

How I Do It: Temporarily Implanted Nitinol Device (iTind)

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ELTERMAN D, GAO B, ZORN KC, BHOJANI N, CHUGHTAI B. How I Do It: Temporarily Implanted Nitinol Device (iTind). *Can J Urol* 2021;28(4): 10788-10793.

Benign prostatic hyperplasia is a common and progressive disease affecting aging men which has a significant impact on quality of life. The second-generation Temporarily Implanted Nitinol Device (iTind) is an FDA approved temporary prostatic urethral device which can be deployed using standard flexible cystoscopy without sedation or

general anesthesia. The device is left in-situ for 5 to 7 days and is then entirely removed in the office, using an open-ended silicone catheter. Prospective, randomized data indicate that iTind has favorable functional and sexual patient outcomes. Readers will familiarize themselves with iTind, significant historical studies and the technique for deploying iTind using a flexible cystoscope in the office setting.

Key Words: BPH, prostate, TMIST, iTind

Introduction

Overview of procedure/technology

Benign prostatic hyperplasia (BPH) is a common disease affecting aging men.¹ Bothersome lower urinary tract symptoms (LUTS) secondary to BPH are a significant burden to the healthcare system, responsible for approximately 4 billion dollars annually in the United States.² Traditional dogma dictates a stepwise approach for BPH management involving lifestyle

alteration, medical therapy and surgery. When lifestyle alteration fails, medical and surgical therapy are frequently complicated by unwanted functional and sexual side effects such as erectile dysfunction (ED), decreased libido, and ejaculatory problems.^{3,4} Sexual health surveys indicate that maintenance of sexual function is significantly prioritized by patients suffering from BPH, with postoperative erections and ejaculatory function important to 95% and 92% of men respectively regardless of age.⁵ To address these treatment shortcomings, innovative minimally invasive surgical therapies (MIST) for the treatment of BPH have been developed.

True Minimally Invasive Surgical Therapy (TMIST) is a novel concept within MIST that bridges medical therapy and surgical therapy.⁶ TMIST is an off-the-

Accepted for publication July 2021

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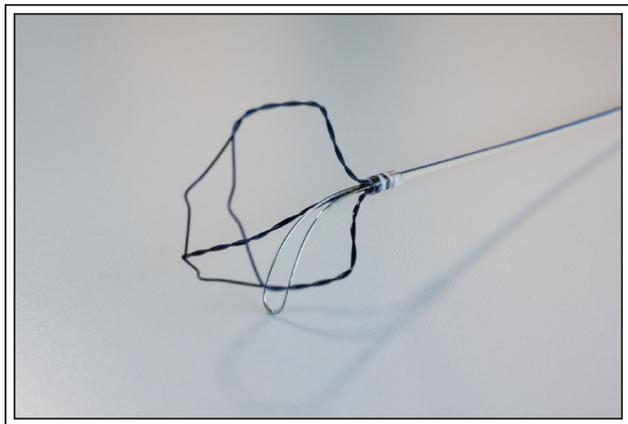


Figure 1. Second-generation Temporarily Implanted Nitinol Device (iTind) consisting of an anti-migration anchoring leaflet, three elongated intertwined nitinol struts connected at the distal end, and polyester retrieval suture.

shelf BPH therapy that can be performed in a urology office without general anesthesia using a flexible cystoscope. TMIST represents an efficient and cost-effective bridge between medical therapy and surgical therapy and may decrease operating room burden and healthcare costs, while improving patient satisfaction.⁶

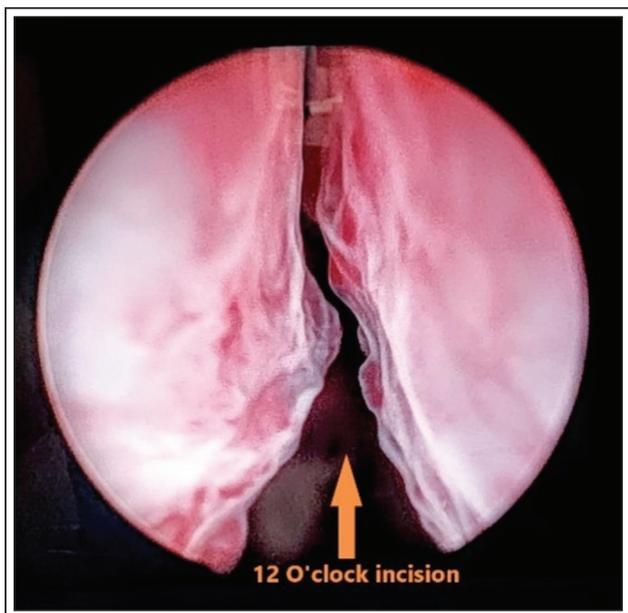


Figure 2. Three nitinol struts apply continuous ischemic pressure, and through subsequent tissue necrosis, three new channels are made to reshape and expand the bladder neck and prostatic urethra. This is an example of the resulting incision at 12 o'clock.

