The Safety and Effectiveness of Transurethral Water Vapor Ablation of Prostate: Literature review

Seungji Lee[1], Jiae Im[1], Jieun Yun[1], Worlsook Lee[1], Chaemin Shin[1]

[1]National Evidence-based Healthcare Collaborating Agency (NECA), Seoul, Korea, Rep. of
Seungji Lee (seungji@neca.re.kr), Acceptance Code: HTA66

1. Abstract

Objective

Benign prostatic hyperplasia (BPH) is a common cause of lower urinary tract symptoms (LUTS) in older men, resulting from the enlargement of the transition zone around the peri-urinary tract. LUTS includes frequent urination, night urination, urinary urgency, and urinary retention. This study aims to determine the safety and effectiveness of transurethral water vapor ablation of the prostate in BPH patients with LUTS.

Methods

A literature review was conducted to assess the effectiveness of transurethral water vapor ablation of the prostate. Guidelines were collected from the Guidelines International Network, the Korean Medical Guideline Information Center, and five clinical society websites, along with additional manual searches.

Results

The review included two medical textbooks (McAninch & Lue, 2020; Partin et al., 2020) and five guidelines (Canadian Urological Association, American Urological Association, National Institute for Health and Care Excellence, European Association of Urology, and Japanese Urological Association and the Japanese Society of Internal Medicine).

Textbooks and guidelines indicate that most patients undergoing this procedure had no adverse events, with mild to moderate symptoms resolving within three weeks for those affected. Minor and serious adverse events were comparable to other BPH treatments. The technique is noted for preserving sexual function and has lower rates of ejaculatory dysfunction and urinary incontinence compared to Transurethral resection of the prostate (TURP) and Holmium laser enucleation of the prostate (HoLEP), indicating acceptable safety.

Effectiveness is demonstrated by symptom improvement, enhanced quality of life, and a low re-procedure rate. It is recommended for patients with BPH (30–80 cc) with LUTS.

Conclusion

The New Health Technology Assessment Committee determined Transurethral water vapor ablation of prostate in patients with BPH with a prostate volume of 30–80 cc with LUTS a safe and effective technique, and announced through the Korean Ministry of Health and Welfare bulletin No. 2023-14 (25 January 2023).

2. Textbooks

Table 2.1 Textbooks(1)_McAninch & Lue, 2020

Smith and Tanagho's general urology
chapter 38 Disorders of the bladder, prostate, and seminal vesicles Benign Prostatic Hyperplasia ▶ Treatment After patients have been evaluated, they should be informed of the various therapeutic options for BPH. It is advisable for patients to consult with their physicians to make an informed decision on the basis of the relative efficacy and side effects of the treatment options. Specific treatment recommendations can be offered for certain groups of patients. For those with mild symptoms (IPSS score 0 ~ 7), watchful waiting is generally advised. On the other end of the therapeutic spectrum, absolute surgical indications include urinary retention refractory to medical management and attempts at catheter removal, recurrent urinary tract infection, recurrent gross hematuria, bladder stones, renal insufficiency, or large bladder diverticula. A. Watchful Waiting(...) B. Medical Therapy(...) C. Surgical Therapy 8. Water vapor therapy (Rezum)—This day procedure can be performed under sedation and can be used in men with a median lobe. During transurethral procedure water vapor is injected into the transition zone of the prostate. Using convective heat transfer, this causes acute necrosis as the water vapor condenses to water within the injected prostatic tissue. The area is irrigated with saline, which aids in cooling the tissue.

IPSS, international prostate symptoms score
Citation: McAninch JW, Lue TF. Smith and Tanagho's general urology: McGraw Hill Professional; 2020.

Table 2.2 Textbooks(2)_Partin et al., 2020

Campbell Walsh Wein Urology
chapter 146 Minimally Invasive and Endoscopic Management of Benign Prostatic Hyperplasia Non-LASER Options Convective Radiofrequency Water Vapor Thermal Therapy **Introduction.** Convective radiofrequency (RF) water vapor thermal therapy, marketed as Rezūm (NxThera, Inc., Maple Grove, MN), utilizes convective rather than conductive energy to ablate prostatic tissue. Rezūm utilizes RF power to generate thermal therapy in the form of water vapor, which is injected transurethrally into the transition zone of the prostate. The water vapor is injected at 103°C for 9 seconds at a pressure slightly above interstitial pressure, facilitating the dispersion of water vapor through the cellular interstices via convective energy. As the water vapor comes into contact with prostatic tissue, it condenses from steam to a liquid, releasing 540 calories of energy per gram onto the exterior cell membrane of the tissue, which causes cell death and tissue necrosis in a spherical ablative lesion of 1.5 to 2.0 cm, which has been confirmed by MRI and pathologic studies (Bhowmick et al., 2004, Dixon et al., 2015a,b; Hahn and Özişik, 2012, Mynderse et al., 2015). Unlike conductive energy, which is used in transurethral needle ablation (TUNA) and transurethral microwave thermotherapy (TUMT), convective energy requires the application of lower energy levels for a shorter duration to induce tissue necrosis (Bhowmick et al., 2004). Water vapor therapy only uses 4 kJ per procedure to produce cell necrosis compared with TUNA (20 kJ), TUMT (86 kJ), and other laser ablative technologies (250 kJ). An additional advantage of water vapor therapy over other minimally invasive technologies include its ability to respect the natural collagen barriers that compartmentalize the prostate, limiting its effect to the hyperplastic tissue of the transitional zone and precluding thermal effects outside of the desired treatment area. Lastly, water vapor therapy

preserves ejaculatory function, unlike transurethral vaporization of the prostate (TUVP) and TURP.

