NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of transurethral water vapour 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, heated water vapour is injected into the prostate using a special probe that is passed up the urethra. The heat from the vapour destroys some of the prostate tissue, reducing its size.

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 November 2017.

Procedure name

- Transurethral water vapour 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

Lower urinary tract symptoms caused by benign prostatic hyperplasia commonly affect men over 50. Stromal and epithelial cells increase in number, causing the prostate to increase in size. It often occurs in the periurethral region of the prostate, with large discrete nodules compressing the urethra. Symptoms include hesitancy during micturition, 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, then surgical options include transurethral resection of the prostate (TURP), transurethral vaporisation, holmium laser enucleation , prostatic artery embolisation or prostatectomy (see the NICE guideline on lower urinary tract symptoms in men). Insertion of prostatic urethral lift implants has been introduced more recently as an alternative treatment for lower urinary tract symptoms caused by benign prostatic hyperplasia. Potential complications of surgical procedures include bleeding, infection, urethral strictures, incontinence and sexual dysfunction.

What the procedure involves

Transurethral water vapour ablation is usually done as day case surgery using local anaesthetic, and sometimes sedation.

A device similar to a rigid cystoscope is advanced into the prostatic urethra. Under direct visualisation, a retractable needle is inserted into the prostate and water vapour (at a temperature of about 103 degrees centigrade) is delivered for 8 to 10 seconds. At the same time, saline irrigation is used to cool and protect the surface of the urethra. Conductive heat transfer disrupts cell membranes in the prostate, leading to rapid cell death and necrosis. The needle is retracted and repositioned several times so that thermoablation can be repeated in different areas of the gland, including the median lobe. The aim is to reduce the size of the prostate, leading to improvement in lower urinary tract symptoms 1 to 3 months after treatment, without impairing sexual function.

Patients may have to take antibiotics and have a urinary catheter for some days after the procedure. Some activities, including sexual intercourse, should be avoided for up to 1 month.

Outcome measures

International Prostate Symptom Score (IPSS)

The IPSS is a validated questionnaire often used to assess symptoms of benign prostatic hyperplasia (BPH). It is also referred to as the American Urological Association BPH Symptom Score Index. It includes questions on 7 dimensions: feeling of incomplete bladder emptying, frequency, intermittency, urgency, weak stream, straining and nocturia (referring to the previous month) and each involving assignment of a score from 1 to 5. 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 (IIEF)

The IIEF is a validated 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).

Benign prostatic hyperplasia impact index (BPHII)

The BPHII is a validated self-administered questionnaire used to assess the impact on quality of life caused by urinary symptoms in men with BPH. It is formed of 4 questions about urinary problems during the past month regarding physical discomfort, worry about health, how bothersome symptoms are, and whether the symptoms are interfering with usual activities. Scores range from 0 (no symptoms) to 13 (severe symptoms).

Overactive bladder (OAB) symptom score

The OAB symptom score uses a self-reported questionnaire to quantify OAB symptoms: daytime frequency, night-time frequency, urgency and urgency incontinence. Patients are asked to rate their symptom severity on a Likert scale with the maximum (worst) scores of 2, 3, 5, and 5. The overall score is a sum of all individual questions scores and ranges from 0 to 15. A more severe OAB is indicated by a higher score. The scoring system is designed to place more weight on urgency and urgency incontinence than on frequency.

Overactive Bladder Questionnaire Short Form (OAB-q SF)

The OAB-q SF is a self-administered patient-reported outcomes tool with 2 scales assessing symptom ‘bother’ and health-related quality of life (HRQL) in patients with OAB. The instrument consists of 19 items with 6 items assessing symptom bother (unique dimension) and 13 items assessing health-related quality of life (coping, concern, sleep and social interaction). The subscales are summed and transformed into scores ranging from 0 to 100. The symptom-bother and the HRQL scales are inversely related: a high symptom-bother score indicates greater symptom severity and a high HRQL scale score indicates better quality of life.

Male Sexual Health Questionnaire for Ejaculatory Dysfunction (MSHQ-EjD)

The MSHQ is a validated questionnaire used to assess the degree of ejaculatory dysfunction in men. Its long form includes 3 domains: erection scale (3 items), ejaculation scale (7 items) and sexual satisfaction scale (6 items). There are 9 additional items (2 items measuring bothersome symptoms linked to erection and

ejaculation, and 7 items measuring sexual activity and desire). The MSHQ short form (MSHQ-EjD-SF) includes 2 domains: ejaculatory function (3 items) and bother/satisfaction (1 item).

International Continence Society male incontinence score - short form (ICSMIS-SF)

The ICSMIC-SF is a validated, self-administered questionnaire used to assess the impact of urinary incontinence on quality of life. The instrument is composed of 11 items, 5 assessing voiding and 6 assessing incontinence. The total score is obtained from the simple sum of each question's individual score. Higher scores represent worse quality of life.

Uroflowmetry:

Uroflowmetry is used to measure the maximum urinary flow rate (Qmax) and voided volume. Flow-rate measurements may be inaccurate if the voided volume is less than 150 millilitres (mL). Qmax values below the threshold of 15 mL/second suggest bladder outlet obstruction.

Efficacy summary

International prostate symptom score (IPSS)

In a randomised control trial (RCT) and case series of 197 men with benign prostatic hyperplasia (BPH), mean IPSS was statistically significantly lower in patients who had water vapour ablation (WVA, 10.8±6.5) compared with the sham group (17.5±7.6, $p<0.0001$) at 3-month follow-up. In the same study, people having sham were invited to crossover to the treatment group and paired outcomes were compared at 3-month follow-up, then patients were followed up for 1 year. Mean IPSS scores were statistically significantly lower in the crossover group after WVA (9.8±6) compared with the paired sham (18±7.6, $p=0.0004$) at 3-month follow-up, and mean IPSS scores were still statistically significantly reduced from baseline assessment (8.6±6.6, $p<0.0001$) at 1-year follow-up. In the same study, 136 men who had WVA were followed-up for 3 years. Mean preoperative IPSS statistically significantly reduced from baseline to 1-year follow-up (10.3±6.7, $p<0.0001$), which was maintained at 3-year follow-up (10.4±6.1, $p<0.0001$)[1-4].

In a case series of 131 men who had WVA, mean IPSS statistically significantly reduced from baseline to 3 to 6 month follow-up (9.8±6.9, $p<0.0001$) and the improvement was sustained at 12-month follow-up (10.1±7.2, $p<0.0001$)[5].

In a case series of 65 patients who had WVA, mean IPSS statistically significantly reduced from baseline to 1-month follow-up (14.8±8.4, p<0.001) and at 2-year follow-up (9.6±6.5, p<0.001)[6-8].

Benign prostatic hyperplasia impact index (BPHII)

In the RCT and case series of 197 men, mean BPHII was statistically significantly lower in patients who had WVA (2.9±2.9) compared with sham (4.7±3.5, p=0.0003) at 3-month follow-up. In the same study, patients crossing over to the WVA group had statistically significantly lower mean BPHII scores (2.6±2.6) compared with the 3-month follow-up after sham (4.9±3.5, p=0.024) and this remained statistically significantly lower at 1-year follow-up (1.6±2.3, p<0.0001). In the same study, mean BPHII scores statistically significantly improved from baseline to 1-year follow-up (2.3±3, p<0.0001) in patients who had WVA, and this was maintained (2.4±2.9, p<0.0001) at 3-year follow-up[1-4].

In the case series of 65 patients who had WVA, mean BPHII scores statistically significantly improved from baseline to 1-month follow-up (5.5±3.6, p=0.034) and this was maintained at 2-year follow-up (2.3±2.5, p<0.001)[6-8].