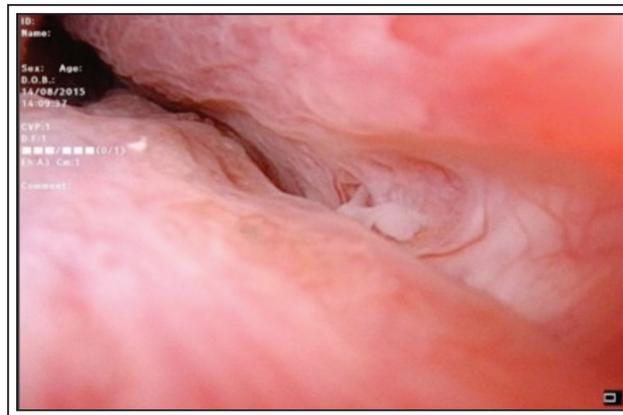


Figure 3. Deep 5 o'clock incision at 12 months follow up.

The second-generation Temporarily Implanted Nitinol Device (iTind) (Medi-Tate, Hadera, Israel/Olympus Corporation, Tokyo, Japan) is an FDA approved TMIST deployed in the bladder neck and prostatic urethra.⁷ Consisting of an anti-migration anchoring leaflet, three elongated intertwined nitinol struts connected at the distal end, and polyester retrieval suture, iTind is placed utilizing a standard flexible cystoscope,⁸ Figure 1. The three nitinol struts apply continuous ischemic pressure, and through subsequent tissue necrosis, three new channels are made to reshape and expand the bladder neck and prostatic urethra. After 5 to 7 days, the device is completely removed by pulling the polyester retrieval suture through a standard open-ended silicone catheter to compress the iTind device, Figures 2 and 3.⁸

Significant historical studies

There is one prospective study for the first generation TIND which was a 4 single wire nitinol device. Porpiglia et al performed a single center, single-arm, prospective study with 32 patients and published their 3 year results in 2018.⁸ Improvements in IPSS, IPSS QoL, and Qmax were sustained through 3 years. Additionally, no patients required retreatment nor experienced reduced sexual function.

Current literature for second generation iTind consists of two prospective studies and one randomized controlled trial. Amparore et al published 3 year results of their prospective multicenter study in 2020. Eighty-one men with prostate volumes less than 75 cm³ showed sustained improvements in IPSS (20.7 to 8.55), IPSS QoL (3.96 to 1.76), and Qmax (7.71 mL/s to 15.2 mL/s).⁹ Soon after, De Nunzio et al published 6 month results of their study in which 70 men were enrolled with an expanded inclusion criteria of prostate volumes less

than 120 cm³.¹⁰ Similar to Amparone's study, iTind showed significant improvements in IPSS (21.2 to 8.3), IPSS QoL (4.1 to 2.0), and Qmax (7.3 to 12.0) at 6 month follow up. No sexual side effects were reported.

Chughtai, Elterman et al published the first multicenter, prospective, sham controlled, single-blinded RCT at the end of 2020.¹¹ A total of 185 men were randomized between iTind and sham control. Prostate volumes of 25 cm³ to 75 cm³ and moderate-to-severe symptomatic BPH (IPSS ≥ 10) were included. The sham control consisted of the insertion and removal of an 18F silicone Foley catheter. There was a 40% reduction in IPSS at 3 months (22.4 versus 12.6) that sustained through 12 months (21.6 versus 12.7). Similar improvements were seen in IPSS QoL at 3 months (4.55 versus 2.54) and 12 months (4.51 versus 2.45) in addition to Qmax at 3 months (8.63 versus 13.6) and 12 months (8.42 versus 11.9). The retreatment rates within 1 year were reported at 4.7%. Common self-limiting complications (Clavien-Dindo 1 and 2) included transient hematuria, dysuria and urgency.