Technique.

The Rezūm system is composed of a generator with a handheld delivery device that includes a transurethral rigid cystoscope and an 18-gauge retractable needle with 12 vapor-emitting holes located at the tip of the delivery device (Fig. 146.7). It utilizes saline irrigation solution to enhance visualization and cool the surface of the urethra. The vapor needle penetrates the prostate at a fixed length of 10.25 mm and is deployed at the 3 o'clock and 9 o'clock positions starting 1 cm distal to the bladder neck, leaving approximately 1 cm between injection sites to create contiguous overlapping thermal lesions distally until the proximal edge of the verumontanum (Fig. 146.8). The procedure can also be modified for patients with a median lobe, giving it an advantage over other minimally invasive procedures. It was developed as a minimally invasive procedure intended for the outpatient setting. Water vapor thermal therapy can be performed with oral sedation, conscious sedation, or a regional prostate block.

Outcomes

Single-Cohort Studies.

In the first-in-man study reported by Dixon et al. (2015a), researchers analyzed histopathologic specimens of 7 patients treated with water vapor thermal therapy followed by suprapubic prostatectomy. Tissue staining of the extirpated adenomas demonstrated nonviable tissue from the steam injection, thrombosed vasculature, and general preservation of the prostatic urethral epithelium. The excised tissue did not show carbonization or heat fixation effects, and no thermal effects were observed outside of the prostate. A second cohort of 15 patients underwent water vapor thermal therapy followed by gadolinium-enhanced MRI 1 week after surgery. MRI confirmed treatment defects in the transition zone, with the largest defect volume of 35.1 cm^3 and no thermal effects observed in the peripheral zone.

A subsequent prospective, nonrandomized single-arm pilot study of 65 patients by Dixon et al. (2015b) demonstrated the safety and efficacy of water vapor thermal therapy in men with moderate to severe LUTS. Patients were evaluated at 1 week, 1 month, 3 months, 6 months, and 12 months post-treatment. The mean baseline was IPSS 21.6, QoL score 4.3, Qmax 7.9 mL/sec, and PVR 92.4 mL.Subjects demonstrated a sustained statistically significant improvement in IPSS, Qmax, and QoL at all time points out to 12 months. A total of 36 patients were catheterized immediately after the procedure or before discharge, with an average catheterization time of 5.6 days. An additional 11 patients were catheterized after release for an average catheter time of 4.3 days. IIEF scores did not change significantly from 1 to 12 months, and although PSA level initially increased at 1 week and 1 month, PSA returned to baseline values by 3 months. A total of 125 AEs were reported by 45 patients, the most common being urinary retention (33.8%), dysuria (21.5%), urinary urgency (20%), UTI (20%), hematuria (13.8%), and poor stream (13.8%).

Comparative Studies.

The largest reported study to date includes a randomized controlled trial of 197 men who underwent either water vapor thermal therapy (136 subjects) or sham procedure (61 subjects), with 53 patients from the sham group crossing over to the treatment group after 3 months. Inclusion criteria included prostate volume less than 80 g and PVR less than 250 mL; men who had urinary retention were excluded. The most recent 2-year data confirmed long-term efficacy with a 51% reduction in IPSS, 4.2 mL/ sec improvement in Qmax, and 50% improvement in QoL at 24 months (Roehrborn et al., 2017). Patients who underwent treatment of a median lobe showed similar improvement in IPSS and Qmax as those without a median lobe who underwent water vapor therapy (McVary et al., 2016a). Although there were initial changes in PSA (fivefold increase at 1 week), PSA returned to baseline by 3 months (Mynderse et al., 2015).

Sexual function was assessed using IIEF and Male Sexual Health Questionnaire-Ejaculatory Dysfunction (MSHQ-EjD) scores. No changes were noted in the treatment group at 3 months, and

Campbell Walsh Wein Urology

ejaculatory bother improved by 31% at 12 and 24 months (McVary et al., 2016b; Roehrborn et al., 2017). No de novo ED was reported in the treatment group, although six (4.4%) men reported decreased ejaculatory volume, and four men (2.9%) reported anejaculation. Authors stipulated that this may have occurred if the initial treatment was delivered too proximal to the bladder neck. For all subjects, the retreatment rate was 3.7% at 24 months (Roehrborn et al., 2017).

Complications.

The majority of patients who underwent treatment with water vapor thermal therapy did not report any adverse events. Of those patients who did report an adverse event, events were typically mild to moderate in severity and resolved within 3 weeks. Of the 189 subjects who underwent water vapor thermal therapy, four patients experienced a procedure-related serious adverse event, one developed de novo extended urinary retention, one experienced a bladder neck contracture and bladder stone at 6 months, one developed urosepsis after cystoscopy performed in the follow-up period, and one developed nausea and vomiting caused by alprazolam requiring overnight hospitalization for observation. The most common nonserious procedure-related adverse events included dysuria, hematuria, urinary frequency and urgency, hematospermia, and urinary tract infection (McVary et al 2016a; Roehrborn et al., 2017).

Conclusion.

