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iTIND: the second-generation temporary implantable nitinol device for minimally invasive treatment of benign prostatic hyperplasia

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***Abstract*:** iTIND is the second-generation version of the temporary nitinol implantable device (TIND), which has emerged over the past decade as one of the latest additions to the library of minimally invasive surgeries now available to treat bothersome lower urinary tract symptoms (LUTS) caused by benign prostate enlargement. While the key procedural steps remain the same, it now carries specific modifications designed to improve its efficacy and safety profile further. With the option to perform implantation under local anaesthesia, it can be delivered on an ambulatory basis and in the office setting. While the formal position of iTIND in current guidelines is yet to be determined, 12-month data demonstrates that it can improve both objective and subjective outcome measures, which are sustained at short-term follow up.

Keywords: alternative therapies, BPE, BPH, iTIND, LUTS, minimally invasive, TIND

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Introduction

Bothersome lower urinary tract symptoms (LUTS) caused by benign prostate enlargement (BPE) is a condition of prevalence, which has been confirmed by a number of community-based, longitudinal studies.[1,2] It is estimated to affect over one-third of men over 60 years of age to a moderate or severe extent.[3] The sequelae are far reaching, and the burden of this disease can be both psychological and socio-economic. Management initially includes lifestyle advice and medical therapies such as α-blockers and 5α-reductase inhibitors.[4] However, side-effects associated with pharmacotherapy, including postural hypotension and sexual dysfunction, can lead to reduced patient tolerance, poor compliance and early discontinuation accordingly. Approximately 25% of men over 50 years who develop LUTS due to BPE will require surgical intervention.[5] While transurethral resection of the prostate (TURP) has served as the gold standard surgical treatment for many years, efforts have always been going on to develop alternatives that deliver high efficacy rates while sustaining sexual function and minimising morbidity.[6] Minimally invasive alternatives include laser-based methods such as holmium laser enucleation of the prostate (HoLEP), greenlight photo-vaporisation of the prostate and thulium laser enucleation of the prostate.[7–10] Newer treatment options also include prostate artery embolisation, UroLift® (PUL), aquablation and rezum.[11–15]

iTIND is the second-generation version of the temporary implantable nitinol device, TIND (TIND; Medi-Tate, Or Akiva, Israel), which has undergone a number of improvements.[16] This mechanical device has now undergone a number of changes as part of its evolution. The aim of this article is to provide an overview of this modified version of the device.

What is the device?

The iTIND serves to re-model the bladder neck and the prostatic urethra. The device comprises of three elongated struts, which are configured at 12, 5, and 7 o'clock positions using interlaced

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Table 1. Inclusion and exclusion criteria for iTIND.

Inclusion	Exclusion
Size <60 cc	History of prostate cancer
Age >50 years	Previous prostate surgery for example, TURP
IPSS >12	History of urethral stricture
Qmax >12 ml/s	Bladder stones
	Active infection
	Urinary retention

IPSS, international prostate symptom severity score; iTIND, second-generation temporary implantable nitinol device; Qmax, maximum urinary flow rate; TURP, transurethral resection of the prostate.

nitinol wires.[17] The size of the newer device is the same (5 cm × 3.3 cm) as the first-generation model and is intended to match the dimensions from the bladder neck to the external urinary sphincter. In addition to the extra strut, which the first-generation device had, the tip was pointed and covered by a soft plastic material. This cover was designed to help avoid bladder injury. However, in order to minimise risk of damage to mucosa, this tip has now been removed and the resultant, open-end appearance is often described as being similar to that of a tulip flower. There remains an anchoring leaflet, which is attached to a nylon wire. The procedural steps are the same for the first- and second-generation devices. The device itself is left *in situ* for approximately 5 days. Maximal expansion of the structure is reached by this point and, through a process of localised ischemic necrosis from where the struts have compressed the encroaching tissue, longitudinal channels are created. From this remodelling process and channel formation, improved urinary outflow is established.

