NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of prostatic urethral temporary implant insertion 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. In this procedure, local anaesthesia or light sedation is used and a tiny wire device (implant) is inserted into the urethra. It expands to create new permanent channels in the lining of the urethra. It stays in place for 5 to 7 days and is then removed. The aim is to increase the flow of urine.

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Abbreviations

Word or phrase	Abbreviation
Benign prostatic hyperplasia	BPH
Confidence interval	CI
International Index of Erectile Function	IIEF
International Prostate Symptom Score	IPSS
Interquartile range	IQR
Lower urinary tract symptoms	LUTS
Postvoid residual	PVR
Sexual Health Inventory for Men	SHIM
Standard deviation	SD
Transurethral resection of the prostate	TURP
Visual analogue scale	VAS

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 professional opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This overview was prepared in November 2021.

Procedure name

- Prostatic urethral temporary implant insertion for lower urinary tract symptoms caused by benign prostatic hyperplasia.

Professional societies

- British Association of Urological Surgeons.

Description of the procedure

Indications and current treatment

LUTS caused by BPH commonly affect men aged over 50. BPH results from an increase in number of stromal and epithelial cells. These cells are typically 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.

NICE's guideline on lower urinary tract symptoms in men describes current treatment options. Mild symptoms are usually managed conservatively. Medicines such as alpha blockers and 5-alpha-reductase inhibitors may also be used. If other treatments have not worked, there are several possible surgical options, including TURP, transurethral vaporisation, holmium laser enucleation, prostatic urethral lift implant insertion, prostatic artery embolisation and prostatectomy. Potential complications of some of these surgical procedures include bleeding, infection, urethral strictures, incontinence and sexual dysfunction.

What the procedure involves

The aim of prostatic urethral temporary implant insertion is to relieve symptoms of BPH by creating new channels in the urethra to increase the flow of urine. The aim of using a temporary implant is to avoid complications from an implant left in place long term.

Local anaesthesia or light sedation is used. A folded device made from nitinol is inserted into the prostatic urethra under direct visualisation using a cystoscope. The device is opened in the urethra. Over the following days, the pressure applied by struts in the device creates areas of ischaemia in the prostatic urethra and bladder neck. This makes new longitudinal channels through which urine can flow. After 5 to 7 days, lidocaine gel and a flexible silicone extraction catheter are inserted into the urethra and the device is removed. Insertion and removal of the device are both done as day-case procedures.

Outcome measures

IPSS

The IPSS is a validated questionnaire used to assess symptoms of BPH. It is also referred to as the American Urological Association BPH Symptom Score Index. It includes questions on 7 dimensions during the previous month (feeling of incomplete bladder emptying, frequency, intermittency, urgency, weak stream, straining and nocturia) and scored from 1 to 5. Higher scores represent worse symptoms. An IPSS 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. The response yields a score for quality of life (ranging from 0 to 6, with 0 representing 'delighted' and 6 representing 'terrible').

IIEF

The IIEF questionnaire includes 15 questions divided into 5 domains: erectile function, orgasmic function, sexual desire, intercourse satisfaction and overall satisfaction. The total score ranges from 1 to 75, from worst to best.

SHIM

The SHIM questionnaire (also known as the IIEF-5) is a modified version of the 15-item IIEF. It has 5 questions and the total score ranges from 5 to 25, with lower scores indicating more severe erectile dysfunction.

Efficacy summary

Symptom improvement

In a randomised controlled trial of 185 patients, 79% who had a prostatic temporary implant insertion and 60% who had a sham procedure had an improvement in IPSS of 3.0 points or more at 3 months compared with baseline (p=0.029) in the intention-to-treat population. The mean improvement in IPSS was 9.0 points in the implant group and 6.6 points in the control group (p=0.063). At 12 months, the mean change in IPSS urinary symptoms score in patients who had a temporary implant inserted (per-protocol population) was -9.25 (95% CI -11.0 to -7.4, p<0.0001). The mean change in IIEF score was 4.5 (95% CI 0.2 to 8.8, p=0.01; Chughtai, 2021).

In a single-arm trial of 81 patients, the mean reduction in IPSS score in the intention-to-treat population was 9.2 at 4 weeks, 11.1 at 6 months, 11.2 at

12 months, 10.1 at 24 months and 10.3 at 36 months (p<0.0001 for all periods; Amparore, 2021).

In a single-arm trial of 70 patients, the mean change in IPSS urinary symptoms score was -11.7 at 4 weeks, -13.4 at 3 months and -12.7 at 6 months (p<0.01 for all periods). The Incontinence Symptom Index questionnaire total score changed by -0.5 at 4 weeks (p=0.21), and by -0.3 at 3 and 6 months (p=0.14; De Nunzio, 2020).

In a single-arm trial of 32 patients, the mean IPSS reduced by 39% at 3 weeks, 47% at 6 months, 45% at 1 year, 23% at 2 years and 19% at 3 years (p<0.001; Porpiglia, 2018).

Quality of life

In the randomised controlled trial of 185 patients, at 3 months, the mean IPSS quality-of-life score improved from 4.6 to 2.7 in the implant group and from 4.9 to 3.4 in the control group (p=0.264) in the intention-to-treat population. At 12 months, the mean change in IPSS quality-of-life score in patients who had a temporary implant inserted (per-protocol population) was -1.90 (95% CI -2.2 to -1.4, p<0.0001; Chughtai, 2021).

In the single-arm trial of 81 patients, the mean improvement in IPSS quality-of-life score was -1.68 at 4 weeks, -1.93 at 6 months, -2.06 at 12 months, -1.77 at 24 months and -1.78 at 36 months in the intention-to-treat population (p<0.0001 for all periods; Amparore, 2021).

In the single-arm trial of 70 patients, the mean change in IPSS quality-of-life score was -2.4 at 4 weeks, -2.5 at 3 months and -2.2 at 6 months (p<0.01 for all periods; De Nunzio, 2020).

In the single-arm trial of 32 patients, the median quality-of-life score was 2 at 24 and 36 months compared with 3 at baseline (Porpiglia, 2018).

Peak urinary flow rate

In the randomised controlled trial of 185 patients, at 3 months, the mean peak urinary flow rate improved from 8.7 ml/second to 13.1 ml/second in the implant group and from 8.5 ml/second to 11.4 ml/second in the control group (p=0.230) in the intention-to-treat population. At 12 months, the increase in peak urinary flow in patients who had a temporary implant inserted (per-protocol population) was 3.52 ml/second (95% CI 2.0 to 5.0, p<0.0001; Chughtai, 2021).

In the single-arm trial of 81 patients, the mean improvement in peak urinary flow rate was 4.63 ml/second at 4 weeks, 5.28 ml/second at 6 months,

5.97 ml/second at 12 months, 6.82 ml/second at 24 months and 6.15 ml/second 36 months in the intention-to-treat population (p<0.0001 for all periods; Amparore, 2021).

In the single-arm trial of 70 patients, the mean change in peak urinary flow rate was 5.8 ml/second at 4 weeks, 4.5 ml/second at 3 months and 4.6 ml/second at 6 months (p<0.01 for all periods; De Nunzio, 2020).

In the single-arm trial of 32 patients, the mean peak urinary flow increased by 37% at 3 weeks, 61% at 6 months, 67% at 1 year, 54% at 2 years and 41% at 3 years (p<0.001; Porpiglia, 2018).

