NICE advice

Aquablation robotic therapy for lower urinary tract symptoms caused by benign prostatic hyperplasia

Medtech innovation briefing
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Summary

- The **technology** described in this briefing is Aquablation robotic therapy. It is used for transurethral water jet ablation for lower urinary tract symptoms caused by benign prostatic hyperplasia.
- The **innovative aspects** are that transurethral water jet ablation does not use heat to remove prostate tissue and the technology can be used with prostates of any shape and size.
- The intended **place in therapy** would be as an alternative to standard care for people with lower urinary tract symptoms caused by benign prostatic hyperplasia that needs surgical intervention.

- The **main points from the evidence** summarised in this briefing are from 5 studies: 1 randomised controlled trial, 2 prospective studies and 2 single-arm studies, including a total of 562 people with benign prostatic hyperplasia. They show that Aquablation therapy is as effective as transurethral resection of the prostate for the removal of prostate tissue for people with benign prostatic hyperplasia.
- **Key uncertainties** around the evidence or technology are that the initial cost of the technology is higher than comparator technologies, but the company claims that long-term cost savings are likely. Further direct comparative evidence comparing Aquablation therapy with other technologies is needed.
- **Experts advised** that the technology is innovative compared with standard care and offers additional benefits such as an increased ability to preserve sexual function and the potential to offer day-case procedures.
- The **cost** of Aquablation robotic therapy is £2,872 per patient, based on volume pricing. The capital cost is covered in this, which also includes a per patient consumable cost of £1,925 (excluding VAT).

The technology

Aquablation robotic therapy (Procept BioRobotics) is a technology used for the removal of obstructions for people with lower urinary tract symptoms (LUTS) caused by benign prostatic hyperplasia (BPH). The system consists of a robotic handpiece, console and conformal planning unit. Resection and removal of prostate tissue is done using a water jet from the robotic handpiece placed within the urethra. This method is known as transurethral water jet ablation. Transrectal ultrasound is used before the procedure to map out the region of the prostate to be resected and allow real-time imaging of tissue resection during the procedure. Positioning is confirmed using visual markers on a computer screen and the surgeon can plan the depth and angle of resection using the system software. Once the surgical mapping is complete, a high-speed jet of saline is delivered to the prostate at various flow rates based on the depth of penetration needed. The ablated tissue is aspirated through ports in the handpiece and can be used for histological analysis. After resection is completed, haemostasis is done around the bladder neck using focal thermal energy from a standard resectoscope. The procedure is usually done with the patient under general or spinal anaesthesia.

Innovations

Resection of prostate tissue using transurethral water jet ablation does not use heat, unlike other resection techniques, which reduces the risk of complications from thermal injury. Other advantages of the technology are that it can be used on prostates of any size and shape and has the potential to preserve sexual function.

Current care pathway

Mild LUTS caused by BPH is usually managed conservatively. Drugs such as alpha blockers and 5-alpha-reductase inhibitors may also be used. If these treatments have not worked, there are a range of surgical options that may be considered. These include transurethral resection of the prostate, transurethral vaporisation, holmium laser enucleation, transurethral incision of the prostate, insertion of prostatic urethral implants and prostatectomy.

The following publications have been identified as relevant to this care pathway:

- NICE guideline on managing LUTS in men
- NICE interventional procedures guidance on transurethral water jet ablation for LUTS caused by benign prostatic hyperplasia
- NICE interventional procedures guidance on insertion of prostatic urethral lift implants to treat LUTS secondary to benign prostatic hyperplasia
- NICE medical technologies guidance on the PLASMA system for transurethral resection and haemostasis of the prostate
- NICE medical technologies guidance on GreenLight XPS for treating benign prostatic hyperplasia.

Population, setting and intended user

Aquablation therapy is intended to be used to treat people with LUTS caused by BPH. The technology will be used by a urologist in secondary care when drug treatments and conservative management options have failed. The manufacturer provides a training program for Aquablation therapy at no additional cost, which is to be completed before using the system. Follow-up training via online modules and surgical observation is also

available. The company states that surgeons need approximately 10 to 12 cases to develop sufficient familiarity with the system.