Convective water thermal therapy ablation of the prostate for the treatment of LUTS/BPH utilizes new technology to provide durable efficacy evident at 2 years of follow-up. It offers the ability to target hyperplastic prostatic tissue within the transition zone, while avoiding delivery of high energy outside of the desired treatment area. Patients will benefit from improvement in clinical symptoms as measured by IIEF, Qmax, and QoL scores, including patients with a median lobe. Water vapor thermal therapy should be used cautiously in patients with a gland greater than 80 g and in men who have urinary retention. Water vapor thermal ablation therapy boasts a favorable safety profile and a low retreatment rate, and it can be used in the office or outpatient setting using minimal anesthesia, making it an attractive option for both providers and patients, particularly those concerned with preserving sexual function.

KEY POINTS

- Patients electing PUL or water vapor thermal ablation therapy should be warned that long-term durability is uncertain, though long-term uncontrolled data are available.
- In appropriate patients, PUL and water vapor thermal ablation therapy are less likely to affect erection and ejaculation than conventional therapies.

AE, adverse event; BPH, benign prostatic hyperplasia; ED; erectile dysfunction; IIEF, international index of erectile function; IPSS, international prostate symptoms score; LUTS, lower urinary tract symptoms; MRI, magnetic resonance imaging; MSHQ-EjD, male sexual health questionnaire-ejaculation domain; PSA, prostate specific antigen; PUL, prostatic urethral lift; PVR, post-void residual; Qmax, maximum flow rate; QoL, quality of life; RF, radiofrequency; TUMT, transurethral microwave thermotherapy; TUNA, transurethral needle ablation; TURP, transurethral resection of the prostate; TUVP, transurethral vaporization of the prostate

Citation: Partin AW, Wein AJ, Kavoussi LR, Peters CA, Dmochowski RR. Campbell Walsh Wein Urology, E-Book: Elsevier Health Sciences; 2020.

3. Guidelines

Table 3.1 Guidelines(1)_CUA 2022, 2018

Canadian Urological Association guideline: Male lower urinary tract symptoms/ benign prostatic hyperplasia: 2022
2.4. Surgical therapy 2.4.7. Minimally invasive techniques **Convective water vapour energy ablation**: Ablations using the Rezum® system (uses the thermodynamic principle of convective energy transfer) report significant improvement of IPSS and Qmax at three months and sustained until 12 months(McVary et al., 2015), with preservation of erectile and ejaculatory function(McVary et al., 2016). Recent five-year results have confirmed durability of the positive clinical outcomes, with a 57% reduction in IPSS, 45% increase in quality of life, and 44% increase in Qmax. Surgical retreatment rate is 4.4% at five years(McVary et al., 2021). → **We suggest that the Rezum system of convective water vapor energy ablation may be considered an alternative treatment for men with LUTS interested in preserving ejaculatory function with prostates < 80 cc, including those with a median lobe (conditional recommendation, evidence level C).**
Canadian Urological Association guideline on male lower urinary tract symptoms/benign prostatic hyperplasia (MLUTS/BPH): 2018 update
2.4. Surgical therapy 2.4.6. New and emerging therapies **Convective water vapour energy ablation**: Ablation using the Rezum® system (uses the thermodynamic principle of convective energy transfer), report significant improvement of IPSS and Qmax at three months and sustained until 12 months with preservation of erectile and ejaculatory function. Reported two-year results have confirmed durability of the positive clinical outcome. → **We suggest that Rezum system of convective water vapour energy ablation may be considered an alternative treatment for men with LUTS interested in preserving ejaculatory function, with prostates < 80 cc, including those with median lobe (conditional recommendation based on moderate-quality evidence).**

BPH, benign prostatic hyperplasia; IPSS, international prostate symptoms score; LUTS, lower urinary tract symptoms; Qmax, maximum flow rate

Citation: Elterman D, Aubé-Peterkin M, Evans H, Elmansy H, Meskawi M, Zorn K, et al. UPDATE – 2022 Canadian Urological Association guideline on male lower urinary tract symptoms/benign prostatic hyperplasia (MLUTS/BPH). Can Urol Assoc J. 2022:16.

Nickel JC, Aaron L, Barkin J, Elterman D, Nachabé M, Zorn KC. Canadian Urological Association guideline on male lower urinary tract symptoms/benign prostatic hyperplasia (MLUTS/BPH): 2018 update. Can Urol Assoc J. 2018;12(10):303-12.