Method and technique

Patient assessment

Patients should be evaluated using standard methods as per urological society guidelines which may include review of medical history, physical exam, completion of validated questionnaires, uroflow studies and volumetric assessment. We also obtain a volumetric assessment of the prostate through cross-sectional imaging or transrectal ultrasound to characterize prostate volume and anatomy for surgical planning as a large obstructive median lobe should be avoided with iTind. The pivotal iTind study (MT-03) included men with prostates between 25 cm³ to 75 cm³ and no significant median lobe. Standardized questionnaires such as the IPSS and IIEF may also be conducted to track patient progress over time.

Patient preparation

The patient is positioned in dorsal lithotomy and prepped and draped in usual fashion for flexible cystoscopy. Local and oral anesthetic are administered as below:

- Intraurethral lidocaine jelly 2% 10 cc, clamp penis for 10 minutes
- Antibiotic prophylaxis (based on local antibiogram and AUA guidelines)
- Consider diazepam – 1 (PO dose 2 mg)
- Consider oxycodone/acetaminophen – 1 (PO dose 2.5 mg/325 mg – 5 mg/325 mg)

- Consider celecoxib – 1 (PO dose 200 mg 1 hour before the procedure)
- Consider prostate block with 0.25% bupivacaine 30 cc
- Consider intravesical lidocaine 2% 50 cc

We have found that using regular lubricating gel with cystoscopy is typically acceptable for patient comfort. Other MISTs have described using inhaled nitrous or methoxyflurane (Penthrox) for patient analgesia without requiring intravenous medication or monitoring of vitals.

Deploying iTind

The iTind is a temporary implant that reshapes the bladder neck and prostatic urethra and is completely removed after 5 to 7 days, Figure 4. The benefit of iTind being a TMIST is that diagnostic cystoscopy and therapeutic delivery of the device can be performed simultaneously in one office procedure with no additional special equipment or anesthesia required. The surgeon simply requests for iTind during flexible cystoscopy and a nurse or assistant can open the device off the shelf and hand it to the surgeon to deploy.

The iTind technique was originally reported using a rigid cystoscope. Patients were either sedated or a prostate block was administered while the device was passed through the outer rigid sheath into the bladder. The outer sheath was then removed and the rigid scope was then passed alongside the iTind's guidewire and into the bladder. The operator would then manipulate the guidewire to orient the iTind with the anterior strut at 12 o'clock and the anchoring leaflet at 6 o'clock. A blue line is present along the entire shaft of the iTind guidewire and should be at the 12 o'clock position to confirm the anchoring leaflet is correctly positioned at 6 o'clock. The iTind was then positioned into the prostatic fossa such that the anchoring leaflet sat just behind the bladder neck and in-front of the verumontanum. The rigid scope would then be removed once the positioning was confirmed and not obstructing the external sphincter. The guidewire was

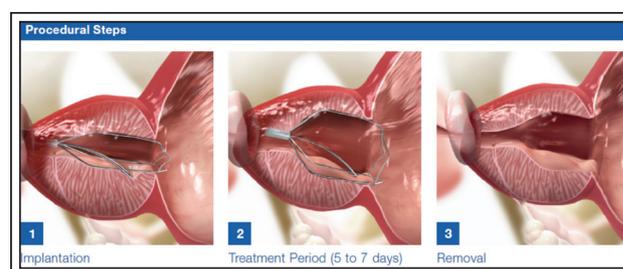


Figure 4. iTind procedural steps. Courtesy of Olympus.

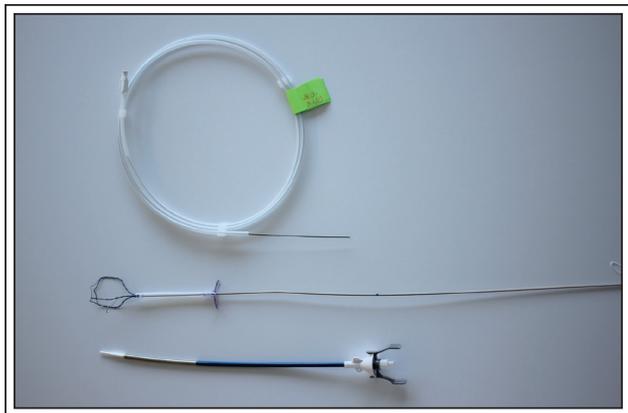


Figure 5. iTind device with ureteral access sheath and PTFE guidewire.

then removed by untying the slipknot and the retrieval suture to be taped using Tegaderm upon the penile shaft for future retrieval.

