iTind
RESHAPING BPH TREATMENT

Medi-Tate iTind System

INSTRUCTIONS FOR USE

Manufacturer **Medi-Tate Ltd.**

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Made in Israel

⚠ CAUTION

Before using the Medi-Tate iTind System, read the entire instructions for use.

⚠ CAUTION

Federal law restricts this device to sale by or on the order of a physician.

INTRODUCTION

INTENDED USE:
The iTind System is intended for the treatment of symptoms due to urinary outflow obstruction secondary to benign prostatic hyperplasia (BPH) in men age 50 and above.

The iTind System includes:

FOR INSERTION: 1 iTind device, supplied sterile (EO) by Medi-Tate.

FOR REMOVAL: 1 Retrieval Snare, supplied sterile (EO) by Medi-Tate.

BEFORE YOU BEGIN

Make sure that you have a suitable cystoscope so that proper device positioning can be visualized:

- **OPTION 1:** Rigid cystoscope – 19Fr and up.
- **OPTION 2:** Access Sheath or similar instrument – 12Fr (inner lumen) and up and cystoscope for the positioning, (Flexible or Rigid 15.5 Fr and up).

The iTind system is supplied sterile and is comprised of a device crimped inside an introducer sheath and pre-mounted on a dedicated guidewire and a retrieval snare.

A. iTind device (shown here in expanded configuration)

B. Anchoring leaflet

C. Guidewire (inside protective cover)

D. Introducer sheath

E. Retrieval suture

F. Retrieval Snare

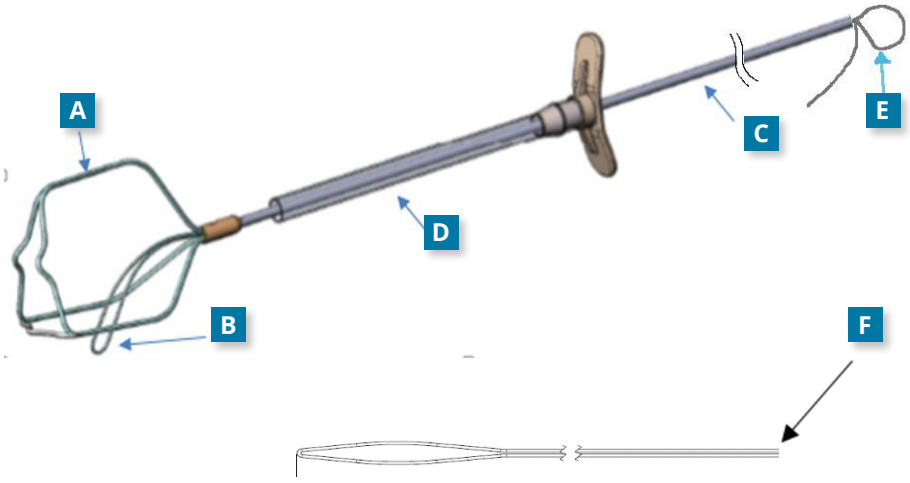


Figure 1: The iTind System

CONTRAINDICATIONS

- Active urinary tract infection or prostatitis.
- Artificial urinary sphincter or any implant (metallic or nonmetallic) within the urethra.
- Any patient condition which, to the implanting physician's opinion, may cause complications during the deployment of the device.
- Prostate cancer.
- Bladder cancer.
- Bladder atonia, neurogenic bladder disorder, or other neurological disorder impacting bladder function as the sole etiology of urinary dysfunction; or urinary obstruction due to causes other than BPH, including urethral stricture.