PVR volume

In the randomised controlled trial of 185 patients, at 3 months, the mean PVR volume decreased from 60.8 ml to 59.4 ml in the implant group and increased from 61.9 ml to 66.9 ml in the control group (p=0.781) in the intention-to-treat population. At 12 months, the mean change in PVR volume in patients who had a temporary implant inserted (per-protocol population) was -0.16 ml (95% CI -24.6 to 24.3, p=0.9039; Chughtai, 2021).

In the single-arm trial of 81 patients, the mean change in postvoid volume was -21.44 ml at 4 weeks, -21.54 ml at 6 months, -27.69 ml at 12 months, -32.86 ml at 24 months and -36.11 ml at 36 months in the intention-to-treat population (p<0.001 for all periods; Amparore, 2021).

In the single-arm trial of 70 patients, the mean change in PVR volume was -19. ml at 4 weeks, -37.4 ml at 3 months and -22.6 ml at 6 months (p=0.13, 0.11 and 0.12; De Nunzio, 2020).

Sexual function

In the randomised controlled trial of 185 patients, the mean SHIM score improved by 0.45 points after 12 months (95% CI -1.0 to 1.9, p=0.3155) in patients who had a temporary implant inserted (per-protocol population). Results were not reported for the control arm (Chughtai, 2021).

In the single-arm trial of 70 patients, the mean improvement in ejaculatory function score on the Male Sexual Health Questionnaire was 1.5 at 4 weeks, 1.8 at 3 months and 2.0 at 6 months (p<0.01 for all periods). The SHIM score improved by 1.9 at 4 weeks, 2.3 at 3 months and 2.2 at 6 months (p=0.09, 0.07, 0.06; De Nunzio, 2020).

Need for medication

In the single-arm trial of 32 patients, all patients were able to stop LUTS-related medical therapy 3 months after the implantation. However, 3 patients (9%) needed it again within 12 or 24 months of treatment (Porpiglia, 2018).

Patient satisfaction

In the single-arm trial of 32 patients, the median Expanded Prostate Cancer Index Composite question 32 score was 5 (corresponding to extremely satisfied) throughout follow up. The differences at different time points were not statistically significant (p=0.180; Porpiglia, 2018).

Safety summary

Overall

There were 16 serious adverse events within 30 days of the procedure in 10 (8%) patients who had a temporary implant inserted and 2 serious adverse events in 2 (4%) patients who had a sham procedure in the randomised controlled trial of 185 patients. Serious procedure-related events were reported in 3 (2%) patients in the implant group (5 events). In total, there were 109 adverse events in 45 (38%) patients in the implant group, of which 81 were procedure related (Chughtai, 2021).

Dysuria

Dysuria within 30 days of the procedure was reported in 23% (27/118) of patients who had a temporary implant inserted and 9% (5/57) of patients who had a sham procedure in the randomised controlled trial of 185 patients (Chughtai, 2021).

Dysuria within 1 month of the procedure was reported in 7% (6/81) of patients in the single-arm trial of 81 patients (Amparore, 2021).

Dysuria was reported in 17% (12/70) of patients in the single-arm trial of 70 patients (De Nunzio, 2020).

Haematuria

Haematuria within 30 days of the procedure was reported in 14% (16/118) of patients who had a temporary implant inserted and no patients who had a sham procedure in the randomised controlled trial of 185 patients (Chughtai, 2021).

Haematuria within 1 month of the procedure was reported in 12% (10/81) of patients in the single-arm trial of 81 patients (Amparore, 2021).

Transient haematuria was reported in 19% (13/70) of patients in the single-arm trial of 70 patients. In addition, 1 patient had gross haematuria that was treated by endoscopic fulguration (De Nunzio, 2020).

Urinary urgency

Urinary urgency within 30 days of the procedure was reported in 5% (6/118) of patients who had a temporary implant inserted and 1 patient who had a sham procedure in the randomised controlled trial of 185 patients (Chughtai, 2021).

Urgency within 1 month of the procedure was reported in 11% (9/81) of patients in the single-arm trial of 81 patients (Amparore, 2021).

Urgency was reported in 13% (9/70) of patients in the single-arm trial of 70 patients (De Nunzio, 2020).

Urinary frequency

Urinary frequency syndrome within 30 days of the procedure was reported in 7% (8/118) of patients who had a temporary implant inserted and 1 patient who had a sham procedure in the randomised controlled trial of 185 patients (Chughtai, 2021).

Frequency was reported in 7% (5/70) of patients in the single-arm trial of 70 patients (De Nunzio, 2020).

Urinary incontinence

Transient urinary incontinence while the device was in place was reported in 8% (6/70) of patients in the single-arm trial of 70 patients (De Nunzio, 2020).

Urinary incontinence because of device displacement was reported in 1 patient in the single-arm trial of 32 patients. This resolved after the device was removed on day 1 after insertion (Porpiglia, 2018).

Urinary retention

Urinary retention within 30 days of the procedure was reported in 6% (7/118) of patients who had a temporary implant inserted and no patients who had a sham procedure in the randomised controlled trial of 185 patients. In addition, 1 patient had urinary retention between 1 and 3 months after implant insertion (Chughtai, 2021).

Urinary retention within 1 month of the procedure was reported in 10% (8/81) of patients in the single-arm trial of 81 patients (Amparore, 2021).

Acute urinary retention was reported in 4% (3/70) of patients in the single-arm trial of 70 patients, all of whom had treatment with temporary catheterisation (De Nunzio, 2020).

Urinary retention on the same day as device implantation was reported in 1 patient in the single-arm trial of 32 patients (Porpiglia, 2018).

Infection

Urinary tract infection within 30 days of the procedure was reported in 2% (2/118) of patients who had a temporary implant inserted and no patients who had a sham procedure in the randomised controlled trial of 185 patients. One patient who had a temporary implant inserted had urinary tract infection between 1 and 3 months after implant insertion. The other patient had a urinary tract infection between 3 and 12 months after implant insertion. In the same study, sepsis within 30 days of the procedure was reported in 1 patient who had a temporary implant inserted (Chughtai, 2021).

Urinary tract infection within 1 month of the procedure was reported in 6% (5/81) of patients in the single-arm trial of 81 patients (Amparore, 2021).

Genitourinary infection within 30 days of the procedure was reported in 6% (2/32) of patients in the single-arm trial of 32 patients, both of whom had treatment with antibiotics (Porpiglia, 2018).

Pain

Pain within 30 days of the procedure was reported in 1 patient who had a temporary implant inserted and no patients who had a sham procedure in the randomised controlled trial of 185 patients (Chughtai, 2021).

Pain within 1 month of the procedure was reported in 10% (8/81) of patients in the single-arm trial of 81 patients (Amparore, 2021).

Need for further treatment

Two patients had TURP or laser treatment (not further described) within 1 month of the primary procedure in the single-arm trial of 81 patients. A further 5 patients (6%) had TURP or laser treatment 1 to 12 months after the primary procedure (Amparore, 2021).

Anecdotal and theoretical adverse events

In addition to safety outcomes reported in the literature, professional experts 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, professional experts did not describe any additional anecdotal or theoretical adverse events.

The evidence assessed

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to prostatic urethral temporary implant insertion for LUTS caused by BPH. The following databases were searched, covering the period from their start to 25 October 2021: 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 inclusion criteria 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.