With greater international experience using the iTind, it became apparent to several surgeons that the technique could be further refined to enhance patient comfort with the use of a standard flexible cystoscope. This advancement would truly allow this procedure to be brought into the urology office and obviate the need for sedation or a prostate block. The introduction of the collapsed iTind into the bladder required a delivery system which was easy to insert, readily available, inexpensive, and comfortable to the patient. A 12/14Fr ureteral access sheath and standard PTFE guidewire solved this problem, Figure 5. During initial flexible cystoscopy, a standard PTFE guidewire is utilized to maintain access into the bladder. The flexible cystoscope is removed and the ureteral access sheath is inserted over the PTFE guidewire. A ureteral access sheath can be introduced comfortably and atraumatically through the urethra and into the

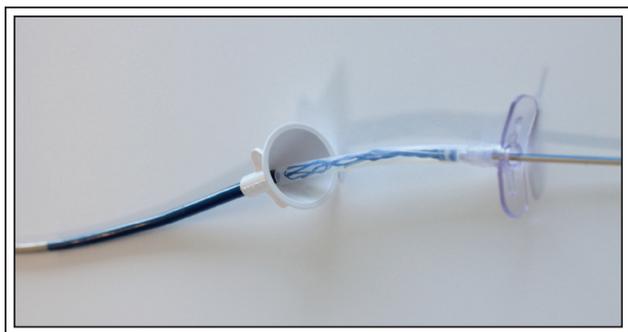


Figure 6. Collapsed iTind being delivered into Olympus UroPass ureteral access sheath.

bladder. Once the iTind has been delivered through the ureteral access sheath and into the bladder where it can expand, Figure 6, the ureteral access sheath is backed out of the urethra. A lubricated, standard flexible cystoscope can then be passed comfortably alongside the iTind guidewire and into the bladder. At the level of the meatus the operator can twist and manipulate the covered retrieval suture to orient the iTind within the bladder. The 12 o'clock strut and its opposing 6 o'clock anchoring leaflet are oriented and pulled back gently to the bladder neck. A blue line is present along the entire shaft of the iTind guidewire and should be at the 12 o'clock position to confirm the anchoring leaflet is correctly positioned at 6 o'clock. The flexible scope is positioned at the verumontanum just distally to allow for direct visualization as the iTind is pulled into the prostatic urethra. The anchoring leaflet slides over the bladder neck inferiorly and seats itself just proximal (in front) of the verumontanum. The iTind guidewire can be removed by untying the slipknot, leaving the retrieval suture in place. The retrieval suture is then coiled and placed on the dorsum of the penis and secured using a Tegaderm with steri-strips or paper tape. Men should be sent home with either an absorbent pad in their undergarment to accommodate any wicking that may occur on the retrieval suture.

Since iTind is performed using a flexible cystoscope under local anesthesia only (with no permanent implant) it can easily be brought up as an alternative to indefinite oral medical therapy.

We use the Olympus UroPass ureteral access sheath (12/14Fr in the 24 cm length). Important advantages of this access sheath include a clip system which keeps the sheath dilator tip position during placement, hydrophilic coating to facilitate reduced friction during passage, stainless steel reinforcement which helps keep the iTind collapsed during its passage, and an atraumatic 12Fr tip. Other comparable ureteral access sheaths can be used, provided their inner lumen is large enough to accommodate the collapsed iTind (12F).

Managing indwelling iTind

While most patients describe the iTind procedure as being "a little uncomfortable", patient experience may vary and a small percentage of patients report more than mild to moderate discomfort. We recommend counselling and preparing your patients for the possibility that they may experience some of the following symptoms and ensuring that they have the necessary tools available to them during the 5 to 7 days to manage comfortably. Below are our recommendations for maximizing patient comfort and recovery.

TABLE 1. Medications

Consider following medications in a graduated fashion. At discharge: (at the discretion of the physician)

- Phenazopyridine 100 or 200 mg orally as needed (max 3 times per day) for duration of iTind
- NSAID and Tylenol orally as needed as per label, do not exceed maximal dosing
- Consider Codeine 30 mg orally as needed (max 3 times per day)
- Consider Prednisone 25 mg/day for 5 days
- Consider Oxybutynin 5 mg as needed (max 3 times per day)

Patients may describe a feeling of dysuria associated with pain or pressure in the perineal area while iTind is deployed. We recommend discharging patients with ample analgesics to be taken in a graduated fashion depending on severity of discomfort for the duration of iTind, Table 1. All patients should consider taking acetaminophen and/or NSAIDs (as per label, do not exceed maximal dosing) for reduction of inflammation and pain during recovery. An opioid such as codeine (one 30 mg tablet as needed, max 3 times per day) and local urinary tract anesthetic such as phenazopyridine (100-200 mg TID as needed) may also be prescribed. In cases of breakthrough pain, it is also possible to prescribe patients an oral dose of steroids to reduce swelling and inflammation (prednisone 25 mg daily for 5 days). These aforementioned medications should be used judiciously, as their side-effects may be more severe than the discomfort from the iTind.