WARNINGS AND PRECAUTIONS

General Warnings and Precautions:

- The iTind System should only be used by clinicians trained in endo-urological procedures and the management of their complications.
- The risks of implanting the iTind System in patients with blood coagulation disorders, compromised immune systems, or any other conditions that would compromise healing should be carefully considered against the possible benefits.
- The iTind system is for single use. Do not re-sterilize or reuse any part of the system.
- The iTind System components should be disposed safely after use according to local regulation.
- Non-functional or defective items should not be used and should be returned to Medi-Tate.
- Do not use any part of the iTind System beyond the indicated expiration date.
- Do not use the iTind System if the package was opened or damaged.
- Do not use the iTind System if the patient has a known allergy to Nickel.
- While the device is in the body, it is better to avoid planned MRI, in order not to compromise the quality of the image. However, a patient with an implant can be scanned safely in an MR system under the following conditions:
    - Static magnetic field of 1.5 Tesla or 3 Tesla, only;
    - Maximum spatial gradient magnetic field of 4,000 gauss/ cm (40 T/m);
    - Maximum MR system reported, whole body averaged specific absorption rate (SAR) of 2 W/kg for 15 minutes of scanning (i.e., per pulse sequence) in the Normal Operating Mode.

OPERATING INSTRUCTIONS

Patient Preparation:

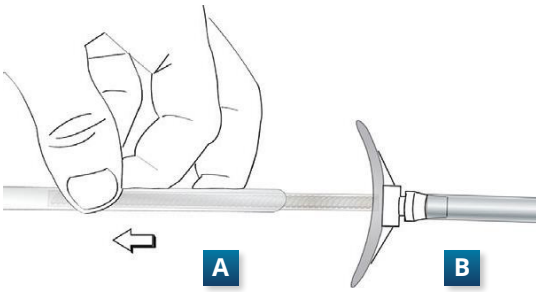
Prior to the procedure and at the physician's discretion, the patient should receive anesthesia: spinal anesthesia is not recommended. Prophylactic antibiotics should be given per local hospital or clinic practice.

System Preparation:

1 Open the iTind system box and withdraw the iTind device from the pouch in a sterile environment.

- **A.** Protective cover
- **B.** Introducer sheath

2 Carefully withdraw the iTind device from the protective cover without disconnecting or breaking the introducer sheath.

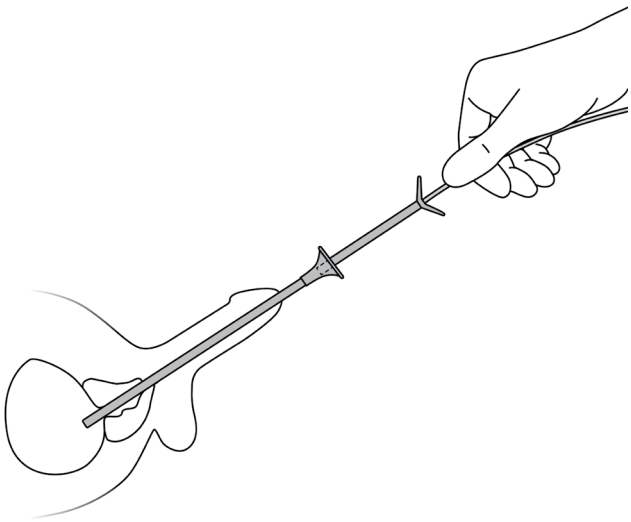


Placement of the iTind device in the bladder:

1 Insert a liberal amount of local anesthetic gel, into the urethra.

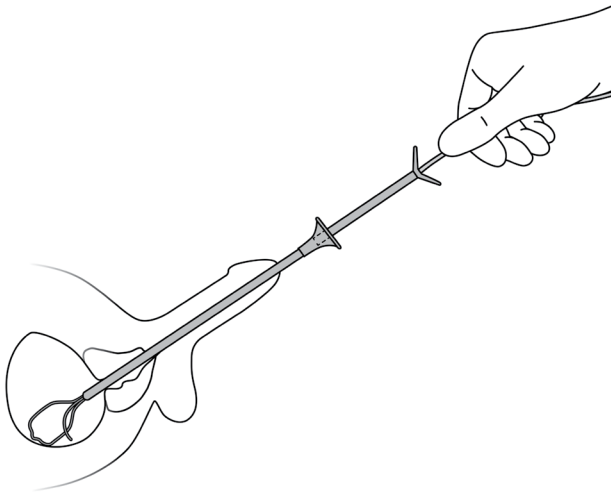
2 Instrument the patient with a sheath according to minimal size defined above:

- **A.** rigid cystoscope or similar
- **B.** access sheath:
  - **i.** place a 0.035 inch. or 0.038 inch. diameter wire guide with the desired length into the urethra and pass into the bladder to establish a working tract.
  - **ii.** Grasp the sheath just below the instrument adaptor and advance the dilator/sheath assembly over the wire guide and into the bladder.
  - **iii.** While holding the sheath in position unlock the fitting and remove the dilator.



3 Insert the crimped device into the sheath and advance it until opens up in the bladder.

! **Note: a slight pull may be felt as the iTind device expands upon entry to the bladder.**

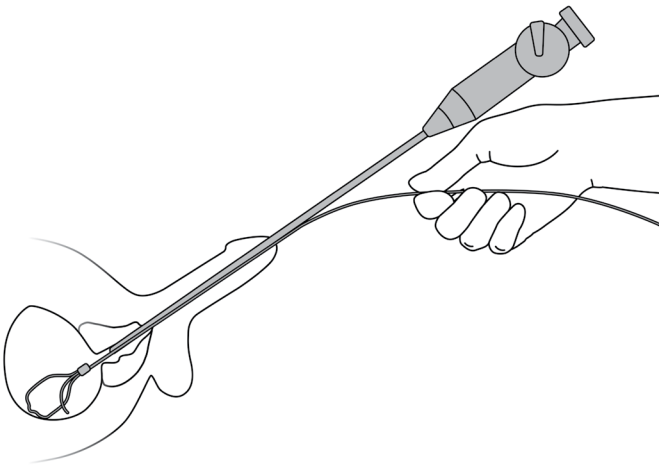


4 Remove the sheath used for insertion while leaving the device in the bladder.

Positioning of the iTind device:

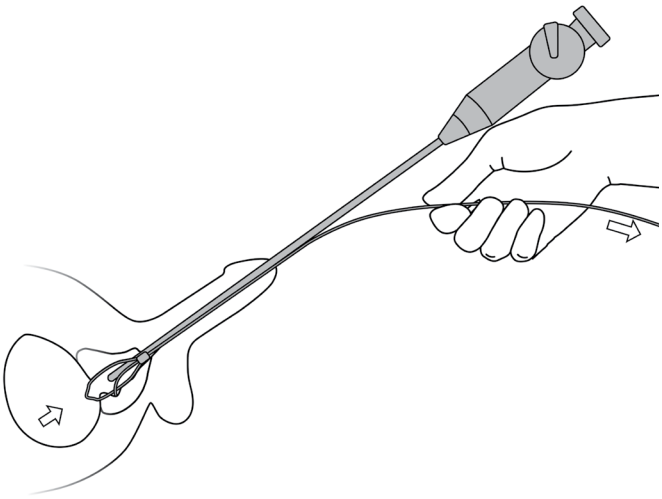
5 Advance a cystoscope (and optics) in parallel to the iTind device guidewire.

6 Inflate the bladder with saline to enable visibility and easy rotation of the iTind device.



7 Position the cystoscope so that the iTind device is visible in the bladder. Rotate the iTind's guidewire so that the blue line proximal to the device is at the 12 o'clock position and the anchoring leaflet is down at the 6 o'clock position.

8 Slowly pull the cystoscope optics back until the bladder neck is visible.



9 Carefully pull the iTind device into the prostatic urethra using the guidewire, until the anchoring leaflet slides snugly over the bladder neck.

10 While being careful not to displace the device, move the cystoscope optics past the external sphincter and ensure it is not being held open by the iTind device.