Table 3.2 Guidelines(2)_EAU 2022

Management of Non-Neurogenic Male Lower Urinary Tract Symptoms (LUTS), incl. Benign Prostatic Obstruction (BPO): European Association of Urology Guidelines 2022
5.3 Surgical treatment 5.3.4 Alternative ablative techniques 5.3.4.3 Alternative ablative techniques under investigation 5.3.4.3.1 Convective water vapour energy (WAVE) ablation: The Rezum system Mechanism of action: The Rezum system uses radiofrequency power to create thermal energy in the form of water vapour, which in turn deposits the stored thermal energy when the steam phase shifts to the liquid phase upon cell contact. The steam disperses through the tissue interstices and releases stored thermal energy onto prostatic tissue effecting cell necrosis. (...) Efficacy: In a multicentre RCT, 197 men were enrolled and randomised in a 2:1 ratio to treatment with water vapour energy ablation or sham treatment(McVary et al., 2016). At three months relief of symptoms, measured by a change in IPSS and Qmax were significantly improved and maintained compared to the sham arm, although only the active treatment arm was followed up to twelve months. No relevant impact was observed on PVR. Quality of life outcome was significantly improved with a meaningful treatment response of 52% at twelve months. Further validated objective outcome measures such as BPH impact index (BPHII), Overactive Bladder Questionnaire Short Form for OAB bother, and impact on QoL and ICS Male Item Short Form Survey for male incontinence demonstrated improvement of symptoms at three months follow-up with sustained efficacy throughout the study period of twelve months. The reported two-year results in the Rezum cohort arm of the same study and the recently reported four-year results confirmed durability of the positive clinical outcome after convective water vapour energy ablation(Roehrborn et al., 2017; McVary et al., 2019). Surgical retreatment rate was 4.4% over four years(McVary et al., 2019). A Cochrane review found no studies comparing convective radiofrequency water vapour thermal therapy to any other active treatment form, such as TURP(Kang et al., 2020). Tolerability and safety: Safety profile was favourable with adverse events documented to be mild-to-moderate and resolving rapidly. Preservation of erectile and ejaculatory function after convective water vapour thermal therapy was demonstrated utilising validated outcome instruments such as IIEF and Male Sexual Health Questionnaire-Ejaculation Disorder Questionnaire(McVary et al., 2016). Practical considerations: There are two SRs of the Rezum cohort studies. One concludes that Rezum provides improvement in BPH symptoms that exceeds established minimal clinically important difference thresholds, preserves sexual function, and is associated with low surgical retreatment rates over four years. Therefore, suggesting that it may be a valuable addition to the urological armamentarium to treat LUTS in men with BPH(Miller et al., 2020). The other, a Cochrane review reported that the certainty of evidence ranged from moderate to very low, with study limitations and imprecision being the most common reasons for down-grading of the evidence(Kang et al., 2020). Randomised controlled trials against a reference technique are needed to confirm the first promising clinical results and to evaluate mid- and long-term efficacy and safety of water vapour energy treatment.

BPH, benign prostatic hyperplasia; BPHII, benign prostatic hyperplasia impact index; ICS, international continence society; IIEF, international index of erectile function; IPSS, international prostate symptoms score; LUTS, lower urinary tract symptoms; OAB, overactive bladder; PVR, post-void residual; Qmax, maximum flow rate; QoL, quality of life; RCT, randomised controlled trials; SR, systematic review; TURP, transurethral resection of the prostate

Citation: Gravas S, Cornu J, Gacci M, Gratzke C, Herrmann T, Mamoulakis C, et al. Management of non-neurogenic male lower urinary tract symptoms (LUTS), incl. benign prostatic obstruction (BPO). Eur Urol. 2022.

Table 3.3 Guidelines(3)_AUA 2021

Management of Lower Urinary Tract Symptoms Attributed to Benign Prostatic Hyperplasia: AUA GUIDELINE
Water Vapor Thermal Therapy (WVTT)
36. WVTT should be considered as a treatment option for patients with LUTS/BPH provided prostate volume 30 ~ 80 cc. (Moderate Recommendation; Evidence Level: Grade C)
WVTT utilizes convective radiofrequency to create stored thermal energy in the form of steam, which is delivered transurethrally via a specialized device into the transition zone. The steam travels through the transition zone, denaturing tissue and thereby ablating the adenoma to create an opening. A double-blind RCT (n = 197) compared WVTT (also referred to as transurethral destruction of prostate tissue by radiofrequency generated water thermotherapy) with SHAM(McVary et al., 2016a; McVary et al., 2016b; Roehrborn et al., 2017). Mean age of study participants was 63 years. Patients had a mean baseline IPSS of 22 and a mean prostate volume of 45 cm^3. The study excluded men with prostate volume < 30g and > 80g and did not exclude men with obstructing middle lobes or median bars. Response to treatment through 3 months, based on an improvement in IPSS of ≥ 30% or ≥ 8 points, was significantly greater in the WVTT group (74%) compared to the SHAM group (31%) (RR: 2.4; 95% CI: 1.6, 3.5). Mean changes from baseline in IPSS and IPSS-QoL at 3 months were greater in the WVTT group compared to the SHAM group with a MDD of > 3 points (MD: -6.9; 95% CI: -9.1, -4.8). Three-year results showed sustained improvements for the IPSS, IPSS-QoL, and Q max, with scores remaining significantly improved from baseline(McVary et al., 2018); Q max improvement was > 50% from 3 to 24 months and 39% at 36 months(Bent et al., 2006). At 36 months in the intent-to-treat population of the original 136 participants, mean change from baseline in IPSS was -11.0 points and the mean score was 10.4 points, representing a 50% improvement from baseline. Mean IPSS-QoL was improved from baseline by 49% at 3 years.
37. WVTT may be offered as a treatment option to eligible patients who desire preservation of erectile and ejaculatory function. (Conditional Recommendation; Evidence Level: Grade C)
Compared to many other surgical interventions, WVTT has a higher likelihood of preserving sexual function. In the RCT comparing WVTT to SHAM, the original 136 patients randomized to WVTT are expected to be followed for five years(McVary et al., 2016b). Few harms occurred in the WVTT group between months 3 and 12. A decrease in ejaculatory volume was reported by 2% of participants(McVary et al., 2016a; McVary et al., 2016b; Roehrborn et al., 2017; McVary et al., 2018). At 36 months, no de novo ED was reported, but dysuria was reported by 1% of participants(McVary et al., 2016a; McVary et al., 2016b; Roehrborn et al., 2017; McVary et al., 2018). At 48 months, there was a significant change in IIEF-EF scores compared to baseline (p = 0.03), but there was not a significant change at the other follow-up intervals(McVary et al., 2019). Function scores associated with ejaculation, assessed by the MSHQ-EjD, were significantly improved at 36 and 48 months following treatment (p = 0.005 and p = 0.003) but not at 12 and 24 months(McVary et al., 2018). Bother scores associated with ejaculation, assessed by the MSHQ-EjD, were significantly improved at 12, 24, and 36 months but not at 48 months following treatment(McVary et al., 2019).