Maximum urinary flow (Qmax)

In the RCT and case series of 197 men, mean maximum urinary flow was statistically significantly higher in patients who had WVA (16.1±7.3 mL/second) compared with sham (10.8±4.0 mL/second, p<0.0001) at 3-month follow-up. In the same study, patients crossing over to the WVA group had statistically significantly higher maximum urinary flow (mean 16.4±7.1 mL/second) compared with the previous 3-month follow-up after sham (10.4±3.8 mL/second, p<0.0001), and maximum urinary flow was still statistically significantly increased from baseline assessment (mean 16.2±7.9, p<0.0001) at 1-year follow-up. In the sane study, mean maximum urinary flow statistically significantly improved from baseline to1-year follow-up in patients who had WVA (15.5±6.7, p<0.0001) and this increase was maintained (13.2±4.8, p<0.0001) at 3-year follow-up[1-4].

In the case series of 131 patients, mean maximum urinary flow statistically significantly increased from baseline to 3 to 6 month follow-up (11.6±7.7 mL/second, p=0.04) but the improvement was not maintained at 12-month follow-up (10±5 mL/second, p=0.4)[5].

In the case series of 65 patients who had WVA, mean maximum urinary flow statistically significantly improved from baseline to 1-month follow-up (9.9±3.9 mL/second, p<0.001) and this was maintained at 2-year follow-up (12±6.2, p<0.001)[6-8].

Post-void residual urine volume (PVR)

In the RCT and case series of 197 men, mean PVR was not statistically significantly different in patients who had WVA (71.8±72.2 mL) compared with sham (92.7±77.8 mL, p=0.108) at 3-month follow-up. In the same study, mean PVR was not statistically significantly different from baseline values in patients crossing over to the WVA group (-17%, 83.8±80.5, p=0.6), at 1-year follow-up. In the same study, mean PVR values were statistically significantly reduced in patients who had WVA (55.1±61.9 mL, p=0.0004) at 3-year follow-up[1-4].

In the case series of 131 patients, mean PVR statistically significantly reduced from baseline to 3 to 6 month follow-up (85.8±167.3 mL, p<0.0001) and the improvement was maintained at 12-month follow-up (77.3±122.1 mL, p<0.0001)[5].

In the case series of 65 patients who had WVA, mean PVR statistically significantly improved from baseline to 1-month follow-up (67.1±64.4 mL, p=0.037) but the difference was no longer statistically significant at 6-month follow-up (-25%, -21.4±88.3, p=0.071) or 2-year follow-up (62.8±83.9 mL, p=0.307)[6-8].

Quality of life

In the RCT and case series of 197 men, quality of life (QOL) assessed by the IPSS-QOL question was statistically significantly better in patients who had WVA (mean 2.3±1.5) compared with sham (mean 3.5±1.5, p<0.0001) at 3-month follow-up. In the same study, patients crossing over to the WVA group had statistically significantly better mean IPSS-QOL scores (1.9±1.4) compared with the previous 3-month follow-up after sham (3.7±1.5, p=0.0024). In the RCT and case series of 197 men, mean IPSS-QOL scores were statistically significantly reduced from baseline to 1-year follow-up 1 in patients who had WVA (2.1±1.5, p<0.0001) and this reduction was maintained (2.1±2.3, p<0.0001) at 3-year follow-up[1-4].

In the case series of 131 patients, mean IPSS-QOL scores statistically significantly reduced from baseline to 3-month follow-up (2.3±1.5, p<0.0001) and the improvement was maintained at 1-year follow-up (2.5±1.4, p<0.0001)[5].

In the case series of 65 patients who had WVA, mean IPSS-QOL scores statistically significantly improved from baseline to 1-month follow-up (2.9±1.8, p<0.001) and this was maintained at 2-year follow-up (1.8±1.4, p<0.001)[6-8].

Overactive bladder (OAB) symptoms

In the RCT and case series of 197 men, mean OAB symptom scores were statistically significantly better in patients who had WVA (24.9±18) compared with sham (31.9±20.7, p=0.022) at 3-month follow-up. In the same study, mean OAB health related quality of life (HRQL) scores were statistically significantly better in patients who had WVA (82±17.5) compared with sham (74.9±19.3, p=0.001) at

3-month follow-up. Similarly, men in the sham group crossing over to have WVA had a statistically significantly improved mean OAB-HRQL score (89.1±12.6, p<0.00001) and OAB symptom score (15.2±12.4, p<0.00001) at 1-year follow-up. In the same study, mean OAB-HRQL scores statistically significantly improved from baseline to year-1 follow-up in patients who had WVA (83.7±18.2, p<0.0001) and this increase was maintained (84.6±15.4, p<0.0001) at 3-year follow-up. Similarly, mean OAB symptom scores statistically significantly reduced from baseline to year-1 follow-up in patients who had WVA (20.6±18.4, p<0.0001) and this was maintained (21.6±16.2, p<0.0001) at 3-year follow-up[1-4].

Erectile function

In the RCT and case series of 197 men, erectile function (EF) assessed using the erectile function-specific question of the international index of erectile function (IIEF-15) was not statistically significantly different in patients who had WVA (22.7±8.4) compared with sham (mean 21.0±9.1, p=0.795) at 3-month follow-up. Overall, there was no statistically significantly difference in mean IIEF scores between patients who had WVA compared with sham at 3-month follow-up. In the same study, patients crossing over to the WVA group did not have statistically significantly better IIFE scores (mean 16.6±11.3) compared with the previous 3-month follow-up after sham (17±10.5, p=0.597), but the improvement became statistically significant at 1-year follow-up (18.8±10, p=0.018). In the same study, minimal clinically important improvement in EF (defined as minimal IIEF-EF score increase of 2 points for men with mild erectile dysfunction, 5 for moderate erectile dysfunction and 7 for patients with severe erectile dysfunction) assessed by the IIEF questionnaires (EF question) were reported by 32 % (29/90) of sexually active men at 3-month follow-up and by 27% (21/77) of sexually active men at 12-month follow-up. The mean IIEF-EF question scores were not statistically significantly different from baseline values in patients who had WVA throughout follow-up of 3 years (p=0.112)[1-4].

In the case series of 131 men, no sexual function data were collected using validated questionnaires but all patients were asked about sexual function. There was no de novo erectile or ejaculatory dysfunction[5].

In the case series of 65 patients who had WVA, mean IIEF-15 scores were statistically significantly worse than baseline values at 1-month follow-up (10.3±11.6, p=0.0019) but the difference lost statistical significance at 3-month follow-up (14.5±11.9, p=0.201), 6 months (15.4±12, p=0.102) and 12 months (14.1±11.8, p=0.210). At 2-year follow-up, mean IIEF-15 score was statistically significantly improved from baseline (15.5±11.5, p=0.006)[6-8].

Ejaculatory function

In the RCT and case series of 197 men, there was no statistically significantly difference in the male sexual health questionnaire for ejaculatory function scores (MSHQ-EjD) for men who had WVA (mean 9.7±4.5) compared with sham (mean 9.6±4.3, p=0.443), or in MSHQ-EjQ bother scores in men who had WVA (mean 1.8±1.7) compared with sham (mean 1.8±1.8, p=0.623) at 3-month follow-up. Similarly, at 3-month follow-up, MSHQ-EjD function (mean 8.9±5.2, p=0.283) and bother (mean 1.7±1.7, p=0.678) scores were not statistically significantly improved after WVA, compared with the 3-month follow-up after sham. Mean MSHQ-EjQ function scores (9.1±4.6, p=0.484) and mean MSHQ-EjQ bother scores (2.1±1.9, p=0.297) were also not statistically significantly improved in the crossover group at 1-year follow-up. In the same study, mean MSHQ-EjD function scores statistically significantly reduced from baseline to 3-year follow-up in patients who had WVA (8.5±4.5, p=0.003). Mean MSHQ-EjD bother scores also statistically significantly reduced from preoperative values to 1-year follow-up (1.5±1.5, p=0.0015) and the reduction was maintained (1.6±1.5, p=0.006) at 3-year follow-up[1-4].

In the case series of 65 patients who had WVA, ejaculatory function assessed by IIEF-15 question-9 mean scores was not statistically significantly improved from baseline to 1-month follow-up (1.8±2.3, p=0.151) and at 2-year follow-up (2.7±2.2, p=0.095). Similarly, mean MSHQ-EjD function scores did not statistically significantly improve from baseline values at any point during follow-up. The MSHQ-EjD bother score did not statistically significantly improve for most of the follow-up period but had statistically significantly improved at the 2-year follow-up (0.8±2.5, p=0.035)[6-8].