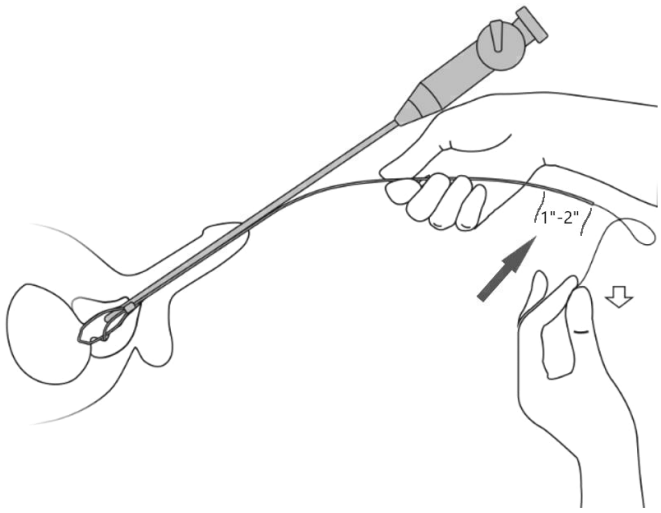
Accurate iTind device positioning must always be verified visually.

NOTE: The iTind device can be repositioned if required as long as the guidewire has not been cut.

- **Option 1: push the iTind device back into the bladder with the help of the guidewire and repeat steps 9-11.**
- **Option 2: guide a sheath up the guidewire, re-crimp the iTind device into the sheath and remove device from the body. Repeat steps 3-11.**

11 To enable removal of the guidewire, loosen the tied suture by pulling it gently. In case the knot cannot be released, cut the guidewire approximately 1-2 inches from the end where the knot is with surgical scissors and carefully remove it from the urethra, exposing the retrieval suture. Empty the bladder of saline with the help of the scope. Remove the scope from the urethra.

NOTE: At this point iTind device implantation is complete and repositioning is no longer possible. If repositioning is required, a new iTind device must be used.

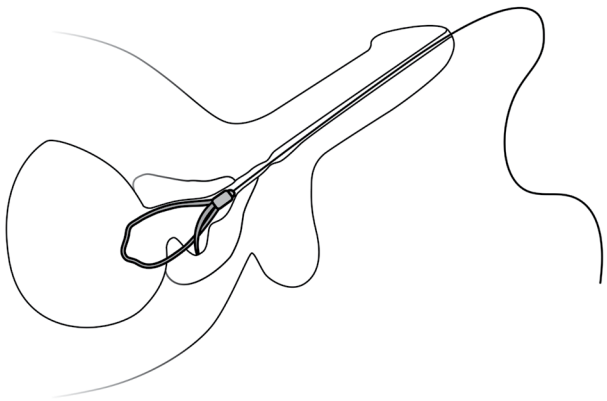


12 Fold the retrieval suture into a loop and loosely fasten it to the patient's penis using adhesive tape.

Make sure to leave enough slack when fastening the suture to avoid irritation of the meatus.

Instruct the patient not to pull or cut the suture while the iTind device is implanted.

NOTE: The iTind device should remain in place for 5-7 days before it is removed.



iTind Device Removal:

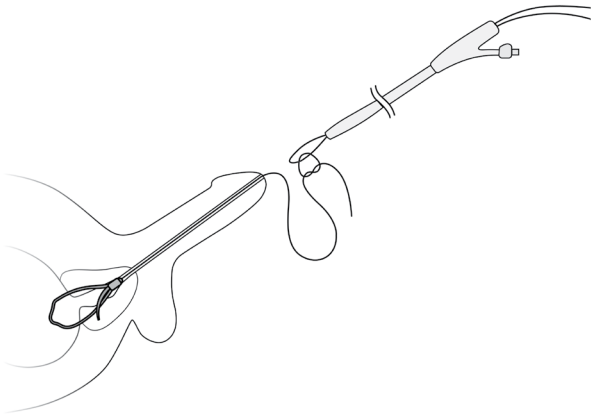
BEFORE YOU BEGIN

Make sure that you have a suitable removal sheath:

- Open ended Foley catheter – 22Fr and up **OR**
- **In US Only:** Removal Kit (20Fr Removal Tube + Snare) **OR**
- Access Sheath or similar instrument – 12Fr (inner lumen) and up **OR**
- Rigid scope – 19Fr and up