BPH, benign prostatic hyperplasia; CI, confidence interval; ED; erectile dysfunction; IIEF-EF, international index of erectile function-erectile function; IPSS, international prostate symptoms score; IPSS-QoL, IPSS quality of life; LUTS, lower urinary tract symptom; MD, mean difference; MDD, minimally detectable difference; MSHQ-EjD, male sexual health questionnaire-ejaculation domain; Qmax, maximum flow rate; RCT, randomized controlled trials; RR, relative risk; WVTT, water vapor thermal therapy

Citation: Lerner LB, McVary KT, Barry MJ, Bixler BR, Dahm P, Das AK, et al. Management of lower urinary tract symptoms attributed to benign prostatic hyperplasia: AUA guideline part II—surgical evaluation and treatment. J Urol. 2021;206(4):818-26.

Table 3.5 Guidelines(3)_AUA 2018 ~ 2020

Surgical Management of Lower Urinary Tract Symptoms Attributed to Benign Prostatic Hyperplasia: AUA Guideline Amendment 2020
Statement 18. Water vapor thermal therapy may be offered to patients with LUTS attributed to BPH provided prostate volume < 80g. (Moderate Recommendation; Evidence Level: Grade C). Statement 19. Water vapor thermal therapy may be offered to eligible patients who desire preservation of erectile and ejaculatory function. (Conditional Recommendation; Evidence Level: Grade C).
Surgical Management of Lower Urinary Tract Symptoms Attributed to Benign Prostatic Hyperplasia: AUA Guideline Amendment 2019
17. Water vapor thermal therapy may be offered to patients with LUTS/BPH provided prostate volume < 80g; however, patients should be counseled regarding efficacy and retreatment rates. (Conditional Recommendation; Evidence Level: Grade C). 18. Water vapor thermal therapy may be offered to eligible patients who desire preservation of erectile and ejaculatory function. (Conditional Recommendation; Evidence Level: Grade C).
Surgical Management of Lower Urinary Tract Symptoms Attributed to Benign Prostatic Hyperplasia: AUA Guideline 2018
17. Water vapor thermal therapy may be offered to patients with LUTS/BPH provided prostate volume < 80g; however, patients should be informed that evidence of efficacy, including longer-term retreatment rates, remains limited. (Conditional Recommendation; Evidence Level: Grade C) 18. Water vapor thermal therapy may be offered to eligible patients who desire preservation of erectile and ejaculatory function.(Conditional Recommendation; Evidence Level: Grade C)

BPH, benign prostatic hyperplasia; LUTS, lower urinary tract symptoms

Citation: Parsons JK, Dahm P, Köhler TS, Lerner LB, Wilt TJ. Surgical management of lower urinary tract symptoms attributed to benign prostatic hyperplasia: AUA guideline amendment 2020. J Urol. 2020;204(4):799–804.
Foster HE, Dahm P, Kohler TS, Lerner LB, Parsons JK, Wilt TJ, et al. Surgical management of lower urinary tract symptoms attributed to benign prostatic hyperplasia: AUA Guideline Amendment 2019. J Urol. 2019;202(3):592–8.
Foster HE, Barry MJ, Dahm P, Gandhi MC, Kaplan SA, Kohler TS, et al. Surgical management of lower urinary tract symptoms attributed to benign prostatic hyperplasia: AUA guideline. J Urol. 2018;200(3):612–9.

Table 3.6 Guidelines(4)_NICE 2020

Rezum for treating lower urinary tract symptoms secondary to benign prostatic hyperplasia: NICE 2020
1. Recommendations 1.1 Evidence supports the case for adopting Rezum for treating lower urinary tract symptoms (LUTS) caused by benign prostatic hyperplasia (BPH) in the NHS. Rezum relieves LUTS and improves quality of life. 1.2 Rezum is a minimally invasive procedure. It should be considered as a treatment option for people with: • moderate to severe LUTS (International Prostate Symptoms Score [IPSS] typically 13 or over) and • a moderately enlarged prostate (typically between 30 cm^3 and 80 cm^3). 2. The technology Technology 2.1 Rezum is water vapour (steam) therapy for treating lower urinary tract symptoms (LUTS) associated with benign prostatic hyperplasia (BPH). The technology uses water vapour to destroy excess prostate tissue with the aim of relieving symptoms. The water vapour is injected into the prostate through a single-use device attached to a

urological endoscope. The process is intended to disrupt cell membranes, leading to cell death and shrinking the prostate. The intention is to relieve obstructive symptoms without interfering with surrounding tissues that might impair sexual function.

The vapour is injected for 9 seconds during treatment. The number of times this has to be done in each lobe of the prostate depends on the length of the prostatic urethra. It can be customised to the configuration of the gland. A maximum number of 15 full injections can be done with each delivery device although fewer injections are needed for most treatments. The procedure is usually done in the NHS under general anaesthesia or local anaesthesia with sedation, and lasts up to 20 minutes.