Incontinence

In the RCT and case series of 197 men, the impact of incontinence on quality of life assessed by the short-form International Continence Society male incontinence score (ICSMIS-SF) statistically significantly reduced from baseline to 1-year follow-up in patients who had WVA (3±2.8, p<0.0001) and this was maintained (3±2.6, p<0.0001) at 3-year follow-up. In the same study, mean ICSMIS-SF scores statistically significantly reduced from baseline to 1-year follow-up in patients who crossed over to the WVA group (3.2±2.6, p=0.018) and this reduction (mean 2.6±1.8, p<0.0001) was maintained at 1-year follow-up[1-4].

Prostate volume

In the case series of 65 men who had WVA, mean prostate volumes reduced by 14% (-8.5 cm^3) at 1-month follow-up, by 23% (-14.2 cm^3) at 3 months and by 29% (-17.7 cm^3) at 6-month follow-up, p value not reported[6-8].

Reoperation

In the RCT and case series of 197 men who had WVA, reoperation rate was 4% (6/135) at 3-year follow-up[1-4].

In the case series of 131 patients who had WVA, reoperation rate was 2% (3/131) at 12-month follow-up[5].

Safety summary

Damage to other tissue

Ablation outside the prostate happened in 1 patient in the case series of 65 patients. Follow-up at 1, 3 and 6 months showed complete resolution of the extraprostatic ablation without negative sequelae[6-8].

Bleeding

Haematospermia was reported by 7% (10/136) and haematuria by 13% (17/136) of men in the RCT and case series of 197 patients[1-4].

Haematuria was reported by 14% (9/65) of patients in the case series of 65 patients[6-8].

Infection

Suspected urinary tract infection was reported by 4% (5/136) of men, urinary tract infection (proven with culture) in 3% (4/136) and epididymitis in 3% (4/136) of men who had WVA in the RCT and case series of 197 patients[1-4].

Suspected urinary tract infections was reported by 20% (13/65) of patients and fever by 5% (3/65) of patients in the case series of 65 patients. Urethral secretion (without haematuria or stones) was reported by 5% (5/65) of patients and terminal dribbling was reported by 3% (2/65) of patients in the same study[-8].

Pain

Dysuria was reported by 17% (23/136) of patients and pelvic pain or discomfort by 3% (4/136) after WVA in the RCT and case series of 197 patients[1-4].

Pain or discomfort was reported by 11% (7/65) of patients and dysuria was reported by 22% (14/65) of patients in the case series of 65 patients. Scrotal pain or discomfort was reported by 3% (2/65) of patients in the same study[6-8].

Urinary retention

De novo urinary retention was reported by 1 patient in the RCT and case series of 197 men[1-4]. Acute urinary retention was reported by 4% (5/136) of men in the same study[1-4].

Acute urinary retention happened in 11% (14/131) of patients in the case series of 131 patients who had WVA[5].

Incontinence

Urinary incontinence was reported by 1 patient in the case series of 65 patients[6-8].

Other urinary problems

Urinary frequency was reported by 7% (9/136) of patients and urinary urgency by 6% (8/136) in the RCT and case series of 197 patients[1-4].

Urinary frequency, urgency, frequency and urgency, haematuria and nocturia were reported by less than 4% (5/131) of patients in the case series of 131 patients (frequencies not reported by adverse event)[5].

Nocturia was reported by 8% (5/65), urinary urgency by 20% (13/65), urinary frequency by 6% (4/65) and poor stream by 14% (9/65) of patients in the case series of 65 patients[6-8].

Vesical catheterisation

Catheterisation before discharge from hospital was needed in 55% (36/65) of patients because of precautionary catheter use (15 patients), inadequate voiding (14), haematuria (6), or dysuria (1), events that are often associated with rigid cystoscopy, in the case series of 65 patients. The median duration of catheter use was 4.1 days. An additional 11 patients (17%) needed catheterisation after discharge for a median of 3.8 days because of urinary retention or for travel convenience[6-8].

Nausea and vomiting

Nausea or vomiting requiring hospitalisation was reported by 1 patient each in the RCT and case series of 197 men who had WVA[1-4].

Ejaculatory problems

Decreased ejaculatory volume was reported by 3% (4/136) of men and anejaculation by 3% (4/136) of men who had WVA in the RCT and case series of 197 patients[1-4].

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 no anecdotal adverse events. They considered that the following were theoretical adverse events: urethral stricture, potential for thermal damage to the bladder urethra and rectum and difficulty in controlling bleeding.

The evidence assessed

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to transurethral water vapour ablation for lower urinary tract symptoms caused by benign prostatic hyperplasia. The following databases were searched, covering the period from their start to 7th November 2017: 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 benign prostatic hyperplasia.
Intervention/test	Transurethral water vapour 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 393 patients from 1 randomised control study and case series[1-4] and 2 case series[5-8].

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 vapour ablation for lower urinary tract symptoms caused by benign prostatic hyperplasia

Study 1, 2, 3 and 4 McVary KT (2016a, 2016b, 2017) and Roehrborn (2017)

Details

Study type	**RCT**
Country	US
Recruitment period	2013 to 2014
Study population and number	**n=197** (136 RFTT, 61 sham) men with BPH related moderate to severe LUTS. A total of 188 patients had RFTT in the randomised and crossover studies.
Age and sex	**RFTT**: 63±7.1 years, all males **Sham**: 62.9±7.0 years, all males
Patient selection criteria	Inclusion criteria: Men with moderate to severe symptomatic BPH, age>50 years, IPSS≥13, prostate volume of 30 to 80 cc, maximum urinary flow rate of ≤15 mL/s, PVR<250 ml, Exclusion criteria • Prostate specific antigen level higher than 2.5 ng/mL with free prostate-specific antigen less than 25% (unless biopsy result was negative) • Active urinary tract infections or 2 separate infections within 6 months. A more comprehensive list of exclusion criteria is available from https://clinicaltrials.gov/ct2/show/study/NCT01912339?sect=X4301256 Men with median lobe were not excluded and could be treated at the discretion of the physician investigator.
Technique	All subjects were washed out of α-blockers, anticholinergics, daily doses of phosphodiesterase-5 inhibitors (4 weeks), oestrogen, androgen-suppressing drugs, anabolic steroids, type II 5α-reductase inhibitors. Daily drug use of any medication for LUTS or ED was prohibited for the duration of the study. All patients had uroflowmetry and questionnaires applied after washout period and within 1 week of treatment. These were repeated at follow-up visits. Each 0.5ml radiofrequency water vapour injection is convectively delivered and dispersed circumferentially to create a 1.5 to 2 cm lesion and remains confined to the prostate zones. The control procedure closely replicated the experience of RFTT and the surgical barrier prevented subject visualisation of treating physician and device. All RFTT were done in office-based or ambulatory surgery settings, receiving only oral analgesia.
Follow-up	**3 years**
Conflict of interest/source of funding	The authors declared that this was a study sponsored by NxThera Inc, manufacturer of the Rezūm device. NxThera were given the opportunity of reviewing the manuscript

Analysis

Follow-up issues: Comparative outcomes for RFTT and control group were documented after 3-month follow-up when treatment assignment for all subjects was unblinded. Subjects in the treatment arm were re-evaluated at 6, 12, 24 and 36 months. Total expected follow-up is 5 years for the crossover subjects. Currently, data is available for the 3-year follow-up period.

A total of 72% (97/135) patients who had RFTT were available for the 3-year follow-up. Of the 38 patients excluded from the analysis, 14 were lost to follow-up, 7 withdrew consent (1 with a cancer diagnosis), 5 were censored for the use of BPH medications and 4 were censored for the use of testosterone at the time of follow-up, 2 missed a clinic visit and 6 had a secondary treatment for LUTS.