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.
Population	Patients with LUTS caused by BPH
Intervention/test	Prostatic urethral temporary implant insertion
Outcome	Articles were retrieved if the abstract contained information relevant to the safety and/or efficacy.
Language	Non-English-language articles were excluded unless they were thought to add substantively to the English-language evidence base.

List of studies included in the IP overview

This IP overview is based on 368 patients from 1 randomised controlled trial and 3 single-arm trials (Chughtai, 2021; Amparore, 2021; De Nunzio, 2020; Porpiglia, 2018).

Other studies that were considered to be relevant to the procedure but were not included in the main summary of the key evidence are listed in the appendix.

Summary of key evidence on prostatic urethral temporary implant insertion for lower urinary tract symptoms caused by benign prostatic hyperplasia

Study 1 Chughtai B (2021)

Study details

Study type	Randomised controlled trial
Country	US and Canada (16 sites)
Recruitment period	2015 to 2018
Study population and number	n=185 (128 prostatic urethral temporary implant, 57 sham control) Men with symptomatic BPH
Age	Mean 61.5 years (implant group), 60.1 years (sham group), p=0.1284
Patient selection criteria	Inclusion criteria: men 50 years or older, IPSS 10 or higher, peak urinary flow rate 12 mL/sec or less with a 125 mL voided volume, prostate volume between 25 and 75 cc, and normal urinalysis, complete blood count, and biochemistry. Excluded patients had a PVR volume more than 250 mL, obstructive median lobe, prostate specific antigen higher than 10 ng/ml or free PSA less than 25%, without a subsequent negative prostate biopsy, previous prostate surgery, prostate or bladder cancer, neurogenic bladder or sphincter abnormalities, or confounding bladder pathologies based on medical history, recent cystolithiasis or haematuria, active urinary tract infection, compromised renal function, severe respiratory disorders, known immunosuppression, active antithrombotic or antiplatelet treatment, cardiac disease, including arrhythmias and uncontrolled diabetes mellitus.
Technique	Device: second generation iTind (Medi-Tate Ltd, Israel) The sham procedure was the insertion and removal of an 18F silicon Foley catheter to simulate both the implantation and retrieval procedures. Throughout the procedure, the surgeon gave verbal description as if deploying the iTind device, after which the catheter was removed. A similar protocol was followed for the removal. Although the iTind device was deployed through a rigid cystoscope, a Foley catheter was used to minimise the risk of procedure-related morbidity. Patients in both the device and control groups were draped to prevent them from seeing the treating physician and the device. All patients on BPH-related medications started a wash-out period before implantation: 1 month for alpha-blockers and 6 months for 5-alpha-reductase inhibitors.
Follow up	12 months
Conflict of interest/source of funding	The study was sponsored by Medi-Tate Ltd. The corresponding author is a consultant for Medi-Tate Ltd, Olympus, Boston Scientific, and Medeon Bio.

Analysis

Follow up issues: Of the 128 patients randomised to have temporary implant insertion, 10 did not have the procedure. At the 3-month follow up, data was missing for 29% (34/118) of patients in the implant group and 28% (16/57) of patients in the control group. Of the 118 patients who had a temporary implant inserted, 12-month data was analysed for 78 (66%).

Study design issues: Prospective, randomised, controlled, multicentre, single-blinded study. Patients were randomised in 2:1 ratio to either temporary implant or control groups using permuted blocks stratified by centre by using a central electronic data program. The primary endpoint compared the percentage of patients with a reduction of at least 3 points in IPSS at 3 months between the groups. Unblinding of the sham arm was done at 3 months. Intention-to-treat analysis was used at 3 months and per protocol at 6 months. A sample size of 180 patients was estimated to provide at least 85% power to meet the study primary endpoint (with an expected response rate of 75% in the implant group and 51% in the sham group).

Study population issues: Baseline characteristics were similar among the 2 groups, except for the Charlson Comorbidity Index, with the implant group having a higher score (2.52 compared with 1.26, p<0.001).

Key efficacy findings

Number of patients analysed: 185 (128 prostatic urethral temporary implant insertion, 57 sham control)

Improvement in IPSS of 3 points or more at 3 months (intent-to-treat)
- Implant group=78.6%
- Control group=60%, p=0.029

Improvement in IPSS of 7 points or more at 3 months (intent-to-treat)
- Implant group=72.6%
- Control group=50%, p=0.048

97% of patients that responded to treatment at 3 months remained responders at 12 months.

Mean improvement in IPSS at 3 months (intent-to-treat)
- Implant group= -9.0 (SD 8.5)
- Control group= -6.6 (SD 9.5), p=0.063

Improvement in IPSS quality of life score from baseline to 3 months (intent-to-treat)
- Implant group=reduction from 4.6 (SD 1.3) to 2.7 (SD 1.8) at 3 months
- Control group=reduction from 4.9 (SD 1.0) to 3.4 (SD 2.0) at 3 months, p=0.264

Improvement in peak urinary flow rate from baseline to 3 months (intent-to-treat)
- Implant group=improved from 8.7 (SD 3.3) ml/sec to 13.1 (SD 7.1) ml/sec
- Control group=improved from 8.5 (SD 2.4) ml/sec to 11.4 (SD 5.3) ml/sec, p=0.230

Improvement in PVR volume from baseline to 3 months (intent-to-treat)
- Implant group=decreased from 60.78 (SD 56.35) ml to 59.44 (SD 56.43) ml
- Control group=increased from 61.9 (SD 54.2) ml to 66.9 (SD 65.1) ml, p=0.781

Functional results at 6 weeks (per protocol analysis), mean (SD)

Outcome	n (paired)	baseline	follow up	change	95% CI	p value
IPSS Urinary Symptoms Score	96	22.37 (6.92)	12.80 (7.40)	-9.57 (8.29)	-11.3 to -7.9	<0.0001
IPSS Quality of life	96	4.66 (1.31)	2.83 (1.88)	-1.83 (1.97)	-2.2 to -1.4	<0.0001
Qmax (mL/second)	73	8.01 (2.21)	13.33 (10.50)	5.32 (10.33)	2.9 to 7.7	<0.0001
PVR (mL)	73	65.08 (60.66)	49.90 (55.82)	-15.26 (63.88)	-30.3 to -0.3	0.0244
SHIM score	96	12.92 (7.49)	12.83 (8.06)	-0.10 (7.00)	-1.5 to 1.3	0.8165
IIEF score	96	36.86 (20.04)	40.31 (22.40)	3.47 (18.56)	-0.4 to 7.3	0.0738

Functional results at 3 months (per protocol analysis), mean (SD)

Outcome	n (paired)	baseline	follow up	change	95% CI	p value
IPSS Urinary Symptoms Score	80	22.38 (6.84)	12.57 (6.95)	-9.48 (8.49)	-11.4 to -7.6	<0.0001
IPSS Quality of life	80	4.55 (1.27)	2.54 (1.82)	-1.96 (1.86)	-2.3 to -1.4	<0.0001
Qmax (ml/s)	65	8.63 (2.71)	13.55 (6.40)	5.01 (6.39)	3.4 to 6.6	<0.0001
PVR (ml)	65	60.78 (56.35)	59.44 (56.43)	-2.20 (56.59)	(-16.7 to 12.3)	0.7407
SHIM score	80	13.40 (7.26)	13.70 (7.76)	0.40 (7.20)	(-1.2 to 2.0)	0.7078
IIEF score	80	39.28 (19.91)	43.52 (22.24)	3.83 (19.61)	(-0.7 to 8.3)	0.0523