Innovative aspects

2.2 Rezum differs from other prostate treatments because it uses water vapour thermal energy. It does not use a laser and can be used to treat the median or middle lobe.

Intended use

2.3 Rezum is intended for the treatment of prostates with volumes greater than 30 cm^3 (equivalent to 30 g).

2.4 The instructions for use state that Rezum is contraindicated for patients:

- with a urinary sphincter implant
- who have a penile prosthesis.

3. Evidence

Clinical evidence

Relevant evidence comes from 4 studies presented in 10 publications, including 1 randomised controlled trial

3.1 Four studies were relevant to the decision problem in the scope:

- 1 randomised controlled trial (5 publications: McVary et al. 2019, McVary and Roehrborn 2018, Roehrborn et al. 2017, McVary et al. 2016a, McVary et al. 2016b)
- 1 prospective observational study (3 publications: Mynderse et al. 2015; Dixon et al. 2015, Dixon et al. 2016)
- 2 retrospective observational studies (Mollengarden et al. 2018, Darson et al. 2017).

The randomised controlled trial was in 197 people with an International Prostate Symptom Score (IPSS) of 13 or more and an estimated prostate volume between 30 cm^3 and 80 cm^3, who did not have urinary retention and who had no previous surgical interventions for their prostate. The observational studies included people with prostate sizes from 20 cm^3 to 110 cm^3 who had the Rezum procedure. All are nonUK studies.

The evidence suggests that Rezum is clinically effective

3.2 The Rezum II study showed that Rezum was associated with statistically significant improvements in lower urinary tract symptoms (LUTS) compared with sham at the 3-month follow up. These improvements were maintained throughout 4 years of follow up. The treatment benefits of Rezum in relieving LUTS were also seen consistently in the observational studies. The incidence of sexual dysfunction after treatment with Rezum was low, with a few people reporting a decrease in ejaculatory function but little change in erectile function. Overall, the evidence base shows that Rezum is an effective treatment for LUTS in people with benign prostatic hyperplasia (BPH). Rezum also improved quality of life (McVary et al. 2019, Darson et al. 2017; Dixon et al. 2015 and 2016).

There is no evidence that directly compares Rezum with other interventions for BPH

3.3 None of the included studies compared Rezum with other commonly used treatments for BPH. Clinical experts suggested that more invasive treatments such as transurethral resection of the prostate (TURP) were likely to be associated with a more substantial relief of urinary symptoms than Rezum. But there is currently no direct evidence to support this. Similarly, there are no direct comparisons of Rezum with UroLift, holmium laser enucleation of the prostate (HoLEP), or

Rezum for treating lower urinary tract symptoms secondary to benign prostatic hyperplasia: NICE 2020

GreenLight laser. Expert opinion indicated that recruiting participants to clinical trials that directly compare different minimally invasive and invasive treatments is challenging because people often say they prefer to avoid more invasive treatment.

An indirect comparison suggests that Rezum is as effective as UroLift

3.4 In the absence of direct comparative evidence, the company did an indirect comparison of Rezum and UroLift to relieve LUTS. This was based on the results of the Rezum II study and the Luminal Improvement Following prostatic Tissue (LIFT) study (Roehrborn et al. 2017b). Both technologies are minimally invasive procedures to treat LUTS, and the trial designs and study populations were similar. The main exception was that the Rezum II study included people with median lobe obstruction (31.1% of study participants) while the LIFT study did not. Results from the 2 trials indicated that the therapeutic effects of Rezum and UroLift in relieving LUTS were similar. Retreatment rates were different in the 2 trials: 4.4% for Rezum at year 4 and 13.6% for UroLift at year 5.

The clinical experts consider Rezum to be a safe procedure

3.5 The Rezum II study reported 3 procedure-related serious adverse events in the 3-month follow up, including extended urinary retention, and nausea and vomiting, which were considered to be because of the sedative medication. An additional 3 procedure-related serious adverse events were reported with Rezum during the 3- to 12-month follow-up period, including bladder contracture, bladder stone and urosepsis after cystoscopy. The clinical experts did not identify any specific safety concerns with Rezum.

4. Committee discussion

Clinical-effectiveness overview

Rezum is an effective minimally invasive procedure with clinical benefits

4.1 The committee concluded that the evidence from the Rezum II study demonstrated the effectiveness of Rezum in relieving lower urinary tract symptoms (LUTS) associated with benign prostatic hyperplasia (BPH) with a sustained benefit up to 4 years after the procedure. The committee noted that this is supported by the results of the observational studies. The committee noted that there are no studies that directly compare Rezum with other treatments in relieving symptoms in people with BPH, but considered an indirect comparison between Rezum and UroLift, which was drawn from analogous trial data. This suggests that Rezum is at least as effective as UroLift over 4 years. The clinical experts explained that these 2 minimally invasive procedures are used in similar cohorts of populations in clinical practice and that, in their experience, both procedures provide a similar degree of symptom relief. They also noted that Rezum is versatile in treating different shapes of prostate.