1 Liberally insert anesthetic gel into the meatus and into both ends of the Sheath.

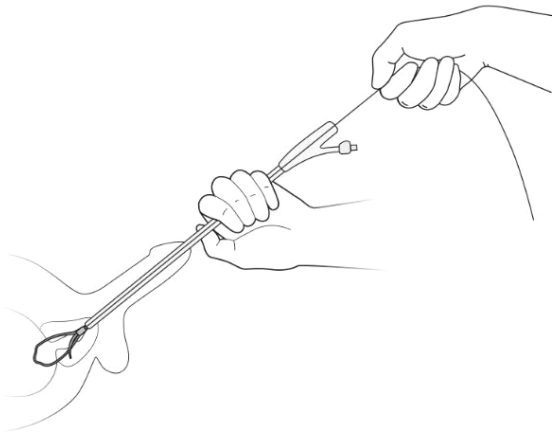
2 Open the sterile retrieval snare package.



3 Feed the Snare through the Sheath.

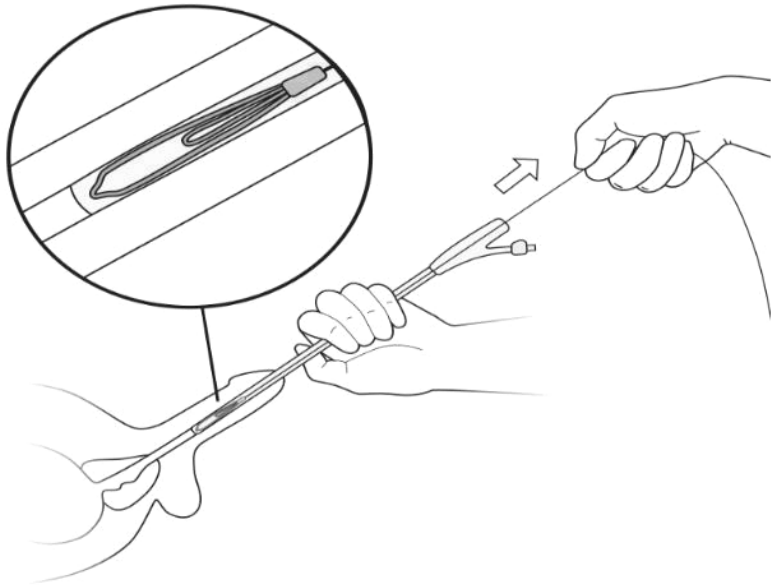
4 Tie the retrieval suture to the loop of the snare and pull the suture through the Sheath all the way out. If required, use a polyester suture USP 1 to extend the iTind device retrieval suture.

While holding the retrieval suture taut, insert the Sheath into the meatus and guide it up the urethra until it meets the iTind device.



5 When the iTind device has been reached, pull the retrieval suture firmly and retract the iTind device into the Sheath. Once the iTind device is folded completely inside the Sheath, remove the Sheath from the urethra.

6 Dispose of the iTind device safely according to local regulation.



NOTE: If the iTind device does not collapse easily, the end of the Sheath may have passed the device. Pull the catheter back 1 inch, tighten the grip on the suture, and re-advance the Sheath to meet the device. If it still hard to collapse, make sure that the suture was threaded through the main opening of the Sheath and not a side hole.

NOTE: If the retrieval suture has been broken and cannot be extended, instrument the patient with a rigid cystoscope (19Fr and more) and use a grasper to grasp the distal end of the device. Pull the iTind device out through the cystoscope sheath.

CLINICAL TESTING SUMMARY

Clinical evidence for the device safety and effectiveness has been established in the pivotal study (MT-03). The data from the pivotal study is consistent with previous OUS pilot study (MT-01) and an additional OUS post-market study (MT-02).