Functional results at 12 months (per protocol analysis), mean (SD)

Outcome	n (paired)	baseline	follow up	change	95% CI	p value
IPSS Urinary Symptoms Score	78	21.64 (6.80)	12.69 (6.35)	-9.25 (6.49)	-11.0 to -7.4	<0.0001
IPSS Quality of life	78	4.51 (1.24)	2.45 (1.79)	-1.90 (1.74)	(-2.2 to -1.4)	<0.0001
Qmax (ml/s)	55	8.42 (2.09)	11.93 (4.89)	3.52 (5.24)	(2.0 to 5.0)	<0.0001
PVR (ml)	55	57.62 (56.16)	58.67 (72.36)	-0.16 (87.01)	(-24.6 to 24.3)	0.9039
SHIM score	78	14.03 (7.41)	14.25 (7.45)	0.45 (5.95)	(-1.0 to 1.9)	0.3155
IIEF score	77	40.01 (19.76)	43.75 (19.85)	4.51 (18.10)	(0.2 to 8.8)	0.0101

Key safety findings

Adverse events within 30 days, number and percentage of patients

	Implant group		control group	
Event	n	%	n	%
Serious adverse events	10 (16 events)	7.8	2 (2 events)	3.5
Procedure related serious events	3 (5 events)	2.3	0	0
All adverse events	45 (109 events)	38.1	10 (19 events)	17.5
All procedure related adverse events	39 (81 events)	33.1	4 (4 events)	7.0
Dysuria	27	22.9	5	8.8
Haematuria	16	13.6	-	-
Micturition urgency	6	5.1	1	1.8
Pollakiuria (urinary frequency syndrome)	8	6.8	1	1.8
Urinary retention	7	5.9	-	-
Urinary tract infection	2	1.7	-	-
Sepsis	1	0.8	-	-
Pain	1	0.8	-	-

Between 1 and 3 months after implant insertion, 1 patient had urinary retention and 1 had urinary tract infection. Between 3 and 12 months after implant insertion, 1 patient had urinary tract infection.

Study 2 Amparore D (2021)

Study details

Study type	Single-arm trial (MT-02)
Country	Italy, Switzerland, Belgium, UK, Spain, Hong Kong (9 sites)
Recruitment period	2014 to 2016
Study population and number	n=81 Men with LUTS secondary to benign prostatic obstruction
Age	Mean 63.9 years
Patient selection criteria	Inclusion criteria: men with an IPSS 10 or above, prostate volume less than 75 ml, a maximum urinary flow rate less than 12 ml/s, a measured PVR less than 250 ml, normal urinalysis, complete blood count and biochemistry values. Exclusion criteria: patients with obstructive median lobe, previous prostate surgery, prostate or bladder cancer, neurogenic bladder or sphincter abnormalities, or confounding bladder pathologies based on medical history, recent cystolithiasis or haematuria, active urinary tract infection, compromised renal function, active antithrombotic or antiplatelet treatment, cardiac disease, including arrhythmias and uncontrolled diabetes mellitus.
Technique	Device: second generation iTIND (Medi-Tate Ltd, Israel) Patients were required to have a washout and discontinue the use of any medications for LUTS secondary to BPH before treatment, 1 month for alpha-blockers and 6 months for 5α-Reductase inhibitors. Devices were retrieved at a mean (SD) of 5.7 (0.9) days after implantation.
Follow up	3 years
Conflict of interest/source of funding	Not reported

Analysis

Follow up issues: Data were available for 50 (62%) patients at 3-year follow up. Of the 81 enrolled patients, 7 were excluded from the final analysis because they had a TURP or holmium laser enucleation of the prostate, 5 were excluded because they needed drug therapy, 9 were excluded because the study site closed, 9 patients withdrew consent and 1 patient died (unrelated).

Study design issues: Prospective, single-arm, multicentre study. Feasibility and safety of the procedure and functional, sexual, and ejaculatory function were assessed up to 36 months. Treatment failure was defined as any surgical treatment for recurrent or persistent LUTS during follow-up. Analysis was done on an intention-to-treat basis, with imputation of missing values using last observation carried forward, and per-protocol with no imputation.

Study population issues: The median prostate volume at baseline was 40 ml (IQR 16 to 69 ml). Of the 81 patients, 10 (12%) had a median lobe, which was identified as a predictor of treatment failure.

Key efficacy findings

Number of patients analysed: 81

Outcome measures by follow up period (intention-to-treat population, n=81), mean (SD)

	4 weeks	6 months	12 months	24 months	36 months
IPSS					
Baseline	22.34 (5.73)	22.34 (5.73)	22.34 (5.73)	22.34 (5.73)	22.34 (5.73)
Follow up	13.12 (8.68)	11.29 (7.82)	11.17 (7.79)	12.21 (7.61)	12.05 (8.13)
Change	-9.22 (8.53)	-11.05 (7.48)	-11.17 (7.71)	-10.13 (7.37)	-10.29 (7.79)
% change	-41.2 (34.5)	-50.0 (31.1)	-49.9 (31.4)	-45.3 (30.8)	-46.1 (34.4)
95% CI	-48.8%, -33.6%	-56.8%, -43.1%	-56.8%, -43.1%	-52.1%, -38.6%	-53.7%, -38.6%
p value	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
Quality of life					
Baseline	4.00 (0.85)	4.00 (0.85)	4.00 (0.85)	4.00 (0.85)	4.00 (0.85)
Follow up	2.32 (1.45)	2.07 (1.39)	1.94 (1.42)	2.23 (1.43)	2.22 (1.44)
Change	-1.68 (1.54)	-1.93 (1.49)	-2.06 (1.62)	-1.77 (1.56)	-1.78 (1.50)
% change	-40.8 (35.5)	-47.2 (34.1)	-49.2 (38.9)	-42.2 (39.6)	-43.3 (39.1)
95% CI	-48.6%, -33.0%	-54.6%, -39.7%	-57.7%, -40.6%	-50.9%, -33.5%	-51.9%, -34.7%
p value	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
Qmax (ml/s)					
Baseline	7.28 (2.55)	7.28 (2.55)	7.28 (2.55)	7.28 (2.55)	7.28 (2.55)
Follow up	11.91 (10.72)	12.56 (6.47)	13.25 (7.97)	14.10 (8.96)	13.43 (8.41)
Change	4.63 (10.49)	5.28 (6.18)	5.97 (7.88)	6.82 (9.10)	6.15 (8.40)
% change	73.8 (163.9)	84.3 (104.3)	96.3 (142.3)	112.7 (163.1)	101.1 (150.3)
95% CI	37.6%, 110.1%	61.3%, 107.4%	64.8%, 127.8%	76.6%, 148.8%	67.9%, 134.4%
p value	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
PVR (ml)					
Baseline	78.72 (56.39)	78.72 (56.39)	78.72 (56.39)	78.72 (56.39)	78.72 (56.39)
Follow up	57.27 (68.78)	57.17 (59.80)	51.02 (69.24)	45.85 (70.79)	42.60 (71.08)
Change	-21.44 (61.20)	-21.54 (64.26)	-27.69 (68.91)	-32.86 (68.14)	-36.11 (69.61)
% change	-24.2 (60.9)	-8.6 (103.4)	-29.0 (91.1)	-43.0 (85.8)	-49.0 (84.5)
95% CI	-38.2%, -10.2%	-32.4%, 15.1%	-50.0%, -8.0%	-62.8%, -23.3%	-68.4%, -29.5%
p value	0.0008	0.0005	<0.0001	<0.0001	<0.0001