Bothersome urinary frequency and urgency may also occur for the duration of iTind due to the proximal end of the device protruding slightly into the bladder. Furthermore, after micturition, the bladder walls may rub against the device and cause further irritation. We recommend lifestyle counselling which includes increased water intake and avoiding bladder irritants such as coffee, tea and alcohol. In severe cases, anticholinergics may also be given (oxybutynin 5 mg as needed, max 3 times per day). The prescriber should be aware that in rare cases, this may increase the possibility of acute urinary retention upon device removal.

The incidence of acute urinary retention while the device is in situ is extremely rare. It is recommended to provide the patient with a medical contact person to notify who is familiar with the procedure. An 8-12Fr foley catheter can be gently placed by an experienced provider through the deployed iTind device in the case of urinary retention. The patient can then have both the foley catheter and device removed at the 5 to 7 day benchmark for a trial of void.

It is important to inform patients that they can expect some mild hematuria, particularly during the first 48 hours following device implantation. Patients should be counselled that this is normal and will self-resolve. Patients should stay well hydrated and be reassured that hematuria is not an issue unless they experience clot retention. Blood thinners may be held if clinically appropriate in severe cases, however this is extremely rare.

Patients may complain of symptoms from the iTind retrieval suture. Patient counselling to not cut or tamper with the retrieval suture is important, as this may affect the positioning of the device and make removal more difficult. The retrieval suture can cause irritation to the patient's meatus, particularly towards the end of the implantation period. It is recommended to leave ample slack when fastening the retrieval suture to minimize chafing. A small amount of petroleum jelly to the meatus may act as a barrier and help reduce irritation from the suture. The retrieval suture can also become damp after voiding. Proper bathroom hygiene with wiping after micturition and absorbent pads will reduce soiling of undergarments.

Removal of iTind

After 5 to 7 days of the iTind left in-situ, the patient returns for device removal in the office. The patient is positioned supine on an exam bed. The Tegaderm or paper tape holding the retrieval suture is removed from the dorsum of the penis. Similar to any catheter insertion, the penis is prepped and a xylocaine gel can be administered into the urethra. Liberally insert lubrication inside the 22Fr open ended silicone foley catheter to facilitate insertion of the iTind retrieval snare. We then place the retrieval snare through the open ended silicone foley catheter. The retrieval suture is withdrawn through the open ended silicone Foley catheter by pulling it through with the retrieval snare. An assistant firmly holds the retrieval suture while the surgeon advances the open-ended catheter until it engages the hub of the iTind. Forward force is applied

on the catheter while slightly turning it, and counter-traction is applied on the retrieval suture. The iTind will collapse inside the lubricated catheter resulting in a feeling of reduced force as the device enters the catheter. The catheter and crimped iTind device is then pulled out of the urethra as one unit.

Symptoms after removal

Following device removal, most patients feel immediate relief of any symptoms experienced while the iTind was in-situ. A small percentage of patients may continue to experience mild dysuria, hematuria, frequency and urgency for up to 2 weeks following device removal and it is recommended to prepare patients for this possibility. Most patients experience an improved urinary stream immediately after device removal. Post removal of the iTind device, patients should successfully void prior to going home. Other patients may take longer to start experiencing a significant improvement in BPH symptoms. It is important to counsel your patient that maximal BPH symptoms relief will be reached 3 months following removal of the device.

At the physician's discretion it is also possible to provide steroids orally to reduce inflammation at the site of the prostatic urethra and bladder neck, and/or to prescribe alpha blockers as a bridge treatment during the implantation period and the 2-3 weeks following device removal. We typically see patients in follow up 4-6 weeks after iTind retrieval.

Discussion and conclusions

iTind is a FDA approved TMIST effective for treating a wide range of prostate glands without the need for general anesthesia or sedation. The technology promises to bridge the gap between conservative medical therapy and more invasive surgical therapy by being deployable using a standard flexible cystoscope in the urology office. Results of prospective studies and recent randomized controlled trials are both exciting and promising and we hope you consider adding iTind to your urological practice. We believe that a standardized technique, such as this, can be easily reproducible for a successful outcome. Like everything that is new, take your time, build your experience and confidence, learn and refine your technique.

Disclosures

Drs Elterman and Chughtai are Olympus consultants. Drs Gao, Bhojani and Zorn have no conflicts to disclose. □

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