Costs

Technology costs

The company estimates the cost per patient to deliver Aquablation therapy is £2,872.42. This is a volume-based price and includes the capital costs, with no separate robotic unit to purchase. This includes a per patient consumable cost of £1,925 (excluding VAT).

Costs of standard care

The cost of standard care is variable depending on the technology used. The costs per patient of some comparator technologies have been taken from supporting documentation in NICE's medical technologies guidance on GreenLight XPS for treating benign prostatic hyperplasia:

- Monopolar transurethral resection of the prostate £3,091.97
- Holmium laser enucleation of the prostate £3,056.66
- Greenlight £2,782.14.

The company claims that the technology is likely to be cost saving compared with standard care because of the following factors: reduced theatre time, reduced length of hospital stay, ability to provide the procedure as day case, reduced retreatment rates and reduced adverse events. But there is limited evidence to support these claims.

Resource consequences

Aquablation therapy is currently being done in 5 NHS centres. The company has estimated that approximately 28,000 people would be eligible for treatment with the technology each year.

Aside from purchasing the system and training staff, no changes in facilities or infrastructure are associated with adopting the technology.

Regulatory information

Aquablation therapy is a CE-marked class I, IIa and IIb medical device.

Equality considerations

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others.

The following equality issues were identified during the development of this briefing: Benign prostatic hyperplasia is most common in people aged over 50. Some people are more prone to prostate enlargement because they are overweight or have an underlying medical condition such as diabetes. Some people may not identify as men but have a prostate. Sex, age, disability and gender reassignment are protected characteristics under the Equality Act 2010.

Clinical and technical evidence

A literature search was carried out for this briefing in accordance with the interim process and methods statement. This briefing includes the most relevant or best available published evidence relating to the clinical effectiveness of the technology. Further information about how the evidence for this briefing was selected is available on request by contacting mibs@nice.org.uk.

Published evidence

Five studies are summarised in this briefing.

One multicentre randomised controlled trial of 181 people (Gilling et al. 2022) is included which compares outcomes for people with benign prostatic hyperplasia (BPH) who had either Aquablation therapy or transurethral resection of the prostate (TURP). There are also 2 single-centre single-arm prospective studies (Whiting et al. 2021 and Desai et al. 2018) which assess the use of Aquablation therapy in people with BPH. A single-arm study carried out at multiple centres across 5 countries is included (Bach et al. 2020). The other study is also a multicentre single-arm study (Zorn et al. 2021), which focuses on a specific

patient subgroup, that is people with large prostates.

Three other studies related to the technology were also identified, but not summarised in this briefing. One study (Gloger et al. 2021) compares the haemostasis of Aquablation therapy with holmium laser enucleation of the prostate. One is a retrospective study (Elterman et al. 2021a) including 2,089 people who underwent Aquablation therapy across 11 countries in Asia, Europe and North America. This study aimed to show how the introduction of focal bladder neck cautery is associated with lower rates of post-procedure bleeding. The other is a meta-analysis (Elterman et al. 2021b) of 425 people who had Aquablation therapy for lower urinary tract symptoms (LUTS) caused by BPH in various prostate anatomies. This meta-analysis includes some of the studies summarised in this briefing.

The clinical evidence and its strengths and limitations are summarised in the overall assessment of the evidence.

Overall assessment of the evidence

The evidence base for Aquablation therapy consists of a randomised controlled trial comparing the technology directly with TURP, and several smaller studies including a single-arm study of people who had Aquablation therapy. The outcomes reported include prostate-health-related outcomes after the procedure, such as urinary flow rates and the International Prostate Symptom Score (IPSS), as well as time taken to complete the procedure, rate of complications which require retreatment, and preservation of sexual function. More evidence is needed to support some of the claimed benefits of the technology, such as reduced theatre time, reduced length of hospital stay, ability to provide day-case procedures, reduced retreatment rates and reduced adverse events. The studies have been done in a wide range of locations, including in the UK. Although the evidence base includes a randomised controlled trial comparing Aquablation therapy against standard care, including TURP, there is a need for further comparative studies comparing Aquablation therapy with other technologies used in current practice, such as holmium laser enucleation of the prostate. Relative to similar technologies for this indication, the total number of studies is small. But there are a number of ongoing studies which may address gaps in the current evidence base.