Outcome measures by follow up period (per-protocol population), mean (SD)

Outcome measure	4 weeks n=78	6 months n=70	12 months n=67	24 months n=51	36 months n=50

IPSS					
Baseline	22.22 (5.62)	21.99 (5.48)	21.70 (5.56)	20.51 (4.58)	20.69 (4.58)
Follow up	11.72 (7.99)	9.75 (7.10)	8.78 6.41	8.51 (5.51)	8.55 (6.38)
Change	-10.50 (8.32)	-12.23 (6.79)	-12.92 (6.92)	-12.00 (6.12)	-12.14 (6.95)
% change	-46.3 (33.2)	-56.4 (27.5)	-59.1 (26.3)	-56.7 (25.6)	-58.2 (32.1)
95% CI	-54.0%, -38.5%	-63.0%, -49.8%	-65.7%, -52.5%	-64.1%, -49.4%	-67.4%, -49.0%
p value	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
Quality of life					
Baseline	4.00 (0.84)	3.97 (0.84)	3.97 (0.87)	3.96 (0.87)	3.96 (0.87)
Follow up	2.08 (1.35)	1.81 (1.30)	1.59 (1.29)	1.76 (1.32)	1.76 (1.32)
Change	-1.92 (1.50)	-2.16 (1.44)	-2.38 (1.60)	-2.20 (1.46)	-2.20 (1.46)
% change	-45.8 (34.4)	-53.3 (32.5)	-56.9 (38.5)	-54.0 (38.5)	-55.6 (37.0)
95% CI	-53.8%, -37.8%	-61.1%, -45.5%	-66.5%, -47.3%	-64.8%, -43.2%	-66.2%, -45.0%
p value	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
Qmax (ml/s)					
Baseline	7.28 (2.49)	7.58 (2.43)	7.61 (2.25)	7.62 (2.25)	7.71 (2.26)
Follow up	11.23 (5.66)	13.69 (6.26)	14.91 (8.06)	16.00 (7.43)	15.20 (6.59)
Change	3.94 (5.22)	6.12 (6.22)	7.30 (8.20)	8.38 (7.93)	7.49 (6.86)
% change	79.4 (167.7)	95.6 (106.5)	111.7 (147.1)	130.8 (132.2)	114.7 (108.5)
95% CI	41.1%, 117.7%	70.1%, 121.2%	74.3%, 149.0%	93.3%, 168.4%	83.2%, 146.2%
p value	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
PVR (ml)					
Baseline	76.17 (55.52)	78.70 (56.11)	73.54 (49.54)	65.84 (38.46)	68.58 (39.53)
Follow up	49.84 (57.27)	48.84 (47.59)	34.03 (54.13)	14.26 (24.05)	9.38 (17.43)
Change	-26.33 (57.59)	-29.86 (60.89)	-39.51 (57.46)	-51.58 (36.68)	-59.21 (37.75)
% change	-26.9 (60.5)	-13.8 (105.9)	-47.8 (72.5)	-75.7 (45.1)	-85.4 (30.7)
95% CI	-41.3%, -12.6%	-39.9%, 12.2%	-66.7%, -28.9%	-88.9%, -62.4%	-94.6%, -76.3%
p value	0.0001	<0.0001	<0.0001	<0.0001	<0.0001

Key safety findings

There were no intraoperative complications. All perioperative complications were self-resolving and graded as Clavien-Dindo 1 or 2.

The median VAS pain score for the procedure was 4 (range 0 to 10). The mean VAS pain score after device removal was 2 (range 0 to 10).

Treatment-related adverse events within 1 month of procedure

- Clavien-Dindo grade 1
  - Haematuria=12.3% (10/81)

  - Dysuria=7.4% (6/81)
  - Urgency=11.1% (9/81)
  - Pain=9.9% (8/81)
- Clavien-Dindo grade 2
  - Urinary tract infection=6.2% (5/81)
- Clavien-Dindo grade 3a
  - Urinary retention=9.9% (8/81); 5 while the device was in place and 3 after removal
- Clavien-Dindo grade 3b
  - Secondary treatment (TURP, laser) = 2.5% (2/81)

Treatment-related adverse events 1 to 12 months after procedure

- Clavien-Dindo grade 3b
  - Secondary treatment (TURP, laser) = 6.2% (5/81)

No adverse events were recorded between 12 and 36 months after the procedure.

None of the patients who were previously sexually active reported a deterioration in sexual or ejaculatory abilities according to the yes/no questions during follow-up.

Study 3 De Nunzio C (2020)

Study details

Study type	Single-arm trial (MT-06)
Country	Italy and Spain (5 centres)
Recruitment period	2018 to 2019
Study population and number	n=70 Men with LUTS secondary to benign prostatic obstruction
Age	Mean 62.3 years
Patient selection criteria	Inclusion criteria: IPSS 10 or above, Qmax less than 12 ml/s, prostate volume less than 120 ml; normal urinalysis and urine culture. Exclusion criteria included: previous prostate surgery, prostate cancer, urethral stricture, bladder stones, urinary tract infections, obstructing median lobe, neurological conditions potentially affecting voiding function.
Technique	Device: iTind (Medi-Tate Ltd, Israel) Patients were not washed out of drug therapy for BPH (alpha-blockers or 5-alpha reductase inhibitors) and did not stop anti-coagulation or anti-platelet therapy before the procedure. Device retrieval was done under local anaesthesia 5 to 7 days after the procedure. All patients discontinued drug therapy for BPH after device retrieval.
Follow up	6 months
Conflict of interest/source of funding	The study was sponsored by Medi-Tate. The authors declared that they had no conflict of interest.

Analysis

Follow up issues: Follow up visits were done at 4 weeks, 3 and 6 months from device retrieval. No losses to follow up were reported.

Study design issues: Prospective, single-arm, multicentre study. The aim was to evaluate the functional outcomes regarding the preservation of urinary continence and sexual function.

Study population issues: The mean prostatic volume at baseline was 37.7 ml (IQR 15 to 80 ml).

Key efficacy findings

Number of patients analysed: 70

All procedures were completed successfully.

At 6 months, erectile and ejaculatory function and urinary continence were preserved in all 70 patients.