MT-01 included 31 subjects completing follow-up to 36 months. This study was conducted outside the United States and was designed as a single-arm, feasibility study. The objective of the study was to assess the safety and efficacy of the TIND System in male subjects age 50 and older with bladder outlet obstruction (BOO) secondary to BPH. The primary efficacy endpoint was to increase maximal urinary peak flow by at least 5 ml/s in at least 75% of patients at 3, 6 and 12 months. The primary safety objective was the incidence of unexpected serious adverse events related to the TIND implant and the implantation/retrieval procedures. Increases in maximal urinary peak flow of 4.1, 4.1 and 4.9 ml/s were attained at the 3, 6 and 12-month time-points. There was a statistically significant increase in peak urinary flow rate (Qmax) from baseline, and reduction in IPSS and QoL scores over 36 months. At 12 months, 25/32 subjects reported an International Prostate Symptom Score (IPSS) improvement of at least 5 points. Four (4) expected early-onset complications were reported and resolved within 30 days without sequelae. Those complications were: urinary retention, transient incontinence, prostatic abscess and urinary tract infection. These were managed via catheter placement, early removal of the device, re-admission/antibiotics, and oral antibiotics, respectively. No further complications were recorded during the follow-up period.

MT-02 was a prospective, single-arm, multi-center, safety and efficacy study on the iTind device. A total of 81 subjects were enrolled in this study. The primary efficacy and safety endpoints were a ≥ 3-point IPSS score reduction in at least 75% of the subjects at 6 months follow-up and the incidence of unexpected serious adverse events related to the device and/or implantation/retrieval procedures, respectively. At the 6-month follow-up visit, (85.3% of treated patients (N=70) reported a ≥ 3-point improvement in IPSS. At the 12-month follow-up visit (, 88.9% of treated patients (n=67) reported a ≥ 3-point improvement in IPSS. Further, patients reported enhanced quality of life, and improvement in mean Qmax, increasing from 7.6 ml/s at baseline to 12 ml/s at 12 months. These findings were also confirmed in the 24-month results, further supporting the durable effect of the iTind procedure.

Three (3.7%) patients experienced serious adverse events that were subsequently resolved within 10 days. The vast majority of complications were low grade, self-limiting, and consisted mostly of hematuria and expected lower urinary tract symptoms, with 43.2% of all patients experiencing some AE (18.5% related; 22.2% device- and procedure-related; 14.8% procedure related). None of the sexually active patients reported any erectile or ejaculatory dysfunction.

The MT-03 pivotal study was an FDA-approved Investigational Device Exemption (IDE) Study, designed as a prospective, parallel, randomized, sham-controlled, multi-center, international clinical trial of the iTind System. A total of 185 subjects were randomized (128 in the iTind group and 57 in Sham) and included in the Intent-to-Treat (ITT) population. A total of 175 patients underwent iTind implantation/Sham treatment, including 118 in the iTind group and 57 in the Sham group. The sham procedure consisted of insertion and removal of a Foley catheter.

The first co-primary endpoint, which was the difference in IPSS score between iTind and Sham groups at 3 months, showed an improvement of approximately 10 points from baseline for the iTind group, which did not achieve statistical significance when compared with the Sham group under the pre-specified statistical model. In addition, 79% of iTind patients were responders (those who showed a ≥ 3-point reduction), compared to 60% in the sham group.

CHANGES IN IPSS AT 3 MONTHS*

Treatment Group	N (baseline)	N (3 months)	IPSS (Baseline)	IPSS (3 months)	IPSS (Change from Baseline)	95% Lower Limit	95% Upper Limit	P-Valve
iTind	127	84	26.7	15.7	-10.6	-11.8	-8.1	NA
Sham	57	40	27.7	19.2	-8.3	-10.1	-4.8	
Sham - iTind	NA	NA	1.0	3.5	2.5	-0.5	5.6	0.104

*SAP Mixed Model; Intent-to-Treat (ITT) Population

The second co-primary endpoint of the study, which was the change in IPSS Score at 12 months compared to the baseline for the iTind group, showed a significant improvement of IPSS scores for the treated group. The sham group could not be compared at 12 months, because their follow up was limited to 3 months to enable them to resume active treatment.

