Interventional procedures

- Insertion of prostatic urethral lift implants to treat lower urinary tract symptoms secondary to benign prostatic hyperplasia. NICE interventional procedures guidance 475 (2014). Available from http://www.nice.org.uk/guidance/IPG475
- Prostate artery embolisation for benign prostatic hyperplasia. NICE interventional procedures guidance 453 (2013). 'This guidance is currently under review and is expected to be updated in 2018. For more information, see https://www.nice.org.uk/guidance/indevelopment/gid-ipg10055
- Laparoscopic prostatectomy for benign prostatic obstruction. NICE interventional procedures guidance 275 (2008) Available from https://www.nice.org.uk/guidance/IPG275
- Holmium laser prostatectomy. NICE interventional procedure guidance 17 (2003). Available from http://www.nice.org.uk/guidance/IPG17

- Transurethral electrovaporisation of the prostate. NICE interventional procedure guidance 14 (2003). Available from https://www.nice.org.uk/guidance/IPG14

Medical technologies

- GreenLight XPS for treating benign prostatic hyperplasia. NICE medical technologies guidance 29 (2016). Available from https://www.nice.org.uk/guidance/mtg29
- UroLift for treating lower urinary tract symptoms of benign prostatic hyperplasia. NICE medical technologies guidance 26 (2015). Available from https://www.nice.org.uk/guidance/mtg26

NICE guidelines

- Lower urinary tract symptoms in men: management. NICE clinical guideline 97 (2010; last updated: June 2015). Available from http://www.nice.org.uk/guidance/CG97

Additional information considered by IPAC

Specialist advisers' opinions

Specialist advice was sought from consultants who have been nominated or ratified by their Specialist Society or Royal College. The advice received is their individual opinion and is not intended to represent the view of the society. The advice provided by Specialist Advisers, in the form of the completed questionnaires, is normally published in full on the NICE website during public consultation, except in circumstances but not limited to, where comments are considered voluminous, or publication would be unlawful or inappropriate. Three Specialist Advisor Questionnaires for transurethral water jet ablation for lower urinary tract symptoms caused by benign prostatic hyperplasia were submitted and can be found on the NICE website.

Patient commentators' opinions

NICE's Public Involvement Programme sent 8 questionnaires to 1 NHS trusts for distribution to patients who had the procedure (or their carers). NICE received 5 completed questionnaires.

Company engagement

A structured information request was sent to 1 company who manufactures a potentially relevant device for use in this procedure. NICE received 1 completed submission. This was considered by the IP team and any relevant points have been taken into consideration when preparing this overview.

Issues for consideration by IPAC

Ongoing trials:

- Waterjet Ablation Therapy for Endoscopic Resection of Prostate Tissue (WATER); NCT02505919; RCT; US, Australia, New Zealand, UK; actual enrolment: 203 patients; actual start date: November 2015; estimated study completion date: February 2020. [Note: this is the same trial that is reported in study 1 of table 2]

- Waterjet Ablation Therapy for Endoscopic Resection of Prostate Tissue II (WATERII); NCT03123250; single group assignment; US, Canada; actual enrolment: 101 patients; actual start date: September 2017; estimated study completion date: January 2019.

References

1. Gilling P, Barber N, Bidair M et al. (2018) WATER: A Double-Blind, Randomized, Controlled Trial of Aquablation vs Transurethral Resection of the Prostate in Benign Prostatic Hyperplasia. Journal of Urology doi: 10.1016/j.juro.2017.12.065. [Epub ahead of print]
2. Desai MM, Singh A, Abhishek S et al. (2018) Aquablation therapy for symptomatic benign prostatic hyperplasia: a single-centre experience in 47 patients. BJU International doi:10.1111/bju.14126
3. Gilling P, Anderson P, Tan A (2017) Aquablation of the prostate for symptomatic benign prostatic hyperplasia: 1-year results. Journal of Urology 197: 1565–72
4. Gilling P, Reuther R, Kahokehr A et al. (2016) Aquablation – image-guided robot-assisted waterjet ablation of the prostate: initial clinical experience. BJU International 117: 923–29
5. Plante M et al. (2018) Symptom Relief and Anejaculation after Aquablation or TURP: Subgroup Analysis from a Blinded Randomized Trial. BJU International doi: 10.1111/bju.14426. [Epub ahead of print]
6. Kasivisvanathan v, Hussain M on behalf of the U.S. WATER investigators (2018) Aquablation versus transurethral resection of the prostate: 1 year United States – cohort outcomes. Can J Urol 25
7. Chughtai B, Thomas D (2018) Pooled Aquablation Results for American Men with Lower Urinary Tract Symptoms due to Benign Prostatic Hyperplasia in Large Prostates (60–150 cc). Advances in Therapy https://doi.org/10.1007/s12325-018-0722-0
8. Desai M, Bidair M, Bhojani N et al. (2018) WATER II (80–150 mL) procedural outcomes. BJU International doi: 10.1111/bju.14360

Additional relevant papers

The following table outlines the studies that are considered potentially relevant to the IP overview but were not included in the main data extraction table (table 2). It is by no means an exhaustive list of potentially relevant studies.