Study design issues: Prospective, multicentre (15 centres in the US), double-blinded RCT. Randomisation (2:1) was done with electronical programming before treatment using permuted blocks of random sizes. Treating physicians were not blinded. Double blinding was maintained until month 3 follow-up for patients and personnel administering the questionnaires. Qualified control subjects had the option to crossover to receive thermal therapy or no treatment. Of the 61 control subjects 87% (53/61) met IPSS and Qmax criteria and were elected for crossover active treatment.

Effectiveness of RFTT was assessed with the IPSS, quality of life, Qmax and BPH impact index; sexual function was evaluated with the IIEF-15 and MSHQ-EjD questionnaires. These were compared with controls at 3-month and to baseline at 1 to 3-year follow-up. The primary end-point analysis per ITT in the RCT included all subjects at the 3-month evaluation including 2 men randomised to the

treatment group who did not receive the treatment or initiate alternate therapy before 3 months. Subjects who reported no sexual intercourse were excluded from the analysis of sexual function.

Study population issues: Baseline characteristic were similar between comparators. Approximately 75% of treatment and control groups had severe LUTS (IPSS≥19), 25% had moderate LUTS (IPSS≤18). At baseline, in the RFTT group 52% of men had ED, 26% had absence of ejaculation and 32% were not sexually active. In the control group 54% had ED, 18% had absence of ejaculation and 33% were not sexually active (no statistically significantly differences between groups).

About 52% in the treatment group and 54% in the controls had erectile dysfunction. The median lobe was identified in 37% (70/188) men and treated in 31% (58/188).

A mean of 4.7±1.7 treatments was delivered to the prostate zones. A mean of 1.6±0.7 treatments were delivered to the median prostate zone. Anaesthesia was varied from 69% of patients received oral sedation only, 21% received prostate block and 10% received intravenous sedation. Some subjects were electively catheterised for an average of 3.6±3.5 days after treatment.

Other issues: This summary compiles 3 publications from the same RCT and crossover study. Sample size power calculations were not reported by the authors.

Key efficacy and safety findings

Efficacy

n=197 (136 RFTT, 61 sham)

Total of **135 men** who had RFTTT (RCT and crossover combined)

Procedural pain VAS – 5.0±2.7 RFTT, 4.9±2.8 rigid cystoscope (controls)

Comparison of mean changes at 3 months between RFTT and control ITT groups

	RFTT Mean±SD (n)			**Sham** Mean±SD (n)			**P value**
Outcome Mean ± SD	**Baseline**	**3 months**	**Change**	**Baseline**	**3 months**	**Change**	
IPSS	22±4.8 (136)	10.8±6.5 (136)	-11.2±7.6	21.9±4.7 (61)	17.5±7.6 (61)	-4.3±6.9	<0.0001
Qmax (mL/s)	9.9±2.3 (136)	16.1±7.3 (133)	6.2±7.1	10.4±2.1 (61)	10.8±4.0 (61)	0.5±4.2	<0.0001
PVR (mL)	82±51.5 (136)	71.8±72.2 (133)	-10.6±68.3	85.5±51.6 (61)	92.7±77.8 (61)	7.2±77.4	0.108
IPSS QoL	4.4±1.1 (136)	2.3±1.5 (134)	-2.1±1.6	4.4±1.1 (61)	3.5±1.5 (61)	-0.9±1.5	<0.0001
BPHII	6.3±2.8 (136)	2.9±2.9 (134)	-3.4±3.5	6.2±2.9 (61)	4.7±3.5 (61)	-1.5±3.0	0.0003
OAB Bother scale	39.6±18 (136)	24.9±18 (133)	-14.6±18.4	39.9±20.7 (61)	31.9±20.7 (61)	-8±17.9	0.022
OAB HRQL	64.5±20 (136)	82±17.5 (132)	17.5±18.8	66.7±16.9 (61)	74.9±19.3 (60)	8.3±15.7	0.001
IIEF erectile function domain	22.6±7.4 (91)	22.7±8.4 (90)	0.1±7.4	21.2±8.3 (40)	21.0±9.1 (40)	-0.3±5.6	0.795
MSHQ-EjD function	9.3±3.1 (91)	9.7±4.5 (90)	0.3±4.3	9.8±3.6 (40)	9.6±4.3 (40)	-0.2±3.2	0.443
MSHQ-EjD bother	2.2±1.7 (91)	1.8±1.7 (90)	-0.4±1.9	2±1.7 (40)	1.8±1.8 (40)	-0.2±1.9	0.623

Erectile function (3 months)

There was no statistically significantly difference in mean scores between patients who had RFTT and controls for any of IIEF-15 domains at the 3-month follow-up.

MCID of change in IIEF erectile function domain score at 3 and 12 months after RFTT

	Month 3 (n=90 sexually active)		**Month 12 (n=77 sexually active)**	
		MCID[2]		MCID[2]
IIEF-EF baseline severity	**n/N**	**Increase, mean±SD**	**n/N**	**Increase, mean±SD**
Severe (1 to 10)	2/7	12.5±4.9	2/3	11.5±3.5
Moderate (11 to 16)	5/15	10.1±4.6	6/13	11.2±4.4
Mild (17 to 25)	18/68	4±2.2	13/61	5.3±2.8
Improved scores	32 % (29/90)		27% (21/77)	

Reoperation

Reoperation rate was 4% (6/135) at 3 years follow-up.

Mean outcome measures at 3 months during control/sham and crossover periods

	Sham Mean±SD (n)			Crossover to RFTT Mean±SD (n)			P value
	Baseline	**3 months**	**Change**	**Baseline**	**3 months**	**Change**	
IPSS	21.9±4.9 (50)	18±7.6 (50)	-3.9±6.7	19.1±6.7 (50)	9.8±6 (50)	-10±7.1	0.0004
Qmax (mL/s)	10.2±2.2 (49)	10.4±3.8 (49)	0.2±3.9	10.1±3.7 (49)	16.4±7.1 (49)	6.3±6.8	<0.0001
IPSS QoL	4.5±1.1 (50)	3.7±1.5 (50)	-0.8±1.5	3.9±1.4 (50)	1.9±1.4 (50)	-2±1.8	0.0024
BPHII	6.2±2.8 (50)	4.9±3.5 (50)	-1.3±2.9	5.5±3.2 (50)	2.6±2.6 (50)	-2.9±3.3	0.024
IIEF-15	16.1±10 (47)	17±10.5 (47)	0.9±6.1	16.7±10.4 (47)	16.6±11. 3 (47)	-0.1±8.9	0.597
MSHQ-EjD Function	9.1±4 (46)	9.4±4.4 (47)	0.6±3.0	9.5±4.2 (46)	8.9±5.2 (47)	-0.4±4	0.283
MSHQ-EjD bother	2.0±1.8 (46)	1.7±1.8 (47)	-0.3±1.7	1.8±1.8 (46)	1.7±1.7 (47)	-0.1±1.9	0.678