The procedure

The patient is given a single dose of antibiotic prophylaxis and lies in the lithotomy position. The mainstay of cases can be achieved with use of local anaesthetic only but light, intravenous sedation can be used to support this as required. In a similar method to PUL, the device is pre-loaded into a custom system (14Fr) and then passed through the cystoscopic sheath (19-22 Fr). Once routine inspection of both bladder and urethra has been performed, the device can be deployed into a full bladder. Under endoscopic vision, it can then be carefully manipulated into the desired position. The anchoring leaflet should be orientated to the 6 o'clock position, under the bladder neck and cranial to verumontanum. With this secured, the device can be carefully retracted so that the nitinol, longitudinal struts are in contact with the encroaching prostatic tissue. Once this has been performed to the surgeon's satisfaction, the plastic sheath covering the nylon wire can be taken off and the wire itself can be shortened. To complete the procedure, the bladder is emptied, and no catheter is required. The total procedural time is less than 10 min. With continuous pressure and resultant ischaemia, the prostatic urethra and bladder neck is remodelled, which creates new channels *via* which urine can flow. While it is yet to be formally assessed, surgeon observation and experience suggests that this procedure carries a short learning curve.

Patients can be discharged on the same day with a regime of simple analgesia. After 5–7 days, patients return to have the device removed. This is achieved *via* retrieval of the nylon wire, using a snare to pull the device into either a cystoscope sheath or an open-ended silicone catheter (20-22Fr).

Patient selection

Based on studies to date, patients require prostate size less than 60cc (Table 1). It has yet to be carried out in patients with previous prostate cancer, prominent median lobe, urethral stricture, concomitant bladder stones or previous prostate surgery. Of note, no published study has performed it in a population sample where the mean prostate size exceeds 40cc.[18]

Current evidence for iTIND

The initial clinical experience with the first-generation version of this mechanical device was reported in a sample of 32 patients by Porpiglia *et al.* in 2015.[19] At 1 year follow up, the international prostate symptom severity score (IPSS) and maximum urinary flow rate (Qmax) scores had improved by –45% and +67% respectively. The early complications were prostate abscess ($n = 1$), urinary tract infection ($n = 1$), transient urinary incontinence caused by device displacement ($n = 1$) and urinary retention ($n = 1$). Extended follow up to 3 years

was later published.[20] No further adverse events were recorded; however, three cases had required re-intervention within 24 months of the initial operation. The final improvement in IPSS and Qmax was –19% and +41%, respectively.

A single-arm, prospective, multi-centre study (MT-02) was performed to report the clinical experience of patients managed with the second-generation version for the treatment of bothersome LUTS due to BPE.[21] A total of 81 patients were involved in this study and follow-up assessments were conducted at 1, 3, 6 and 12 months post-operatively.[10] Study sites included Italy, the United Kingdom (UK), Switzerland, Belgium and Hong Kong. All patients enrolled in this study had an IPSS ⩾10, Qmax <12 ml/s, and prostate volume <75 cc. The mean patient age was 65 years. The devices were retrieved at a mean of 5.9 days after implantation, typically under topical anaesthesia. The results of this study showed the mean Qmax at 1 month follow-up was 11.2 ml/s and continued to improve thereafter, reaching 14.9 ml/s and 16 ml/s at the 12 months and 24 months, respectively. The mean IPSS was 11.7 after 1 month, and this improved further to 8.7 and 8.5 (–60%) at 12 months and 24 months, respectively. No major complications (>Clavien III) were recorded. All the implantations were successful, and all patients were discharged on the same day of surgery. However, during the 12-month period, two patients required subsequent surgery (TURP/HoLEP). In the second year, a further five patients required additional surgery (TURP). Four of these patients who required re-treatment were found to have prominent median lobes. Failure analysis was carried out, and the presence of prominent median lobe was associated with a significantly higher rate of treatment failure ($p < 0.0001$). At the 2 year follow-up mark, no patients reported de novo sexual dysfunction.[22]