Functional results by follow up period, mean (SD)

Outcome measure	4 weeks, n=70	3 months, n=70	6 months, n=70
IPSS Urinary symptoms			
Baseline	21.2 (6.0)	21.2 (6.0)	21.2 (6.0)
Follow up	9.5 (6.8)	7.8 (5.4)	8.3 (6.7)
Change	-11.7 (8.3)	-13.4 (6.4)	-12.7 (6.9)
p value	<0.01	<0.01	<0.01
IPSS Quality of life			
Baseline	4.1 (1.0)	4.1 (1.0)	4.1 (1.0)
Follow up	1.8 (1.4)	1.6 (1.3)	2.0 (1.4)
Change	-2.4 (1.5)	-2.5 (1.6)	-2.2 (1.6)
p value	<0.01	<0.01	<0.01
Peak flow rate (ml/s)			
Baseline	7.3 (2.2)	7.3 (2.2)	7.3 (2.2)
Follow up	13.2 (5.5)	11.8 (5.1)	12.0 (5.4)
Change	5.8 (5.5)	4.5 (5.2)	4.6 (5.5)
p value	<0.01	<0.01	<0.01
PVR (ml)			
Baseline	69.3 (86.8)	69.3 (86.8)	69.3 (86.8)
Follow up	49.2 (74.5)	33.4 (46.2)	48.1 (72.7)
Change	-19.4 (95.4)	-37.4 (90.5)	-22.6 (77.3)
p value	0.13	0.11	0.12
SHIM total score			
Baseline	16.1 (7.7)	16.1 (7.7)	16.1 (7.7)
Follow up	18.0 (7.6)	18.7 (7.7)	18.2 (8.2)
Change	1.9 (4.8)	2.3 (6.9)	2.2 (7.4)
p value	0.09	0.07	0.06
Incontinence Symptom Index questionnaire total score			
Baseline	1.1 (1.9)	1.1 (1.9)	1.1 (1.9)
Follow up	0.6 (1.4)	0.9 (1.7)	0.8 (1.6)
Change	-0.5 (1.7)	-0.3 (1.5)	-0.3 (1.4)
p value	0.21	0.14	0.14
Male Sexual Health Questionnaire – ejaculatory function score (higher scores indicate better function)			
Baseline	9.2 (4.9)	9.2 (4.9)	9.2 (4.9)
Follow up	10.7 (4.6)	11.1 (4.9)	11.2 (4.8)

Change	1.5 (5.1)	1.8 (5.2)	2.0 (4.4)
p value	<0.01	<0.01	<0.01

Key safety findings

There were no intraoperative complications.

The mean VAS pain score was 3.2 after the implantation procedure and showed a gradual decrease to 1.5 by day 7. The mean VAS pain score after the removal procedure was 3.4.

Reported complications

- Total number of complications=75
- Clavien-Dindo grade 1
  - Transient haematuria=18.6% (13/70)
  - Dysuria=17.1% (12/70)
  - Urgency=12.8% (9/70)
  - Frequency=7.1% (5/70)
  - Pain=11.4% (8/70)
  - Transient urinary incontinence (device in situ) = 8.4% (6/70)
- Clavien-Dindo grade 3a
  - Acute urinary retention=4.2% (3/70); 2 were in patients with the device in situ and 1 was 12 hours after device removal. All 3 had treatment with temporary catheterisation.
- Clavien-Dindo grade 3b
  - Gross haematuria=1.4% (1/70); treated by endoscopic fulguration.

Study 4 Porpiglia F (2018) – included in 2018 overview

Study details

Study type	Single-arm trial
Country	Italy
Recruitment period	2010 to 2013
Study population and number	n=32 Patients with BPH-related LUTS
Age	Mean 69.4 years
Patient selection criteria	Inclusion criteria included: age over 50 years, IPSS 10 or above, peak urinary flow (Qmax) 12 ml/s or less, and prostate volume (as assessed by transrectal ultrasound) less than 60 ml. Patients were excluded if they had history of prostate surgery, prostate cancer, urethral stricture, bladder stones, obstructive median lobe, and history of significant medical comorbidities, haemostatic disorders or suspected neurological conditions that could underlie impaired voiding function.
Technique	Device: first generation temporary implantable nitinol device (TIND; Medi-Tate Ltd., Israel) The device was retrieved 5 days after insertion, using rigid urethroscopy in an outpatient setting.
Follow up	36 months
Conflict of interest/source of funding	None

Analysis

Follow-up issues: Patients visited an outpatient setting at 5 days (removal day), 3 and 6 weeks, and 3, 6, 12, 24 and 36 months after the implantation, for assessment of uroflowmetry, IPSS, and IPSS quality of life score. Of the 32 patients, 1 died from a cause unrelated to the procedure, at 26 months after device implantation.

Study design issues: Single-arm, prospective, single-centre trial. The aim was to assess perioperative results, complications (according to Clavien–Dindo classification), functional results, and quality of life. Sexual dysfunction in sexually active patients was investigated by asking the patient: 'after the intervention, did you record any changes in terms of ejaculation?'. Patient satisfaction with the procedure was assessed using Question 32 of the Expanded Prostate Cancer Index Composite questionnaire to the patients during the follow-up visits: 'Overall, how satisfied are you with treatment you received for your prostate disease intervention?', with a choice of 5 possible responses (1 extremely dissatisfied, 2 dissatisfied, 3 uncertain, 4 satisfied, 5 extremely satisfied). Treatment failure during follow-up was defined as the need for any surgical treatment for LUTS related to BPH.

Study population issues: All patients were on alpha blocker therapy at the time of the procedure, with 46% regularly using 5-alpha-reductase inhibitors. The mean prostate volume at baseline was 29.5 mL (SD 7.4).

Key efficacy findings

Number of patients analysed: 32

IPSS - mean percentage changes (SD) compared with baseline

- 3 weeks= -39 (0.3)
- 6 weeks= -50 (0.3)
- 3 months= -55 (0.2)
- 6 months= -47 (0.2)
- 12 months= -45 (0.3)
- 24 months= -23 (0.5)
- 36 months= -19 (0.5)

Peak urinary flow - mean percentage changes (SD) compared with baseline

- 3 weeks= 37 (1)
- 6 weeks= 72 (0.6)
- 3 months= 61 (0.7)
- 6 months= 61 (0.8)
- 12 months= 67 (0.8)
- 24 months= 54 (0.6)
- 36 months= 41 (1)

There was a statistically significant increase in peak urinary flow values over the first 12 months after treatment, peaking at a mean 72% increase by 6 weeks after treatment and remaining steady over the ensuing 12 months ($p<0.001$).

There was also a statistically significant difference between baseline values and the postoperative IPSS and quality of life scores ($p<0.001$). The median quality of life score was 2 at 24 and 36 months after treatment, compared with 3 at baseline.

Medication

All patients were able to discontinue LUTS-related medical therapy 3 months after the implantation, but 3 patients (9%) needed it again within 12 or 24 months of treatment.

Multiple regression analysis did not identify any independent prognostic factors predictive of the need for BPH-related medical therapy after the procedure, increase of peak urinary flow or decrease of IPSS.

Overall, no patients needed any surgical therapy for BPH during follow up. None of the 19 patients reporting preoperative sexual activity reported any ejaculatory dysfunction during follow up.

Patient satisfaction

The median Expanded Prostate Cancer Index Composite question 32 score was 5 (corresponding to extremely satisfied) throughout follow up and the differences at different time points were not statistically significant ($p=0.180$).

Key safety findings

There were no intraoperative complications.

The median VAS pain score 6 hours after the procedure was 2 (IQR 2 to 4).

Complications within 30 days of procedure

- Total=12.5% (4/32)
- Urinary incontinence because of device displacement, n=1 (resolved after device was removed on day 1)
- Urinary retention on the same day as device implantation, n=1
- Genitourinary infection=6.3% (2/32) (treated with antibiotics)

There were no further complications reported during follow up.