Mean outcome measures in crossover subjects after RFTT

Outcome	**3 months**	**p**	**6 months**	**p**	**12 months**	**p**
IPSS (n)	**50**		**49**		**45**	
Baseline	19.9±6.7	p<0.0001	20.1±6.7	p<0.0001	19.4±66.	p<0.0001
Follow-up	9.8±6		10.2±6.9		8.6±6.6	
IPSS QoL (n)	**50**		**49**		**45**	
Baseline	3.9±1.4	p<0.0001	3.9±1.4	p<0.0001	3.8±1.3	p<0.0001
Follow-up	1.9±1.4		2±1.4		1.7±1.2	
Qmax (mL/s) (n)	**49**		**49**		**45**	
Baseline	10.1±3.7	p<0.000	10.1±3.7	p<0.0001	10.3±3.8	p<0.0001
Follow-up	16.4±7.1		16.1±7.2		16.2±7.9	
PVR volume (mL) (n)	**49**		**49**		**44**	
Baseline	95.8±79.2	p=0.096	91.6±75.6	-p=0.06	101±79.2	p=0.6
Follow-up	67.3±64.2		67.3±64.9		83.8±80.5	
BPHII (n)	**50**		**49**		**45**	
Baseline	5.5±3.2	p<0.0001	5.6±3.3	p<0.0001	5.3±3.2	p<0.0001
Follow-up	2.6±2.6		2.3±2.5		1.6±2.3	
IIEF-15 (n)	**29**		**28**		**26**	
Baseline	23.2±6.8	p=0.331	21.8±7.5	p<0.358	22.8±6.6	-18%, p=0.018
Follow-up	21.3±10.3		20.9±9.2		18.8±10	
MSHQ-EjD function (n)	**30**		**28**		**26**	
Baseline	9.9±3.8	p=0.603	9.8±3.9	p=0.177	9.8±3.6	p=0.484
Follow-up	9.7±5.1		8.6±4.9		9.1±4.6	
MSHQ-EjD bother (n)	**30**		**30**		**26**	
Baseline	1.6±1.7	p=0.681	1.8±1.8	p=0.683	1.7±1.7	p=0.297
Follow-up	1.6±1.6		1.8±1.7		2.1±1.9	
ICSMIS-SF (n)	**50**		**49**		**45**	
Baseline	4.3±3	p=0.018	4.4±3	p=0.0023	3.9±2.5	p<0.0001
Follow-up	3.2±2.6		3.3±2.7		2.6±1.8	
OAB HRQL Score (n)	**49**		**48**		**45**	
Baseline	72.5±18.9	p<0.0001	72.2±19.2	p<0.0001	75.2±17.6	p<0.00001
Follow-up	86.7±15.2		86.2±16		89.1±12.6	
OAB Symptom score (n)	**50**		**49**		**45**	
Baseline	33.1±19	p<0.0001	33.4±20.9	p<0.0001	30.1±17.9	p<0.00001
Follow-up	21.4±18.3		20±18.7		15.2±12.4	

Mean outcome changes after convective RFTT from baseline through 3 years (treatment group)

Outcome	1 year	p	2 years	p	3 years	p
IPSS (n)	**121**		**109**		**97**	
Baseline	21.8±4.8	p<0.0001	21.4±4.5	<0.0001	21.4±4.6	p<0.0001
Follow-up	10.3±6.7		10.2±6.2		10.4±6.1	
IPSS QoL (n)	**121**		**109**		**97**	
Baseline	4.4±1.1	p<0.0001	4.3±1.0	p<0.0001	4.3±1.0	p<0.0001
Follow-up	2.1±1.5		2.1±1.4		2.1±1.3	
Qmax (mL/s) (n)	**112**		**99**		**80**	
Baseline	10±2.2	p<0.0001	10±2.2	p<0.0001	9.7±2.0	p<0.0001
Follow-up	15.5±6.7		14.7±6.1		13.2±4.8	
PVR volume (mL) (n)	**118**		**106**		**92**	
Baseline	82.5±51.2	p=0.894	84.9±54	p=0.654	81.5±2.0	p=0.0004
Follow-up	78.6±79.9		84.6±92		55.1±61.9	
BPHII (n)	**121**		**109**		**97**	
Baseline	6.2±2.8	p<0.0001	6.1±2.8	p<0.0001	6.1±2.9	-61%, p<0.0001
Follow-up	2.3±3		2.3±2.7		2.4±2.9	
IIEF-15 (n)	**77**		**71**		**62**	
Baseline	23.3±6.9	p=0.871	22.9±7.3	p=0.408	23.2±7.4	p=0.112
Follow-up	23±8.4		21.8±8.7		21.3±9.1	
MSHQ-EjD function (n)	**78**		**70**		**63**	
Baseline	9.6±3	p=0.278	9.6±3	p=0.351	9.9±3	p=0.003
Follow-up	9.3±4		9.1±4.4		8.5±4.5	
MSHQ-EjD bother (n)	**79**		**70**		**63**	
Baseline	2.2±1.6	p=0.0015	2.2±1.6	p=0.0129	2±1.6	p=0.006
Follow-up	1.5±1.5		1.7±1.7		1.6±1.5	
ICSMIS-SF (n)	**120**		**109**		**97**	
Baseline	4.3±2.8	p<0.0001	4.2±2.4	p<0.0001	4.1±2.3	p<0.0001
Follow-up	3±2.8		3±2.6		3±2.6	
OAB HRQL Score (n)	**120**		**106**		**95**	
Baseline	65.8±18.9	p<0.0001	66.6±18.3	p<0.0001	66.7±18.2	p<0.0001
Follow-up	83.7±18.2		85.6±15.1		84.6±15.4	
OAB Symptom score (n)	**121**		**109**		**97**	
Baseline	39±17.5	p<0.0001	38.2±17.2	p<0.0001	37.5±16.2	p<0.0001
Follow-up	20.6±18.4		20.9±16.6		21.6±16.2	
PSA (ng/mL) (n)	**120**		**109**		**96**	
Baseline	2.1±1.6	p=0.0003	2.1±1.6	p=0.0015	2±1.6	p=0.0947
Follow-up	1.8±1.3		1.8±1.6		1.8±1.7	

Safety

Related serious adverse events	**RFTT**	**Controls**
Nausea[3]	1/136	0/61
Vomiting[3]	1/136	0/61
De-novo urinary retention	1/136	0/61
Non-serious adverse events[4]		
Dysuria	17% (23/136)	2% (1/61)
Haematuria	13% (17/136)	0/61
Urinary frequency	7% (9/136)	3% (2/61)
Urinary urgency	6% (8/136)	2% (2/61)
Acute urinary retention	4% (5/136)	0/61
Suspected urinary tract infection	4% (5/136)	0/61
Urinary tract infection (proven with culture)	3% (4/136)	0/61

Haematospermia	7% (10/136)	0/61
Decreased ejaculatory volume	3% (4/136)	0/61
Anejaculation	3% (4/136)	0/61
Epididymitis	3% (4/136)	2% (1/61)
Pelvic pain of discomfort	3% (4/136)	0/61

[1]Voided volume ≥125 mL

[2]MCID is a minimal IIEF-EF score increase of 2 for men with mild erectile dysfunction, an increase of 5 for moderate erectile dysfunction, and 7 for severe erectile dysfunction.

[3]Requiring hospitalisation overnight for observation

[4]Data extracted from original papers and authors report available from https://clinicaltrials.gov/ct2/show/results/NCT01912339?sect=X4301256#othr

Abbreviations used: BPH, benign prostatic hyperplasia; ED, erectile dysfunction; ICSMI-SF, international continence society male incontinence score - short form; IIEF-15, international index of erectile function; IPSS, international prostate symptom score; ITT, intention to treat; LUTS, lower urinary tract symptoms; HRQL, health related quality of life; MCID, minimal clinical important differences; MSHQ-EjD, male sexual health questionnaire for ejaculatory function; ng, nanogram; OAB, overactive bladder; PSA, prostate specific antigen; PVR, post-void residual urine volume; Qmax, peak urinary flow; QoL, quality of life; RCT, randomised control trial; SD, standard deviation; VAS, visual analogue scale; RFTT, convective radiofrequency thermal treatment.

Study 5 Darson MF (2017)

Details

Study type	**Case series**
Country	US
Recruitment period	2015 to 2017
Study population and number	**n=131 patients** with moderate to severe LUTS due to BPH who had RFTT in 2 group practices
Age and sex	Mean 70.9 (47 to 96) years, males
Patient selection criteria	Consecutive patients with moderate to severe LUTS were offered RFTT as an alternative to medications for symptomatic relief of BPH, after inadequate relief or drug intolerance. Urologists used their own discretion for patient selection with variable prostate sizes, LUTS severity, urinary retention or presence of an obstructing median lobe. Patient selection and treatment did not follow a standardised protocol.
Technique	Analgesia consisted of intravenous sedation (86% [113/131]), general anaesthesia (15% [20/131]) or prostate block (6% [8/131]) followed by posttreatment analgesics.
Follow-up	**12 months**
Conflict of interest/source of funding	The authors declared having consulted for NxThera, manufacturer of the Rezūm device.