While the European Association of Urology guidelines acknowledge the emerging role of this device, no specific recommendation is given, and its formal role is therefore yet to be defined.[23]

Comparison with similar treatment(s)

The modus operandum of this device is mechanical rather than ablative or cavitating, and therefore the alternative that is most similar is arguably UroLift®.[24] Elterman *et al.* reported 3 year clinical and economic outcomes from their single-arm, prospective study.[25] The authors directly compared their findings using the first-generation device with the 3-year outcomes published from the L.I.F.T. study (Luminal Improvement Following Prostatic Tissue Approximation for the Treatment of LUTS secondary to BPE).[26] The latter, a randomised controlled multicentre trial, compared PUL with a sham procedure. In the L.I.F.T study, 5.2 implants were used on average and the authors calculated an overall cost at $4160 CAD ($800 CAD/implant). In comparison, the cost of iTIND per device was reported as $2500 CAD (single implant only). The authors reported superior results associated with iTIND, with regards to IPSS ($p = 0.033$), Qmax ($p = 0.033$) and quality of life (QoL) ($p = 0.192$). However, the sample size was small ($n = 32$) and the study was completely separate, non-matched and non-randomised.[26] Future comparative studies are required to be able to truly validate these early findings by Elterman *et al.*[25] Both do offer strong profiles with respect to preservation of sexual function and are widely accepted as similar in this regard. However, the efficacy, safety and durability of PUL has been studied more extensively to date. A meta-analysis by Cacciamani *et al.* determined that preservation of antegrade ejaculation is sparse among endoscopic treatments such as TURP compared with the newer treatments such as iTIND and PUL.[27] The potential role of these alternatives is therefore of great interest to both clinicians and patients alike.

Advantages and disadvantages

This mechanical device offers a number of potential advantages (Table 2). Requirement for general anaesthesia is obviated and therefore it can be delivered in an office or ambulatory setting. Given the short procedural time, a high number of cases can be performed in an operating session. While yet to be determined and published formally, it would be estimated that cost savings would follow accordingly. A urinary catheter is not required at end of the procedure, which is anticipated to increase patient satisfaction. The modified design, principally the removal of the cranial tip, should also minimise risk of tissue injury on deployment of the device. The mechanism of action allows for preservation of sexual function, which is supported by the clinical studies to date.

Table 2. Advantages and disadvantages of iTIND.

Advantages	Disadvantages
No requirement for general anaesthesia	No Level 1 data
Office or ambulatory setting	No long-term data
No major complications recorded to date	Specialist centre experience reported only
Sexual function preserved	Not suitable for large prostate burdens
Key anatomical structures preserved	No cost data available
Thermal damage avoided	
No ionising radiation	
Short learning curve	

iTIND, second-generation temporary implantable nitinol device.

However, there is a lack of long-term data available for the new device and therefore, the durability of this procedure is yet to be established at this time. It is also yet to be demonstrated in larger prostate volumes or those with obstructive median lobes. Future studies with broader inclusion and exclusion criteria will help delineate the generalisability and reproducibility of this novel surgery.[28]

Future research

At present, the authors know of four registered studies that are currently ongoing. These exist in the UK [ClinicalTrials.gov identifier: NCT03239951], Germany [ClinicalTrials.gov identifier: NCT03994263], North America [ClinicalTrials.gov identifier: NCT02506465] and a multi-centre study across Europe [ClinicalTrials.gov identifier: NCT03395522]. However, these all represent one-arm trials and while such research will augment the available evidence to support this novel procedure, Level 1 evidence in the form of randomised trials would complement this the most. Future studies should aim to include measurement of cost and learning curve as these two elements have yet to be addressed.[29]

Conclusion

The second generation iTIND is a novel and minimally invasive surgery, which can now be offered in the ambulatory setting. 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.

Conflict of interest statement

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