Rezum should be used for men with moderate to severe LUTS with an estimated prostate volume of 30 cm^3 to 80 cm^3

4.2 The committee noted that there is 1 pivotal study that provides the evidence for the efficacy of Rezum. The clinical experts explained that Rezum II was a US study and designed to meet US Food and Drug Administration eligibility criteria. Its major inclusion criteria were: men aged 50 or over who have symptomatic BPH with an International Prostate Symptoms Score (IPSS) of 13 or greater, and with a prostate volume, measured by transrectal ultrasound, of 30 cm^3 to 80 cm^3. The committee concluded that there is limited evidence on the efficacy of Rezum in men outside this cohort. The clinical experts confirmed that, in their clinical practice, this cohort of patients corresponds closely to those that they treat with Rezum and that this encompasses approximately 75% to 85% of the overall population that need treatment to relieve LUTS. The clinical experts also explained that, for people with mild LUTS (IPSS less than 8), first-line treatment is medication or lifestyle change. For people with an estimated prostate volume 120 cm^3 and greater, more invasive surgical interventions are recommended.

Rezum is unlikely to damage surrounding tissue and nerves, and the risk of sexual dysfunction is low

Rezum for treating lower urinary tract symptoms secondary to benign prostatic hyperplasia: NICE 2020

4.3 The clinical experts explained that loss of sexual function is an important concern for people undergoing invasive treatment for LUTS because the invasive procedure is likely to damage nerves on the external surface of the prostate. They also explained that Rezum involves injecting steam into carefully directed and localised areas of the prostate from the inner, urethral surface of the prostate, and this may avoid possible damage to surrounding nerves. The committee considered that the published evidence suggests that sexual function is retained after treatment with the Rezum procedure. It did note, however, a high incidence of sexual inactivity in people included in the Rezum II study and that overall sexual function showed a tendency to decline during study follow up. The experts explained that there are different types of sexual dysfunction. They said that after treatment with Rezum erectile dysfunction is rare, but ejaculatory dysfunction has been reported. Overall, the committee concluded that the risk to sexual function is low with Rezum, and that this may be particularly important to people who are sexually active at the time of treatment. The committee was uncertain, however, about the impact of Rezum on longer-term sexual function because no data are available for longer than 4 years.

Quality of life is an important outcome when considering patient benefit

4.4 The evidence from the Rezum II study and observational studies indicated that treatment with Rezum with significant relief of LUTS is associated with a significant improvement in quality of life, which persists for up to 4 years of follow up. The clinical experts confirmed that, in their experience, people who underwent Rezum express a high level of satisfaction after the procedure.

Side effects and adverse events

Urinary tract infection is a common complication after Rezum

4.5 The clinical experts advised that complications after the Rezum procedure are similar to those after other procedures for LUTS because of BPH and include urinary tract infections (UTIs), bleeding, epididymitis and abscess. The clinical experts also explained that, after the Rezum procedure, a urinary catheter is left in place for 5 to 7 days to allow the dead prostate tissue to drain away. The need for catheterisation, combined with the presence of necrotic tissue, are considered by the clinical experts to be predisposing factors for developing UTIs and, more rarely, urosepsis. This risk is higher for Rezum than UroLift, which usually does not need a post-operative urinary catheter. The clinical experts estimated that the risk of UTIs associated with a urinary catheter is around 5% to 7%, so a short course of prophylactic antibiotics may be prescribed after the procedure. The committee heard that post-procedure UTI rates associated with Rezum may be difficult to record because patients may present to their GP for treatment. It also noted that antibiotic use was not reported in the Rezum II study. The committee concluded that UTI is a common complication after Rezum but the risk of UTI can be reduced using prophylactic antibiotics.

The rate of surgical reintervention is low with Rezum

4.6 The committee noted that the Rezum II study reported a 4.4% rate of surgical retreatment after Rezum over 4 years of follow up. The LIFT study reported a 13.6% rate of surgical retreatment after UroLift over 5 years of follow up. The clinical experts suggested that the average retreatment rate in their experience is low after Rezum, and that retreatment is most likely in the first year after the procedure. The clinical experts explained that, because there is no direct view of the prostate cavity during the Rezum procedure, additional transurethral resection of the prostate (TURP) is sometimes needed to remove residual prostate tissue after Rezum. Overall, the committee concluded that the retreatment rate with Rezum is low and compares favourably with similar treatments like UroLift.

Relevance to the NHS

The evidence for Rezum is broadly generalisable to the NHS

4.7 The clinical experts explained that Rezum is currently done in some NHS trusts and that there

Rezum for treating lower urinary tract symptoms secondary to benign prostatic hyperplasia: NICE 2020

has been an increased demand by people for this procedure in some centres. The committee noted that the published evidence for Rezum is from studies that were done outside the UK. Nonetheless, the clinical experts explained that the study population included in the Rezum II study is similar to the people that they treat with Rezum in their own practices in the NHS. The committee concluded that the evidence is generalisable to UK NHS practice.

NHS considerations overview

Rezum is a day surgery procedure that can be done under local anaesthetic with sedation but it may not be suitable for everyone

4.8 The clinical experts said there are currently 8 different treatments, including Rezum, available in the NHS for people with significant LUTS that have not responded to conservative therapy including medication and lifestyle changes. The clinical experts considered TURP to be the standard of care for LUTS secondary to BPH, but emphasised that treatments need to be offered to people on an individual basis guided by their individual circumstances. Key factors for consideration include: the availability of procedures in their local hospitals, age, prostate gland size and characteristics, and comorbidities. Rezum's advantages over some other technologies are that it is a minimally invasive procedure that can be done under local anaesthesia with sedation, and it takes only around 20 minutes. Despite this, the clinical experts estimated that around two thirds of procedures done in the NHS are under general anaesthetic. People usually do not need an overnight stay in hospital, however. The clinical experts said that Rezum should be avoided in people with prostatitis or confirmed prostate cancer, in people for whom day case treatment is impractical or unsafe, and if there's a risk of increased bleeding, for example if they're having anticoagulant treatment.