Analysis

Follow-up issues: Although the intention was to follow-up as many patients as possible, there was no obligation for patients to comply with follow-up evaluations. Patients were offered follow-up visits at 1, 3, 6 and 12 months.

Study design issues: Pre and post procedure assessments included IPSS, QoL, peak urinary flow rate, voided volume and PVR. The results were reported separately according to LUTS severity: IPSS 8 to 19 and IPSS 20 to 35. Safety events and surgical retreatment rates were monitored prospectively.

The clinically meaningful threshold for improvement was defined as a greater or equal than 3-point increase in IPSS relative to baseline, as suggested by the American Urological Association.

Study population issues: Preoperative mean prostatic volume was 45.1 (range 12.9 to 183) cm^3 and mean PVR was 216 (range 0 to 2,000) ml with 26% (34/131) of patients having a PVR volume ≥250 ml. There were 12% of patient having previous surgery or minimally invasive surgical procedures, including TURP (2% [3/131]), transurethral conductive radiofrequency thermal therapy (7% [9/131]), transurethral microwave thermal therapy (1/131), transurethral microwave thermal therapy and prostatic urethral lift (1/131) and Rezūm RFTT (2% [2/131]). The average preoperative LUTS severity was moderate (IPSS 8 to 19) in 53% (68/131) of patients and severe (IPSS 20 to 35) in 47% (60/131).

The total number of treatments in lateral lobes averaged 4.4 (range 2 to 12). The median lobe or enlarged central zone was identified and treated in 41% (54/131) of patients with an average of 1.6 (range 1 to 6) treatments.

Other issues: None.

Key efficacy and safety findings

Efficacy

n=131

Changes in outcome measures after RFTT by LUTS severity

Outcome measure	IPSS 8 to 35 (all participants) Mean±SD		IPSS 8 to 19 Mean±SD	IPSS 20 to 35 Mean±SD
	3-6 months	12 months	12 months	12 months
IPSS				
n (paired values)	115	87	46	41
Baseline	19.9±6.7	19.4±6.7	14.1±3	25.4±4.1
Follow-up	9.8±6.9	10.1±7.2	8.3±6.6	12±7.3
Change	-10.1±8.8	-9.4±8.7	-5.8±6.5	-13.4±9.2
P value	<0.0001	<0.0001	<0.0001	<0.0001
IPSS QOL				
n (paired values)	104	74	39	34
Baseline	4.3±1.2	4.4±1.3	3.8±1.4	4.9±0.9
Follow-up	2.3±1.5	2.5±1.4	2.3±1.5	2.6±1.3
Change	-2±1.7	-1.9±1.8	-1.5±1.9	-2.3±1.6
P value	<0.0001	<0.0001	<0.0001	<0.0001
Qmax (ml/s)				
n (paired values)	38	7	3	4
Baseline	8.7±4.7	8.5 (3.5)	8.1±4.6	8.8±3.2
Follow-up	11.6±7.7	10±5	9.3±3.2	10.5±6.5
Change	3±9	1.5±5.9	1.2±7.6	1.7±5.5
P value	0.04	0.4	0.57	0.82
PVR (ml)				
n (paired values)	89	35	17	18
Baseline	243.8±316.7	236.6±341.3	281.6±461.6	194.1±168.8
Follow-up	85.8±167.3	77.3±122.1	96.6±166.4	59±55.2
Change	-158±221.8	-159±254.7	-185±340.5	-135±138.9
P value	<0.0001	<0.0001	<0.0001	<0.0001
Voided volume (ml)				
n (paired values)	38	7	3	4
Baseline	192.3±119.4	182.7±119.4	223.7±124.1	151.9±123.7
Follow-up	146.7±100.6	138.4±103.1	120±129.2	152.3±97.7
Change	-45.5±149.8	-44.2±146.6	-104±230.2	0.3±38.4
P value	0.19	0.51	0.36	0.79

Erectile and ejaculatory function
The study did not collect sexual function data via a validated questionnaire but all patients were asked about sexual function and there was no de novo erectile or ejaculatory dysfunction.

Reoperation rate at 12 month follow-up: 2% (3/131)

There were no statistically significantly difference in MCID IPSS between the two centres

Safety

The author reported no perioperative device or procedure related adverse events.

Acute urinary retention: 11% (14/131)

Urinary frequency, urgency, frequency and urgency, haematuria and nocturia: less or equal to 4% (5/131) of patients[1]

[1]Frequencies not reported by type of adverse event.

doing the procedure.	
Abbreviations used: BPH, benign prostatic hyperplasia; IPSS, international prostate symptom score; LUTS, lower urinary tract symptoms; MCID, minimal clinical important differences; PVR, post-void residual urine volume; Qmax, peak urinary flow; QoL, quality of life; SD, standard deviation; VAS, visual analogue scale; RFTT, convective radiofrequency thermal treatment.	

Study 6, 7 and 8 Dixon CM (2015 & 2016) & Mynderse LA (2015)

Details

Study type	**Case series**
Country	Czech Republic, Dominican Republic, Sweden
Recruitment period	
Study population and number	**n=65** men with moderate to severe LUTS secondary to BPH who had RFTT using the Rezūm device
Age and sex	66.6 (range 50 to 90) years, males
Patient selection criteria	Inclusion criteria: Age ≥ 45 years, IPSS ≥ 13, Qmax ≤ 15 ml/s and prostate volume 20 to 120 cm^3, voided volume ≥ 125 ml and PVR < 300ml. Exclusion criteria: Confirmed or suspected prostate or bladder cancer, active urinary tract infection or bacterial prostatitis within the last year. Men taking concomitant drug therapy for LUTS. Individuals with a median lobe were not excluded and could be treated at the physician investigator' discretion.
Technique	Patients had a washout period from antihistamines, antispasmodics (1 week, except if documented evidence of stable dosing for the last 6 months), α-blockers, androgens, gonadotropin-releasing hormone analogues (2 weeks), 5α-reductase inhibitors (6 months), and from the use of antidepressants, anticholinergics, anticonvulsants, β-blockers (unless with documented evidence of stable dosing). Of the 65 patients 79% (51/65) received oral sedation and 21% (14/65) had intravenous sedation. Initial thermal treatment procedures in this pilot study evolved with slight modifications to optimise the water vapour delivery and endoscopic technique. These modifications in dosimetry and technique were guided by serial gadolinium-enhanced MRI to monitor the size and location of ablative lesions, their time course of resolution and the corresponding change in prostate tissue volume. MRI results were available in 59 of 65 patients.
Follow-up	**2 years**
Conflict of interest/source of funding	The authors declared being clinical trial investigators for NxThera and some authors declared being consultants for NxThera. Some authors and the Mayo clinic declared having financial interest in the Analyse 11.0 image and analysis technology used in this research. This study was funded by MxThera, manufacturer of the Rezūm device.

Analysis

Follow-up issues: Post-procedure follow-up happened at 1 week, 1, 3, 6, 12 and 24 months. Eighty-nine percent (58-65) of men completed the 1-year follow-up and 66% (43-65) the 2-year follow-up. In the first 212 months there were 7 patients not completing the study: 3 were lost to follow-up, 2 were relocated and 2 had poor health (1 de novo diagnose of prostate cancer). In the 12 to 24-month follow-up 2 patients died, 2 had other treatments (TURP, open prostatectomy), 4 were lost to follow-up or had a second phase of treatment with RFTT (5 men).

Study design issues: Self-administered questionnaires were completed at follow-up including IPSS, QoL instruments (IPSS QoL, BPHII), and sexual function with the IIEF, IIEF-question 9 for ejaculatory function and the MSHQ-EjD (1 centre). Uroflowmetry, PVR and PSA records were also collected.

An independent urologist adjudicated all reported AEs. Device or procedure related AEs were evaluated using a Clavien-Dindo classification.

Study population issues: Mean prostate volume was 48.6 (19.5 to 110.4) cm^3 and mean IPSS was 21.6 (13 to 35). There were 32% (21-65) of men with moderate LUTS (IPSS ≤18) and 68% (44/65) with severe LUTS (IPSS ≥ 19). There were 48% (31-65) of men with history of erectile dysfunction.