CHANGES IN IPSS SCORE AT 12 MONTHS*

Treatment Group	N (12 months)	Visit	Change from Baseline (at 12 months)	95% Lower Limit	95% Upper Limit	P-Valve
iTind	81	12 Months	-8.7	-10.6	-6.9	< 0.001

*SAP Mixed Model; Intent-to-Treat (ITT) Population

Analyses of the secondary endpoints demonstrated improvement in the iTind group for all the tested
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clinical outcome measures, including urinary flow rate, bladder emptying, and male sexual health at 3 months.

CHANGES IN CLINICAL OUTCOME MEASURES*

		Measurement			Change from Baseline		
Clinical Outcome	**Visit**	**n**	**Mean**	**SD**	**n**	**Mean**	**SD**
Peak Flow Rate (ml/sec)	Baseline	125	8.7	3.3	125	0.0	0.0
	3 Months	82	13.1	7.0	81	4.4	7.0
Post-Void Residual Urine Volume (ml)	Baseline	125	61.6	55.5	125	0.0	0.0
	3 Months	80	55.9	53.2	79	-5.0	55.3
International Index of Erectile Function (IIEF) Score	Baseline	125	38.3	20.7	125	0.0	0.0
	3 Months	84	43.7	22.2	83	4.0	19.1
Sexual Health Inventory for Men (SHIM) Score	Baseline	127	13.2	7.3	127	0.0	0.0
	3 Months	84	13.6	7.8	84	0.4	7.0

*Descriptive Statistics; ITT Population

The most frequent AEs observed in the study included dysuria (22.9% of subjects), hematuria (13.6%), pollakiuria (6.8%), urinary retention (5.9%), and micturition urgency (5.1%). There were 74/109 (68%) adverse events in the iTind group which occurred within 7 days of treatment (while the device was in the body). Most were mild, anticipated and resolved within 1-4 weeks. Of the 109 total AEs, 54 (49.5%) required no intervention, (33.0 %) were managed pharmacologically, 12 (11.0%) were managed non-surgically, and 4 (3.6%) were managed surgically. Of the AEs that were managed surgically, one subject had dental caries, one subject had an upper limb fracture, one subject had worsening of urinary symptoms that led to a transurethral prostatectomy, and 1 subject had worsening hematuria, clots and an inability to void (successfully treated by catheterization, subsequent clot removal, and bladder fulguration).Relevant observed adverse events are listed below.

Preferred Term	Treatment group					
	iTind (N=118)			Sham (N=57)		
	No. Events	No. Subj.	% Subj.	No. Events	No. Subj.	% Subj.
Total AEs	109	45	38.1	19	10	17.5
Dysuria	27	27	22.9	5	5	8.8
Hematuria	17	16	13.6	0	0	0
Pollakiuria	8	8	6.8	1	1	1.8
Urinary retention	8	7	5.9	0	0	0
Micturition urgency	6	6	5.1	1	1	1.8

Most of the AEs in both groups occurred within 90 days from randomization (99 AEs in 44 (37.3%) patients in the iTind group and 15 AEs in 10 (17.5%) patients in sham). Most of the AEs were anticipated. The unanticipated AEs occurred in 12.7% of patients in the iTind group and 10.5% of patients in the sham group. One AE (mild postoperative urinary retention) was found to be related to the procedure. Three AEs (lung neoplasm, urinary retention, and UTI) were not resolved by the time of study completion in one patient in iTind group, and one AE (chest pain) was not resolved in a patient in the sham group. All these AEs were not related to the device. In the Safety Population (all randomized patients for whom study treatment was initiated), there were 29 patients in the iTind group and 15 patients in the sham group who terminated the study early. Among them, 10 in the iTind group, and 3 in the Sham group experienced AEs.