Validity and generalisability of the studies

- Studies included patients from North America, Europe (including the UK) and Asia.
- There is a randomised single-blinded controlled trial, which used a sham control, with a 12-month follow up (Chughtai, 2021). Although there was a relatively high dropout rate in the trial, the proportion of dropouts were similar in the treatment and control groups.
- The randomised controlled trial showed a strong placebo effect associated with the procedure.
- Inclusion criteria varied between the studies, particularly regarding prostate volume.
- One study used a first generation device (Porpiglia et al., 2018) and the other 3 used a second generation device.
- The longest reported follow up was 3 years.

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

- Transurethral water jet ablation for lower urinary tract symptoms caused by benign prostatic hyperplasia. NICE interventional procedure guidance 629 (2018). Available from http://www.nice.org.uk/guidance/IPG629
- Transurethral water vapour ablation for lower urinary tract symptoms caused by benign prostatic hyperplasia. NICE interventional procedure guidance 625 (2018). Available from http://www.nice.org.uk/guidance/IPG625

- Prostate artery embolisation for lower urinary tract symptoms caused by benign prostatic hyperplasia. NICE interventional procedure guidance 611 (2018). Available from http://www.nice.org.uk/guidance/IPG611
- 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
- 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

- The PLASMA system for transurethral resection and haemostasis of the prostate. Medical technologies guidance 53 (2021). Available from https://www.nice.org.uk/guidance/mtg53
- Rezum for treating lower urinary tract symptoms secondary to benign prostatic hyperplasia. Medical technologies guidance 49 (2020) Available from https://www.nice.org.uk/guidance/mtg49
- 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

Professional experts' opinions

Expert advice was sought from consultants who have been nominated or ratified by their professional 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 professional experts, 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.

One professional expert questionnaire for prostatic urethral temporary implant insertion for LUTS caused by BPH was submitted and can be found on the NICE website.

Patient commentators' opinions

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.

Company engagement

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

Issues for consideration by IPAC

- Ongoing trials:
  - A Post Market Prospective, Randomized, Controlled, Multi-center International Study to Assess the Safety of the iTind Compared to TURP in

Subjects With Symptomatic BPH (NCT04757116); randomised controlled trial; n=140; estimated study completion date October 2023.

- One-arm, Multi-center, International Prospective Study to Assess the Efficacy of Medi-tate Temporary Implantable Nitinol Device (iTind) in Subjects With Symptomatic Benign Prostatic Hyperplasia (BPH), (MT-06; NCT03395522); Australia, Austria, France, Germany, Italy, Spain Switzerland; single group assignment; n=200; estimated study completion date October 2021.

References

1. Chughtai B, Elterman D, Shore N et al. (2021) The iTind temporarily implanted nitinol device for the treatment of lower urinary tract symptoms secondary to benign prostatic hyperplasia: a multicenter, randomized, controlled trial. Urology 153: 270−76
2. Amparore D, Fiori C, Valerio M et al. (2021) 3-Year results following treatment with the second generation of the temporary implantable nitinol device in men with LUTS secondary to benign prostatic obstruction. Prostate Cancer and Prostatic Diseases; 2020 24, pages349–357
3. De Nunzio C, Cantiello F, Fiori C et al. (2020) Urinary and sexual function after treatment with temporary implantable nitinol device (iTind) in men with LUTS: 6-month interim results of the MT-06-study. World Journal of Urology 39: 2037–42
4. Porpiglia F, Fiori C, Bertolo R et al. (2018) 3-Year follow-up of temporary implantable nitinol device implantation for the treatment of benign prostatic obstruction. BJU international 122: 106–112

Literature search strategy

Databases	Date searched	Version/files
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	25/10/2021	Issue 10 of 12, October 2021
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	25/10/2021	Issue 10 of 12, October 2021
International HTA database (INAHTA)	20/10/2021	-
MEDLINE (Ovid)	26/10/2021	1946 to October 25, 2021
MEDLINE In-Process (Ovid)	26/10/2021	1946 to October 25, 2021
MEDLINE Epubs ahead of print (Ovid)	26/10/2021	October 25, 2021
EMBASE (Ovid)	26/10/2021	1974 to 2021 October 25
EMBASE Conference (Ovid)	26/10/2021	1974 to 2021 October 25
Epistomonikos	26/10/2021	-

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

Literature search strategy

Number	Search term
1	Prostatic Hyperplasia/
2	Lower Urinary Tract Symptoms/
3	Urinary Bladder Neck Obstruction/
4	Prostatism/
5	(Prostat* adj2 (hyperplas* or adenom* or urethra* or enlarg*)).tw.
6	((bladder* or urinat* or urinar* or urethra*) adj4 (neck* or obstruct* or block* or narrow*)).ti.
7	((bladder* or urinat* or urinar* or urethra*) adj4 (neck* or obstruct* or block* or narrow*)).ab.
8	(LUTS or (low* adj2 urinar* adj2 tract* adj2 symptom*)).tw.
9	(BPO or BPH or BPH-relat* or BPE or prostatism*).tw.
10	or/1-9

11	minimally invasive surgical procedures/
12	((minimall* or non) adj2 invasive adj2 (surg* or treatment* or technolog* or procedure* or technique*)).tw.
13	"Prostheses and Implants"/
14	((temporary or removable) adj4 (implant* or nitinol* or device*)).tw.
15	TIND.tw.
16	or/11-15
17	10 and 16
18	(itind or Medi-tate).tw.
19	17 or 18
20	animals/ not humans/
21	19 not 20

Appendix

The following table outlines the studies that are considered potentially relevant to the IP overview but were not included in the summary of the key evidence. It is by no means an exhaustive list of potentially relevant studies.

Additional papers identified

Article	Number of patients/ follow up	Direction of conclusions	Reasons for non-inclusion in summary of key evidence section
Amparore D, De Cillis S, Volpi G et al. (2019) First- and second-generation temporary implantable nitinol devices as minimally invasive treatments for BPH-related LUTS: systematic review of the literature. Current Urology Reports 20: 47	Systematic review 3 studies	Current evidence suggests that the temporary implantable nitinol devices are promising alternatives to the standard minimally invasive surgical options for BPH-related LUTS. Further studies are needed to confirm the effectiveness over a long-term follow-up.	Only 3 studies are included, all of which are already summarised in the key evidence.
Balakrishnan D, Jones P, Somani BK (2020) iTIND: the second-generation temporary implantable nitinol device for minimally invasive treatment of benign prostatic hyperplasia. Therapeutic Advances in Urology 12: 1–5	Review	While at present, only limited evidence exists to support its use, early results of this modified version are very promising. Key advantages include a strong safety profile and preservation of existing sexual function. Future studies are awaited to help delineate its formal role in current treatment algorithms.	No meta-analysis. Relevant studies have been included in the key evidence summary or appendix.
Bertolo R, Fiori C, Amparore D et al. (2018) Follow-up of temporary implantable nitinol	Systematic review	Current available evidence is limited. Sample size of patients available for analysis is small. Moreover, the duration of follow-up	No meta-analysis. More recent studies have been included.