The mean number of water vapour injections was 4.6 (range 2 to 9). The median lobe was treated in 14 patients with a mean of 1.8 (range 1 to 3) water vapour injections.

Other issues: There were 4 patient receiving BPH medication 1 to 4 months after RFTT for relief of intermittent or residual LUTS. Data from this study was reported in 3 different publications.

Key efficacy and safety findings

Efficacy

n=65 men

Outcome after RFTT including MRI imaging of the prostate

Variable	Time	n	Mean (Range)	Mean Variation	Mean % variation
Whole prostate volume (cm^3)	1 week	44	61.2 (20.4 to 133.2)		
	1 month	42	52.7 (15.4 to 118.4)	-8.5	-14%
	3 months	41	47 (15.3 to 115.4)	-14.2	-23%
	6 months	40	43.5 (16 to 116.6)	-17.7	-29%
Transition zone volume (cm3)	1 week	44	36.3 (9.1 to 87.8)		
	1 month	42	29.8 (8.4 to 80.3)	-6.5	-18%
	3 months	41	25.1 (6.8 to 79.4)	-11.2	-31%
	6 months	40	22.5 (6.6 to 79.3)	-13.8	-38%
Gadolinium defects volume (cm^3)	1 week	44	8.2 (0.5 to 24)		
	1 month	42	3.4 (0.3 to 11.3)	-4.8	-59%
	3 months	41	0.7 (0 to 2.6)	-7.5	-92%
	6 months	40	0.4 (0 to 3.7)	-7.8	-95%

Paired PSA levels at baseline and during 6 months follow-up

	Time point Mean±SD			
PSA (ng/mL)	**Week 1**	**1 month**	**3 months**	**6 months**
n (paired values)	36	20	41	41
Baseline	3.5±3.6	4.3±4.1	3.3±3.4	3.3±3.4
Follow-up	18.7±16	5.6±3.3	3.3±3.8	3.1±3.0
Change	15.2±15.3	1.2±3.5	-0.0±2.5	-0.2±1.9
P value	<0.001	0.131	0.971	0.513

Proportion of patients with IPSS improvement after RFTT

Posttreatment	**IPSS change from baseline n/N (% of patients)**			
	≥25%	**≥50%**	**≥3 points**	**≥5 points**
3 months	86% (53/62)	73% (45/62)	90% (56/62)	82% (51/62)
6 months	87% (55/63)	73% (46/63)	91% (57/63)	84% (53/63)
1 year	83% (48/58)	67% (39/58)	88% (51/58)	81% (47/58)
2 years	84% (36/43)	61% (26/43)	93% (40/43)	79% (34/43)

Baseline, follow-up and change in each outcome measure after RFTT

Outcome measure	1 month	3 months	6 months	12 months	24 months
IPSS					
n (paired volumes)	**64**	**62**	**62**	**58**	**43**
Baseline	21.6±5.5	21.7±5.5	21.5±5.6	21.7±5.7	21.7±5.3
Follow-up	14.8±8.4	8.3±5.8	8.5±7	9.2±6.5	9.6±6.5
Change	-6.8±10	-13.4±7.6	-13.1±8.6	-12.5±7.6	-12.1±7.9
% change, p-value	p<0.001	p<0.001	p<0.001	p<0.001	p<0.001
IPSS QoL					
n (paired volumes)	**64**	**62**	**62**	**58**	**43**
Baseline	4.3±1.1	4.3±1.1	4.3±1.1	4.4±1.1	4.4±1.2
Follow-up	2.9±1.8	1.5±1.4	1.6±1.6	1.7±1.4	1.8±1.4
Change	-1.5±2	-2.8±1.6	-2.7±2	-2.7±1.6	-2.6±1.7
% change, p-value	p<0.001	p<0.001	p<0.001	p<0.001	p<0.001
BPHII					
n (paired volumes)	**62**	**61**	**59**	**56**	**42**
Baseline	6.8±2.9	6.8±2.9	6.8±2.9	6.9±2.8	7.1±2.7
Follow-up	5.5±3.6	2.2±2.4	2±2.6	2±2.3	2.3±2.5
Change	-1.2±4.4	-4.7±3.2	-4.8±3.7	-4.9±3	-4.8±3.5
% change, p-value	p=0.034	p<0.001	p<0.001	p<0.001	p<0.001
Qmax (ml/s)					
n (paired volumes)	**63**	**61**	**60**	**57**	**39**
Baseline	7.9±3.2	8.1±3.2	8±3.1	8.1±3.3	8.3±2.8
Follow-up	9.9±3.9	12.8	12.3±5.3	12.7±6.3	12±6.2
Change	2±4.5	4.7±6.4	4.3±5.5	4.6±6.4	3.7±6.5
% change, p-value	p<0.001	p<0.001	p<0.001	p<0.001	p=0.001
PVR					
n (paired volumes)	**62**	**60**	**58**	**55**	**38**
Baseline	92.1±77.9	89.5±77.3	87.3±74.2	92.2±78.4	78.5±65.8
Follow-up	67.1±64.4	59.6±66.4	65.9±88.5	64.5±72.3	62.8±83.9
Change	-25±92.3	-29.9±78	-21.4±88.3	-27.6±82.9	-15.6±93.1
% change, p-value	p=0.037	p=0.004	p=0.071	p=0.017	p=0.307
IIEF-15					
n (paired volumes)	**60**	**58**	**59**	**55**	**31**
Baseline	13.3±12	12.8±11.8	13.5±12	12.6±11.7	11.8±12.4
Follow-up	10.3±11.6	14.5±11.9	15.4±12	14.1±11.8	15.5±11.5
Change	-3±9.8	1.7±10.1	1.9±8.9	1.5±8.7	3.6±6.8
% change, p-value	p=0.019	p=0.201	p=0.102	p=0.210	p=0.006
IIEF-15 question 9 (ejaculatory function)					
n (paired volumes)	**64**	**62**	**60**	**58**	**33**
Baseline	2.2±2.2	2.2±2.2	2.2±2.2	2.1±2.2	2.1±2.3
Follow-up	1.8±2.3	2.9±2.3	2.6±2.3	2.6±2.3	2.7±2.2
Change	-0.4±2.2	0.7±2.3	0.5±1.9	0.4±1.7	0.5±1.8
% change, p-value	p=0.151	p=0.02	p=0.061	p=0.053	p=0.095
MSHQ-EjD function					
n (paired volumes)	**14**	**14**	**13**	**12**	**8**
Baseline	5.9±4.8	5.9±4.8	5.5±4.7	5.3±4.9	4.6±5.2
Follow-up	5.6±6.1	7.1±5.0	8±4.5	5±4.7	7±4.8
Change	-0.2±3.9	1.2±4.6	2.5±4.9	-0.3±5.8	2.4±5.2
% change, p-value	p=0.841	p=0.339	p=0.585	p=0.884	p=0.234
MSHQ-EjD bother					
n (paired volumes)	**14**	**14**	**13**	**12**	**8**
Baseline	2.3±2.3	2.3±2.3	2.5±2.3	2.3±2.2	2.6±2.2
Follow-up	0.8±0.9	0.9±1.1	1±0.9	0.9±0.8	0.8±2.5
Change	-1.5±2.7	-1.4±2.4	-1.5±2.5	-1.3±2.3	-1.9±2
% change, p-value	-p=0.057	p=0.057	-61%, p=0.06	p=0.071	p=0.035

Safety

There were no perioperative serious device or procedure related AEs.