Gilling et al. (2022)

Study size, design and location

A double-blinded multicentre prospective randomised controlled trial of 181 people with BPH-related LUTS. The study was done in the US, Australia, New Zealand and the UK.

Intervention and comparator

Aquablation therapy, compared with TURP.

Key outcomes

Procedure times, defined as first instrument introduction to insertion of catheter, were similar at 40 minutes for Aquablation and 36 minutes for TURP. Mean resection time was found to be significantly lower in the Aquablation group at 4 minutes compared with 27 minutes for TURP ($p<0.0001$). One Aquablation patient required a blood transfusion, but no TURP patient did. Mean length of hospital stay was 1.4 days in both groups and the urinary catheter was removed at a median of 1 day after surgery in both groups. Procedure-related anejaculation was less common after Aquablation (7%) than TURP (25%), $p=0.0004$.

BPH symptoms were measured using the IPSS. Score improvements were similar across both groups at 12 months, with a reduction of 15.1 points after Aquablation or TURP. Mean maximum urinary flow rates increased significantly ($p=0.863$) in both groups. At 1 year, prostate-specific antigen was reduced significantly in both groups by 1 point ($p<0.01$). Rates of surgical retreatment for BPH within 1 year from the study procedure were 1.5% for TURP and 2.6% for Aquablation therapy, though this difference was not found to be significant.

At 5-year follow up, mean IPSS reduction was 15.1 in the Aquablation group and 13.2 in the TURP group ($p=0.2764$). For people with prostates larger than 50 ml, IPSS reduction was 3.5 points greater in the Aquablation group compared with the TURP group ($p=0.0123$). Peak urinary flow rates showed a mean improvement of 8.7 ml/s or 125% improvement for the Aquablation group, compared with 6.3 ml/s or 89% improvement for TURP. After 5 years, 6% of Aquablation patients needed an additional BPH therapy as a result of recurrent LUTS, whereas 12.3% of people in the TURP arm required additional BPH therapy.

Strengths and limitations

There were many strengths of this study design: people were randomised to either study treatment, people were recruited from multiple centres in different geographical locations, and blinding was preserved until 3 years of follow up. A limitation of the study was that there was a large drop-out after 3-year follow up, which the authors attributed to the impact of the COVID-19 global pandemic. The study authors did not specify the method used or the name of the technology for TURP. The study was also funded by the manufacturer.

Zorn et al. (2021)

Study size, design and location

A multicentre prospective study of 101 people with BPH symptoms and large prostates (80 to 150 cm^3). The study was done in the US and Canada.

Intervention and comparator

Aquablation therapy, no comparator.

Key outcomes

Maximum urinary flow rate increased from 8.7 cc/s to 18.5 cc/s. Post-void residual urinary volume decreased from 131 cm^3 to 51 cm^3 at 3 years. Mean serum prostate-specific antigen also decreased from 7.1 at baseline to 5.0 at 3 years. At 3-year follow up, 6% of treated patients needed BPH medication and an additional 3% required surgical retreatment for LUTS. Subgroup analysis was done for people with moderate symptoms compared to people with severe symptoms. No significant difference was found in any efficacy measure between the subgroups.

Strengths and limitations

This was a prospective study carried out across multiple centres, with scheduled pre-operative and post-operative visits and assessments. Strengths of the study were that it focused on people with large prostates and included follow up for 3 years. A limitation of the study was the lack of a control group, which prevented direct comparison with other treatment approaches. In addition, the study authors did not present results relating to the

procedure itself, such as time taken for resection and average time for the entire procedure.

Bach et al. (2020)

Study size, design and location

A multicentre prospective single-arm trial of 178 people with BPH-related LUTS. The study was done in Germany, New Zealand, Lebanon, Australia and the UK.