During the course of study, 16 serious adverse events (SAE) were observed in 10 patients from the iTind group and 2 SAEs in the sham group. For the iTind group, 2 SAEs occurred during the Device-in-Body phase and 14 SAEs occurred during the Post-Retrieval phase. A total of 5 procedure- and/or device-related SAEs were observed in 3 patients from the iTind group, including urinary retention (n=2), urinary tract infection (n=2), and sepsis (n=1). Only 3 SAEs from 2 iTind patients during the Post Retrieval Phase were found to be possibly related to the device. One patient in the iTind group died from pancreatic cancer complications, which was not related to the device.

Adverse events associated with iTind were comparable to other minimally invasive endourological therapies as well as standard cystoscopy. None of the 118 subjects experienced de novo sustained sexual dysfunction (erectile or ejaculatory dysfunction).

For all patients, the procedure was conducted in the same day. On average it took 12.2±17.1 days and 6.2±17.0 days for iTind patients to return to preoperative activities after implantation procedures and retrieval procedures, respectively, which are similar to the sham patients as well as to other minimally invasive endourological therapies. The implantation procedure was shown to be fairly quick and not to cause more than moderate discomfort, with the mean implantation duration of 4.2 minutes and mean VAS pain score of 4.2.

SUMMARY

The pivotal study met one of the two co-primary endpoints, showing a significant improvement of IPSS scores at 12 months compared to the baseline. For the other co-primary endpoint, IPSS score at 3 months was not statistically significantly better for the iTind treatment group when compared to the sham. Analyses of the secondary endpoints demonstrated improvements in the iTind group for all the tested clinical outcome measures, including urinary flow rate, bladder emptying, and male sexual health at 3 months.

Safety results demonstrated a favorable safety profile for the iTind device, with a low rate of serious adverse events (none were deemed to be definitely related to the device, though several were deemed to be possibly related). After device removal, the rate of additional AEs decreased significantly. Most of the AEs observed in the study were anticipated and were mild with 49.2% resolving without intervention and 34.3% resolving with pharmaceutical intervention.

ADVERSE EFFECTS

The cystoscopy procedure, and/or the presence of the iTind device in the prostatic urethra or the deployment/retrieval procedure, may lead to the following adverse effects:

- Fever, bleeding, pain, UTI, false route of the urethra, dysuria, difficult urination, frequency and urgency, urinary retention and related symptoms, blood in urine (hematuria), urinary incontinence, urethrorrhagia, blood in semen (hemospermia), bladder perforation, urethral and/ or bladder neck strictures, urethral bleeding, prolonged erection and retrograde ejaculation.
- Local irritation and foreign body response.

REPROCESSING INFORMATION

The iTind system is NOT reusable in any way. For this reason, no reprocessing instructions are required.

STORAGE AND TRANSPORTATION

Storage temperature:

- Room temperature. The iTind System and the Removal KIT should be stored in a dry environment and away from sunlight.
- Transportation conditions:

1. For iTind System KIT:
   temperature -35°C to +60°C
   Humidity 15% to 90%.
2. For Removal KIT (**In US Only**):
   Temperature -15ºC to +49ºC
   Humidity 15% to 85%

USE OF ORIGINAL PRODUCTS

The components of the Medi-Tate iTind System are designed for specific use and complement each other.

System components cannot be replaced by a product from another manufacturer, even if the other product or part is comparable or identical to the original product in appearance and dimensions. For instance, materials used from other manufacturers and any structural alterations resulting from the use of products from another source can introduce unforeseen risks to the patient and user.

SYMBOLS and their **DEFINITIONS**

	Single sterile barrier system.		Manufacturer.
	Medical Device		Keep Dry.
	Batch code.		Keep away from sunlight.
	Use by date.		Catalogue number.
	Do not re-use.		Humidity limitation.
	Do not re-sterilize.		Temperature limitation.
	Do not use if package is damaged.		Local distributor address.
	Sterilized using ethylene oxide.		Transportation conditions.
	Consult instructions for use.		MR Conditional.
	Caution, consult accompanying documents.		

Medi-Tate iTind System

INSTRUCTIONS FOR USE

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