	Events	Patients n (%)	Number of AEs by Follow-up			
			0 to 1 month	>1 to 3 months	>3 to 12 months	>12 to 24 months
Serious AEs related	3*	1/65	1	0	0	0
Serious AEs unrelated	14	14% (9/65)	4	1	6	3
Related non-serious AEs						
Urinary retention	24	34% (22/65)	21	2	1	0
Dysuria	14	22% (14/65)	9	4	1	0
Urinary urgency	14	20% (13/65)	10	4	0	0
UTI suspected	13	20% (13/65)	8	4	1	0
Haematuria	10	14% (9/65)	10	0	0	0
Poor stream	10	14% (9/65)	6	3	1	0
Pain/discomfort	7	11% (7/65)	5	2	0	0
Nocturia	6	8% (5/65)	5	1	0	0
Urinary frequency	5	6% (4/65)	4	1	0	0
Urethral secretion (without haematuria or stones)	3	5% (5/65)	2	0	1	0
Fever	3	5% (3/65)	3	0	0	0
Terminal dribbling	2	3% (2/65)	1	0	1	0
Scrotal pain/discomfort	2	3% (2/65)	1	1	0	0
Urinary incontinence	2	2% (1/65)	1	0	0	0
Total Non-serious	**115**		**75% (86/115)**	**19%(22/115)**	**4% (6/115)**	**0%**

In no case was a lesion seen between the prostate and the rectal wall. The mean closest distance to the rectal wall was15.4 mm (range 5.2 to 62.2 mm). Treatment defects were within 1 to 4 mm of the urethra and the prostatic urethra mucosa appeared intact on the gadolinium-enhanced areas of coronal view.

Some patients 55% (36/65) were catheterized before discharge at the discretion of the investigator (precautionary catheter use; 15), or for inadequate voiding (14), haematuria (6), or dysuria (1), events often associated with rigid cystoscopy. The median duration of catheter use was 4.1 days. An additional 11 patients (17%) were catheterized after discharge for a median of 3.8 days related to urinary retention or travel convenience.

*In 3 patients, the treatment was delivered outside the prostrate target. Subsequent 1, 3 and 6-month follow-up imaging showed progressive and complete resolution of the extraprostatic treatment

Abbreviations used: AEs, adverse events; BPH, benign prostatic hyperplasia; BPHII; benign prostatic hyperplasia impact index; IIEF-15, international index of erectile function; IPSS, international prostate symptom score; LUTS, lower urinary tract symptoms; MSHQ-EjD, male sexual health questionnaire for ejaculatory function; OAB, overactive bladder; PSA, prostate specific antigen; PVR, post-void residual urine volume; Qmax, peak urinary flow; QoL, quality of life; RFTT, convective radiofrequency thermal treatment; SD, standard deviation; TURP, transurethral resection of the prostate; UTI, urinary tract infection.

Validity and generalisability of the studies

- There is only one randomised study (with sham group crossover to treatment) on the use of RFTT for BPH. This has adequate blinding and follow-up to 3 years. Five years follow-up data is not yet available
- All studies used the same device and technique and the outcome assessment tools were consistently used across studies
- Loss to follow-up did not seem to have a major impact on the studies outcomes.

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 procedure 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 guidance

- 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 vapour ablation for

lower urinary tract symptoms caused by benign prostatic hyperplasia were submitted and can be found on the NICE website.

Patient commentators' opinions

Section to be inserted if there is patient commentary

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

Section to be inserted if there is no patient commentary at IPAC 1

NICE's Public Involvement Programme will send questionnaires to NHS trusts for distribution to patients who had the procedure (or their carers). When NICE has received the completed questionnaires, these will be discussed by the committee.

Section to be inserted if there is no patient commentary at IPAC 2

NICE's Public Involvement Programme was unable to gather patient commentary for this procedure.

Section to be inserted if patient commentators raised no new issues

The patient commentators' views on the procedure were consistent with the published evidence and the opinions of the specialist advisers. [Add if relevant: See the patient commentary summary for more information.]

Section to be inserted if patient commentators raised new issues

The patient commentators raised the following issues about the safety/efficacy of the procedure, which did not feature in the published evidence or the opinions of specialist advisers, and which the committee considered to be particularly relevant:

- [insert additional efficacy and safety issues raised by patient commentators and highlighted by IPAC, add extra rows as necessary].
- [Last item in list].

[Add if relevant: See the patient commentary summary for more information.]

Company engagement

A structured information request was sent to 1 company who manufacture 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

- All studies were supported by the manufacturers of the device used in this procedure.
-

Ongoing clinical trials:

- NCT02940392 - Rezum FIM Optimization (Rezum FIM), Single group assignment; Dominican Republic; n=15, 5 years follow-up; study start date: February 2012; estimated completion date: June 2018.

- NCT02943070 - Rezum I Pilot Study for BPH (Rezum Pilot), Single group assignment; multicentre (Czech Republic, Dominican Republic and Sweden), n=50, 1 yeas follow-up; study start date: March 2012; study estimated completion date: December 2018.

References

1. McVary KT, Gange SN, Gittelman MC et al. (2016a) Erectile and ejaculatory function preserved with convective water vapor energy treatment of lower urinary tract symptoms secondary to benign prostatic hyperplasia: randomized controlled study. Journal of Sexual Medicine 13(6), 924-33
2. McVary KT, Gange SN, Gittelman MC et al. (2016b) Minimally invasive prostate convective water vapor energy ablation: a multicenter, randomized, controlled study for the treatment of lower urinary tract symptoms secondary to benign prostatic hyperplasia. Journal of Urology 195(5), 1529-38
3. McVarty KT and Roehrborn CG (2017) Three-year outcomes of the prospective, randomised controlled Rezūm system study: convective radiofrequency thermal therapy for treatment of lower urinary tract symptoms due to benign prostatic hyperplasia. Urology, doi: 10.1016/j.urology.2017.10.023. [Epub ahead of print]
4. Roehrborn CG, Gange SN, Gittelman MC et al. (2017) Convective thermal therapy: durable 2-year results of randomized controlled and prospective crossover studies for treatment of lower urinary tract symptoms due to benign prostatic hyperplasia. Journal of Urology 197(6), 1507-1516
5. Darson MF, Alexander EE, Schiffman ZJ et al. (2017) Procedural techniques and multicenter postmarket experience using minimally invasive convective radiofrequency thermal therapy with Rezum system for treatment of lower urinary tract symptoms due to benign prostatic hyperplasia. Research & Reports in Urology 9, 159-168
6. Dixon CM, Cedano ER, Pacik D et al. (2015) Efficacy and safety of Rezum system water vapor treatment for lower urinary tract symptoms secondary to benign prostatic hyperplasia. Urology 86(5), 1042-7
7. Dixon CM, Cedano ER, Pacik D et al. (2016) Two-year results after convective radiofrequency water vapor thermal therapy of symptomatic benign prostatic hyperplasia. Research & Reports in Urology 8, 207-216
8. Mynderse LA, Hanson D, Robb RA et al. (2015) Rezum System Water Vapor Treatment for Lower Urinary Tract Symptoms/Benign Prostatic Hyperplasia: Validation of Convective Thermal Energy Transfer and Characterization With Magnetic Resonance Imaging and 3-Dimensional Renderings. Urology 86(1), 122-7

Literature search strategy

Databases	Date searched	Version/files
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	07/11/2017	Issue 11 of 12, November 2017
HTA database (Cochrane Library)	07/11/2017	Issue 4 of 4, October 2016
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	07/11/2017	Issue 10 of 12, October 2017
MEDLINE (Ovid)	07/11/2017	1946 to October Week 4 2017
MEDLINE In-Process (Ovid)	07/11/2017	November 06, 2017
EMBASE (Ovid)	07/11/2017	1974 to 2017 Week 45
PubMed	07/11/2017	n/a
BLIC	07/11/2017	n/a

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 (Benign adj4 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 Thermal Conductivity/

16 Laser Therapy/ and "Transurethral Resection of Prostate"/

17 ((thermal or heat or vapor or vapour or water or wet) adj4 (energy or conduct* or ablat*)).tw.

18 ((vapor or vapour or water or wet) adj4 (thermal* or heat* or fever* or thermo-ablat* or thermoablat* or thermo-therap* or thermotherap* or ablat* or therap* or treat*)).tw.

19 or/14-18

20 13 and 19

21 rezum.tw.

22 20 or 21

23 Animals/ not Humans/

24 22 not

Appendix

There were no additional papers identified.