Intervention and comparator

Aquablation therapy, no comparator.

Key outcomes

Mean duration of the procedure was 24 minutes, while the total duration of anaesthesia was 50 minutes. Operative time and anaesthesia duration increased by 0.13 minutes per cubic centimetre of prostate tissue and 0.2 minutes per cubic centimetre of prostate tissue, respectively. Median catheterisation time after surgery was 1.9 days and average length of hospital stay was 2.2 days. Five patients (2.7%) underwent blood transfusion in the first week after the procedure and 14 patients (7.9%) were taken back to the operating room for post-procedure bleeding, after which haemostasis was achieved with cautery.

Mean IPSS significantly improved from 21.7 at baseline to 7.1 at 3-month follow up and 6.4 at 12-month follow up ($p<0.0001$). Mean quality-of-life scores improved from 4.7 at baseline to 1.5 at 3-month follow up and 1.4 at 12-month follow up ($p<0.0001$). Follow-up IPSS scores were found to be independent of baseline IPSS. Maximum urinary flow rate increased from 9.9 cc/s to 20.3 cc/s at month 3 and 20.8 cc/s at month 12. Post-void residual also improved from 108 to 47 at 3 months.

Strengths and limitations

Advantages of the study include its prospective multicentre design and recruitment of patients in a non-clinical trial setting. The study involved surgeons with both high and low levels of experience with the Aquablation procedure, and similar levels of symptom relief were seen independent of surgical experience. The lack of a control group and relatively short-term efficacy follow up can be classed as limitations. The study was funded by the

manufacturer.

Whiting et al. (2021)

Study size, design and location

Single centre study of 55 people with BPH having Aquablation therapy, with 12-month follow-up. The study was done in the UK.

Intervention and comparator

Aquablation therapy, no comparator.

Key outcomes

Mean time taken for the procedure was 26.9 minutes. Tissue resection time was not reported. A significant reduction was seen in mean prostate volume from 58.2 cm^3 to 33.2 cm^3 ($p<0.0001$). At 12-month follow up, maximum urinary flow rate showed significant improvements from 9.9 ml/s to 23.9 ml/s. Mean IPSS decreased from 21.7 to 6.1 and mean IPSS quality-of-life score also decreased from 4.8 to 1.4; both results were significant ($p<0.0001$). There was no significant change in scores for erectile function and ejaculatory dysfunction. Clavien grade 2 complications occurred in 14.5% of people.

Strengths and limitations

A significant strength of the study was that it was done in the UK with 1-year follow up. Limitations include the lack of a comparator and the relatively small study population.

Desai et al. (2018)

Study size, design and location

Single centre study of 47 people with BPH having Aquablation therapy, with 3-month follow up. The study was done in India.

Intervention and comparator

Aquablation therapy, no comparator.

Key outcomes

Mean time taken for the procedure was 35 minutes, and tissue resection time was 4 minutes. The mean hospital stay was 3.1 days, and mean duration for urethral catheterisation was 1.9 days. At 3-month follow up, the mean IPSS decreased from 24.4 at baseline to 5.0. Mean IPSS quality-of-life score also decreased from 4.5 to 0.3. Peak urinary flow rate increased from 7.1 ml/s to 16.5 ml/s, and post-void residual urine volume decreased from 119 ml to 43 ml. All of the results at 3-month follow up were found to be significantly different ($p<0.01$).

Strengths and limitations

A significant strength of the study was that a range of surgeons carried out the procedures, some of whom had no prior experience with the technology. There was no long-term follow up as most patients were located in rural areas, so only short-term safety and efficacy could be recorded. These results showed consistency with 3-month results reported in previous studies. The study did not include questions related to sexual function.

Sustainability

The company claims the technology will reduce energy consumption and resource use by reducing length of hospital stay and operating time. There is no published evidence to support these claims.