device (TIND) implantation for the treatment of BPH: a systematic review. Current Urology Reports 19: 44. doi: 10.1007/s11934-018-0793-0		period is intermediate and longer follow-up is required. At the available 3 years follow-up, the TIND implantation is safe, effective, and well tolerated.	
Chung ASJ, Woo HH (2018) Update on minimally invasive surgery and benign prostatic hyperplasia. Asian Journal of Urology 5: 22–27	Review	The results of the first-in-man prospective trial of the temporary implantable nitinol device procedure for treatment of LUTS caused by BPH have been promising. Phase 1, 2 and 4 studies are in progress and further validation of results awaited.	Only includes 1 relevant published study.
Elterman DS, Zorn KC, Chughtai B et al. (2021) Is it time to offer true minimally invasive treatments (TMIST) for BPH? - A review of office-based therapies and introduction of a new technology category. The Canadian Journal of Urology 28: 10580–83	Review	The iTind procedure appears to improve subjective and objective outcomes, but long-term data is lacking.	Relevant cited studies have been included in the key evidence summary or appendix.
Elterman D, Gao B, Zorn KC et al. (2021) How I do it: temporarily implanted nitinol device (iTind). The Canadian Journal of Urology 28: 10788–93	Review	The technology promises to bridge the gap between conservative medical therapy and more invasive surgical therapy. Prospective, randomised data indicate that iTind has favourable functional and sexual patient outcomes.	The main focus of the paper is to describe a standardised technique for doing the procedure.
Franco JVA, Jung JH, Imamura M et al. Minimally invasive treatments for lower urinary tract symptoms in men	Network meta-analysis (Cochrane review)	Minimally invasive treatments may result in similar or worse effects concerning urinary symptoms and quality of life compared to TURP at	Review only includes 1 study (2 reports) on prostatic urethral

with benign prostatic hyperplasia: a network meta-analysis. Cochrane Database of Systematic Reviews 2021, Issue 7. Art. No.: CD013656. DOI: 10.1002/ 14651858.CD013656.pub2.	n=3,017 (27 trials)	short-term follow up. They may result in fewer major adverse events. The effects of these interventions on erectile function is very uncertain. There was limited long-term data.	temporary implant insertion (Chughtai et al., 2021).
Guelce D, Kini M, Thomas D et al. (2019) BPH-related voiding dysfunction-i-Tind. Current Bladder Dysfunction Reports 14: 9–12	Review 7 studies	There is promising evidence for the use of i-Tind as an office-based treatment for BPH. An important consideration, however, will centre on patient selection. There will be a cohort of men who elect to have this minimally invasive procedure over the gold standard TURP. However, this will not be a viable treatment option for men with particularly large prostate volumes.	The cited studies have been included in the key evidence summary or appendix.
Kadner G, Valerio M, Giannakis I et al. (2020) Second generation of temporary implantable nitinol device (iTind) in men with LUTS: 2 year results of the MT-02-study. World Journal of Urology 38: 3235–44	Single-arm trial n=81 Follow up=2 years	iTind treatment for benign prostatic obstruction-related LUTS showed marked and durable reduction in symptoms and improvement of functional parameters and quality of life at 24 months of follow-up. It was found that median lobe may predict failure of iTind treatment.	A longer term follow up of the same study has been included (Amparore et al., 2020).
Madersbacher S, Roehrborn CG, Oelke M (2020) The role of novel minimally invasive treatments for lower urinary tract symptoms associated with	Review	Procedures that can be performed on an outpatient basis are not an alternative for the standard patient needing BPH surgery. Their effect on urinary flow, PVR urine volume or bladder outlet obstruction is less pronounced than that of	Both relevant studies have been included in the appendix.

benign prostatic hyperplasia. BJU International 126: 317–26		TURP. These options appear to be valuable for patients for whom surgery is inappropriate, men who want to avoid medical therapy in general, or those who want to avoid sexual side-effects associated with medical therapy or standard BPH surgery.	
Marcon J, Magistro G, Stief CG et al. (2018) What's New in TIND? European Urology Focus 4: 40–42	Review 2 articles	Preliminary data suggest that TIND is a safe and effective minimally invasive technique for patients with male LUTS. Symptom relief and increase in urinary flow after 36 months are promising. However, long-term results are needed.	More recent studies are included.
Ng BHS, Chung E (2021) A state-of-art review on the preservation of sexual function among various minimally invasive surgical treatments for benign prostatic hyperplasia: Impact on erectile and ejaculatory domains. Investigative and Clinical Urology 62: 148–58	Review	To date, there are very little direct comparative clinical trials among minimally invasive BPH technologies, and further studies are needed to ensure optimal patient selection, analyse cost-effectiveness and counsel patients on longer-term clinical outcomes and safety profile.	No meta-analysis. Relevant studies are included in the key evidence summary or appendix.
Porpiglia F, Fiori C, Amparore D et al. (2019) Second-generation of temporary implantable nitinol device for the relief of lower urinary tract symptoms due to benign prostatic hyperplasia: results of a prospective, multicentre study at	Single-arm trial n=81 Follow up: 12 months	iTIND implantation is feasible, safe and effective in providing relief of BPH-related symptoms, at least until 12 months postoperatively. Sexual and ejaculatory functions are fully preserved. Further studies with a longer follow-up period are needed to assess the durability of these results and to clearly	A more recent publication from the same study with longer follow up is included (Amparore et al., 2020).

1 year of follow-up. BJU International 123: 1061–69		define the indications for iTIND implantation.	
Porpiglia F, Fiori C, Bertolo R et al. (2015) Temporary implantable nitinol device (TIND): a novel, minimally invasive treatment for relief of lower urinary tract symptoms (LUTS) related to benign prostatic hyperplasia (BPH): feasibility, safety and functional results at 1 year of follow-up. BJU international 116: 278–87	Single-arm trial n=32 Follow up: 1 year	TIND implantation is a feasible and safe minimally invasive option for the treatment of BPH-related LUTS. The functional results are encouraging and the treatment significantly improved patient quality of life. Further studies are required to assess durability of TIND results and to optimise the indications of such a procedure.	A more recent publication from the same study with longer follow up is included (Porpiglia et al. 2018).
Suarez-Ibarrola R, Miernik A, Gratzke C et al. (2020) Reasons for new MIS. Let's be fair: iTIND, Urolift and Rezum. World Journal of Urology 39: 2315–27	Review 15 studies (2 on iTIND)	Although iTIND, Urolift, and Rezūm cannot be applied to all bladder outlet obstruction cases resulting from BPH, they provide a safe alternative for carefully selected patients who desire symptom relief and preservation of erectile and ejaculatory function without the potential morbidity of more invasive procedures.	No meta-analysis. Both relevant studies are included.
Tzeng M, Basourakos SP, Lewicki PJ et al. (2021) New endoscopic in-office surgical therapies for benign prostatic hyperplasia: a systematic review. European Urology Focus https://doi.org/10.1016/j.euf.2021.02.013	Systematic review 18 articles	Among the emerging technologies introduced to treat BPH, the in-office prostatic urethral lift, water vapor thermal therapy, and temporary implantable nitinol device systems are promising options for men interested in minimally invasive, well-tolerated therapies that preserve sexual function. Although standard surgical approaches may be more	No meta-analysis. All 3 relevant studies are included in the key evidence summary.

		effective, these advantages are valuable to certain patient populations.	
Yalcin S, Tunc L (2020) Indications, techniques, and role of new minimally invasive benign prostate hyperplasia surgical options. Turkish Journal of Urology 46: S79–S91	Review	Novel emerging techniques for the surgical treatment of BPH related to LUTS are being investigated. These methods, which are still being studied, are promising for the future. As the studies get completed, the indications will become clearer, and these techniques will find their respective places as the personalised treatment options.	No meta-analysis. All 5 relevant studies are included in the key evidence summary or appendix.