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Aljuri N, Gilling P, Roehrborn C (2017) How I do it: Balloon tamponade of prostatic fossa following Aquablation. The Canadian journal of urology 24: 8937–40	Case report n=1	Study reports the use of a balloon catheter to achieve haemostasis.	Case report.
MacRae C, Gilling P (2016) How I do it: Aquablation of the prostate using the AQUABEAM system. Canadian Journal of Urology 23: 8590–3	Review	Aquablation is a new method of prostate ablation showing functional improvement that compares to other benign prostatic hyperplasia technologies. The safety profile of the procedure is also favourable, with no grade III-V adverse events. Longer term data with larger patient numbers are needed, but this technique shows promise to improve lower urinary tract symptoms with the potential for less morbidity than traditional transurethral resection of the prostate.	All included published studies are in table 2.
Nair SM, Pimentel MA, Gilling PJ (2015) Evolving and investigational therapies for benign prostatic hyperplasia. Canadian Journal of Urology 22 (Suppl 1): 82–7	Systematic review	Aquablation shows promise in phase II studies with few side effects and is a relatively an automated procedure, albeit requiring general anaesthesia.	Cited studies are included in table 2.
Pimental MA, Yassaie O, Gilling PJ (2018) The Aquabeam system: a review. Current bladder dysfunction reports. https://doi.org/10.1007/s11884-018-0455-6	Review	Aquablation is not only a technically feasible and safe procedure for symptomatic male bladder outlet obstruction, but has equivalent efficacy to transurethral resection of the prostate with a better safety profile. Ongoing trials are taking place to confirm aquablation's role in the spectrum of minimally invasive treatments for male lower urinary tract symptoms.	All included published studies are in table 2.
Pimentel MA, Nair SM, Gilling PJ (2016) Aquablation™: Early Clinical Results. Current Bladder Dysfunction Reports 11: 130–33	Review	Early phase I and phase II clinical trials show aquablation has a promising safety profile and clinical efficacy. There have been no significant complications in human clinical trials, including urinary	All included published studies are in table 2.

		incontinence and sexual function-related adverse events. A larger multi-centre randomised controlled trial is currently underway to validate these early findings.	
Taktak S, Jones P, Haq A et al. (2018) Aquablation: a novel and minimally invasive surgery for benign prostate enlargement. Therapeutic Advances in Urology 10: 183–8	Review	Early results show this to be a promising surgical strategy with a strong morbidity profile and reduced resection time.	Review without a meta-analysis. All included published studies are in table 2.
Yassaie O, Silverman JA, Gilling PJ (2017) Aquablation of the Prostate for Symptomatic Benign Prostatic Hyperplasia: Early Results. Current Urology Reports 18: 91	Review	Due to the precise prostate mapping, aquablation has also demonstrated favourable sexual and urinary outcomes with no new erectile dysfunction, retrograde ejaculation, or urinary incontinence as often experienced with other techniques. These improvements in functional outcomes at 12 months confirm that aquablation is a safe and effective alternative for BPH treatment.	All included published studies are in table 2.

Literature search strategy

Databases	Date searched	Version/files
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	30/05/2018	Issue 5 of 12, May 2018
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	30/05/2018	Issue 4 of 12, April 2018
HTA database (Cochrane Library)	30/05/2018	Issue 4 of 4, October 2016
MEDLINE (Ovid)	30/05/2018	1946 to Present with Daily Update
MEDLINE In-Process (Ovid) & MEDLINE Epubs ahead of print (Ovid)	30/05/2018	May 29, 2018
EMBASE (Ovid)	30/05/2018	1974 to 2018 Week 22

Trial sources searched

- Clinicaltrials.gov
- ISRCTN
- WHO International Clinical Trials Registry

Websites searched

- National Institute for Health and Care Excellence (NICE)
- NHS England
- Food and Drug Administration (FDA) - MAUDE database
- Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP – S)
- Australia and New Zealand Horizon Scanning Network (ANZHSN)
- EuroScan
- General internet search

The following search strategy was used to identify papers in MEDLINE. A similar strategy was used to identify papers in other databases.

1	Prostatic Hyperplasia/
2	(prostat* adj4 (hyperplasia* or enlarge* or hypertroph* or obstruct*)).tw.
3	(BPH or BPO or BPE).tw.
4	((Adenofibromatous* or Adenofibromyomatous* or adenoma* or glandular* or stromal*) adj4 (hyperplasia* or enlarge* or hypertroph* or obstruct*)).tw.

5	Lower Urinary Tract Symptoms/
6	(low* adj4 urin* adj4 tract* adj4 symptom*).tw.
7	LUTS.tw.
8	Urinary Bladder Neck Obstruction/
9	(bladder adj4 (outflow* or outlet* or neck*) adj4 obstruct*).tw.
10	BOO.tw.
11	Prostatism/ /
12	Prostatism*.tw.
13	or/1-12
14	Ablation Techniques/
15	Robotic Surgical Procedures/
16	aquablat*.tw.
17	((water* or aqua* or saline) adj4 (jet* or ablat* or stream* or therap* or treat* or resection* or pressur* or high velocity)).tw.
18	(waterjet* adj4 (ablat* or stream* or therap* or treat* or resection* or pressur* or high velocity)).tw.
19	or/14-18
20	13 and 19
21	aquabeam*.tw.
22	20 or 21
23	Animals/ not Humans/
24	22 not 23