Recent and ongoing studies

- WATER III: Aquablation versus transurethral laser enucleation of large prostates (80 ml to 180 ml) in benign prostatic hyperplasia. ClinicalTrials.gov identifier: NCT04801381. Status: recruiting. Indication: BPH with urinary obstruction with other LUTS. Devices: Aquablation. Estimated completion date: December 2027. Country: Germany.

- Aquablation versus holmium laser enucleation of the prostate in the treatment of benign prostatic hyperplasia in medium to large sized prostates: a prospective randomised trial. ClinicalTrials.gov identifier: NCT04560907. Status: recruiting. Indication: BPH. Devices: Aquablation. Estimated completion date: November 2027. Country: Germany.
- Aquablation in benign prostatic hyperplasia in Canada. ClinicalTrials.gov identifier: NCT05169892. Status: recruiting. Indication: BPH. Devices: Aquablation. Estimated completion date: December 2026. Country: Canada.
- AQUA: Aquabeam robotic system and ultrasound accessories. ClinicalTrials.gov identifier: NCT05157529. Status: not yet recruiting. Indication: BPH. Devices: Aquablation. Estimated completion date: February 2024. Country: Canada.

Expert comments

Comments on this technology were invited from clinical experts working in the field and relevant patient organisations. The comments received are individual opinions and do not represent NICE's view.

Four out of 5 experts were familiar with or had used this technology before.

Level of innovation

All of the experts agreed that this is a novel technology. Two of the experts said that Aquablation therapy is an ultrasound-guided procedure with advanced planning software to draw contours specific to each individual's anatomy. This feature helps protect key areas of the prostate, such as the ejaculatory ducts, to maintain normal ejaculation. Two experts also said that the technology uses an automated robotic approach to remove prostate tissue via a water jet rather than heat, which most other technologies use.

Potential patient impact

Three experts said that the technology is a safer and more effective treatment for patients, because it carries a lower risk of negative side effects relating to sexual function. The technology has been shown to offer improved rates of maintenance of ejaculation and erection. Two experts mentioned the importance of being able to use the technology with

patients who have large or complex prostate anatomy. Both the shape and the size of the prostate are a limiting factor for other technologies used in standard care. Three experts also commented on the shorter procedure time compared with standard care, and the potential to provide day-case procedures. All of the experts said that people with large prostates and those who are keen to preserve sexual function would particularly benefit from using this technology.

Potential system impact

One expert said that the technology has the potential to replace current standard care because of its efficacy and potential to be used with nearly all sizes of prostate. Three other experts felt that the technology would be used in addition to standard care. The consensus was that the technology has the potential to replace transurethral resection of the prostate and will challenge holmium laser enucleation of the prostate for larger prostates. All of the experts agreed that the initial capital outlay and consumable costs are higher compared with standard care. Some of the experts highlighted the potential cost savings based on the efficiency gains related to completing more procedures per day and reducing hospital stay.

General comments

All of the experts commented that specific training is required before doing procedures and that this is provided by the company. Ongoing training through observation and onsite support is also in place. The experts suggested that the learning curve is relatively short and that no changes to clinical facilities are needed to do the procedure. It was also highlighted that the initial blood transfusion rate following Aquablation therapy was high, but the introduction of focal bladder neck cautery has addressed this issue with a much lower rate of blood loss and rectal perforation being observed.

Expert commentators

The following clinicians contributed to this briefing:

- Dr Evangelos Mazaris, consultant urological surgeon at North West Anglia NHS Foundation Trust. Did not declare any interests.

- Dr Adam Cox, consultant urological surgeon at Aneurin Bevan University Health Board. Did not declare any interests.
- Dr Neil Barber, consultant urological surgeon at Frimley Health NHS Foundation Trust. Contracted as a consultant by the manufacturer.
- Professor Richard Hindley, consultant urologist at Hampshire Hospitals NHS Foundation Trust. Did not declare any interests.
- Dr Philip Charlesworth, consultant urological surgeon at Royal Berkshire Hospital. Did not declare any interests.

Development of this briefing

This briefing was developed by NICE. The interim process and methods statement sets out the process NICE uses to select topics, and how the briefings are developed, quality-assured and approved for publication.

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