Rezum is used to treat patients with benign prostate enlargement but there is no consensus on how to measure prostate size

4.9 The clinical experts said that an enlarged prostate that causes LUTS as a result of prostatic obstruction is caused by prostatic hyperplasia, which is a benign histopathological diagnosis. The clinical experts explained that there is currently no consensus on how prostate size should be estimated or measured in UK clinical practice. They considered that normally imaging would be used to estimate prostate size before surgically invasive treatment. The clinical experts said that imaging modalities could complement information from rectal digital examination of the prostate. Common imaging tools include transrectal ultrasound, cystoscopy and MRI. On the basis of these measurements, the committee heard that Rezum is usually offered to people with moderate prostatic enlargement with a prostate that is typically estimated to be 30 cm^3 to 80 cm^3.

The Rezum procedure is easy to learn

4.10 The clinical experts explained that urologists need specialist training to do the Rezum procedure. This training is provided by the company and includes lectures and simulation training. The clinical experts suggested that Rezum is relatively easy to learn and that the training requirement is minimal. The committee concluded that the amount of training needed to carry out the Rezum procedure is reasonable.

BPH, benign prostatic hyperplasia; HoLEP, holmium laser enucleation of the prostate; IPSS, international prostate symptoms score; LUTS, lower urinary tract symptoms; MRI, magnetic resonance imaging; NHS, national health service; TURP, transurethral resection of the prostate; UTI, urinary tract infection

Citation: National Institue for Health and Care Excellence(NICE). Rezum for treating lower urinary tract symptoms secondary to benign prostatic hyperplasia. 2020. Available from URL: www.nice.org.uk/guidance/mtg49

Table 3.7 Guidelines(4)_NICE 2018

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

1 Recommendations

1.1 Current evidence on the safety and efficacy of transurethral water vapour ablation for urinary tract symptoms caused by benign prostatic hyperplasia is adequate to support the use of this procedure provided that standard arrangements are in place for clinical governance, consent and audit. Find out what standard arrangements mean on the NICE interventional procedures guidance page.

1.2 This procedure should only be done by a urologist with specific training in the procedure, who should carry out their initial procedures with an experienced mentor.

2 The condition, current treatments and procedure

The condition

2.1 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 peri-urethral 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.

Current treatments

2.2 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 the NICE clinical guideline on lower urinary tract symptoms in men). Potential complications of some of these surgical procedures include bleeding, infection, urethral strictures, incontinence and sexual dysfunction.

The procedure

2.3 Transurethral water vapour ablation is usually done as day-case surgery using local anaesthetic including a peri-prostatic block, 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. 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.

2.4 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.

3 Committee considerations

The evidence

3.1 To inform the committee, NICE did a rapid review of the published literature on the efficacy and safety of this procedure. This comprised a comprehensive literature search and detailed review of the evidence from 10 sources, which was discussed by the committee. The evidence included 1 randomised controlled trial (RCT) reported with 1, 2 and 3 years of follow-up in 4 publications, 1 comparative study (also including patients from the RCT) and 3 case series (1 of which was

Transurethral water vapour ablation for lower urinary tract symptoms caused by benign prostatic hyperplasia
reported in 3 publications), and is presented in table 2 of the interventional procedures overview. 3.2 The specialist advisers and the committee considered the key efficacy outcomes to be: improvement of lower urinary tract symptoms, urinary flow rate, and quality of life. 3.3 The specialist advisers and the committee considered the key safety outcomes to be: bleeding, infection, disorders of sexual function, and need for reintervention. 3.4 Fifteen commentaries from patients who had experience of this procedure were received, which were discussed by the committee. Committee comments 3.5 The committee was advised that the procedure may also be effective for patients with an enlarged median prostatic lobe. 3.6 Patients may need a urinary catheter for several days after the procedure. 3.7 The committee noted that this procedure is also known as transurethral water vapour thermal ablation or transurethral steam ablation. 3.8 Patient commentaries were all supportive of the procedure, and most people reported improvement in symptoms.

RCT, randomized controlled trials; TURP, transurethral resection of the prostate
Citation: National Institue for Health and Care Excellence(NICE). Transurethral water vapour ablation for lower urinary tract symptoms caused by benign prostatic hyperplasia[IPG625]. 2018. Available from URL: https://www.nice.org.uk/guidance/ipg625

Table 3.8 Guidelines(5)_JUA 2017

Clinical guidelines for male lower urinary tract symptoms and benign prostatic hyperplasia: Japanese Urological Association & Japanese Society of Internal Medicine
Surgical therapy **Water vapor** (Grade of recommendation: reserved) There is some evidence to support efficacy, although long-term efficacy is uncertain(McVary et al., 2016). It is not approved in Japan.

Reserved, No recommendation made
Citation: Homma Y, Gotoh M, Kawauchi A, Kojima Y, Masumori N, Nagai A, et al. Clinical guidelines for male lower urinary tract symptoms and benign prostatic hyperplasia. Int J Urol 2017;24(10):716–29.