Published in final edited form as:

Urology. 2011 January ; 77(1): 211–216. doi:10.1016/j.urology.2010.06.065.

Novel Artificial Urinary Sphincter in the Canine Model: The Tape Mechanical Occlusive Device (TMOD)

Bahaa S Malaeb, MD^{*,1}, Sean P Elliott, MD¹, Joseph Lee, MD¹, David W Anderson, PE², and Gerald W Timm, PhD^{1,2}

¹Department of Urologic Surgery, University of Minnesota, Minneapolis MN

²GT Urological, LLC, Minneapolis MN

Abstract

Objective—To assess the functionality, occlusive efficiency and biocompatibility of a novel artificial urinary sphincter, the Tape Mechanical Occlusive Device (TMOD), [GT Urological, Minneapolis, MN], following implantation in a live canine model as well as its occlusive efficiency and sizing parameters in human cadavers.

Materials and Methods—Three female canines underwent implantation of the device at the level of the bladder neck. Functionality was assessed starting at two weeks post-implantation up to 9 weeks. The devices were activated at 2 weeks, then deactivated for three, thirty minute sessions per day to permit voiding. Urethral occlusion pressures (UOP) and biocompatibility for systemic toxicity and local tissue response were examined. Additionally, the TMOD was inserted in 3 male cadavers to determine sizing parameters and to assess UOP utilizing pressure profilometry.

Results—In the canine model, UOP increased from a range of 9–42 cm H₂O with TMOD deactivated to a range of 57–82 cm H₂O with the TMOD activated. Pathological examination revealed unremarkable pseudo-capsular tissues surrounding the device. No histological or structural evidence of systemic toxicity was observed. Sizing parameters similar to other urological implants were confirmed in the male cadavers and urethral occlusion pressures increased from 24–30 cm H₂O with the device deactivated to 61–105 cm H₂O with the device activated.

Conclusion—The TMOD meets the current standards for an artificial urinary sphincter in terms of functionality, biocompatibility and achieving desired occlusion pressures following chronic implantation. Additional testing in male canines followed by early human clinical trials is being contemplated.

Key terms

Artificial urinary sphincter; urethral occlusion pressure; urinary incontinence; urological prosthetic devices; urethral surgery

Introduction

Urinary incontinence occurs in 3–15% of men after radical prostatectomy [1–3]. United States Federal Drug Agency-approved surgical options for management of urinary incontinence include injectable urethral bulking agents, male slings or the AMS 800

*Corresponding Author Bahaa S Malaeb, MD, Department of Urologic Surgery, University of Minnesota, 420 Delaware St. SE, MMC 394, Minneapolis, MN 55407, Phone 612 625 8364, Fax 612 626 0428, malae001@umn.edu.

artificial urinary sphincter (American Medical Systems AMS, Minnetonka, MN, USA). Bulking agents and slings are effective in mild to moderate incontinence whereas the AMS 800 is used for all degrees of incontinence. Despite having been approved for use for over three decades, few physicians implant the device. Indeed, in 2005 only 38 urologists implanted more than 10 devices each and on average only 1 device was implanted for every 3 practicing urologists [4]. Reasons for low acceptance may be related to the physician experiencing difficulty in placing the device or the patient experiencing difficulty in operating it.

We have developed the Tape Mechanical Occlusive Device (TMOD), [GT Urological LLC, Minneapolis, MN]: a 1-piece device for male urinary incontinence that utilizes a spring-loaded mechanism to apply constrictive circumferential pressure on the urethra. As a 1-piece device it facilitates surgical implantation. Additionally, we anticipate that the manually controlled ON and OFF buttons will be easier for the patient to manipulate through the scrotum than the pump bulb of the AMS 800. The current study evaluates the functionality and biocompatibility of the device following implantation in canines and examines the sizing and occlusion efficiency in human cadavers.

Materials and Methods

Device Description

The TMOD is a totally implantable, one-piece artificial urinary sphincter (figure1) with no tubes or wires penetrating the intact skin. It consists of an occlusive tape and a conduit tape, both made of micro-porous expanded polytetrafluoroethylene (ePTFE) with pore size selected to prevent tissue in-growth connected to a control mechanism. The conduit tape originates at the control mechanism and the occlusive tape connects to the conduit tape. The conduit tape is of sufficient length to allow placement of the occlusive tape at the bulbous or penoscrotal urethra without creating undue tension on the conduit tape. The scrotally implanted control mechanism consists of a titanium casing, housing a nickel-cobalt-chromium alloy spring (Elgiloy®, Elgiloy Specialty Metals, Elgin, IL) that applies tension to Teflon®-coated polyester sutures running through the conduit and occlusive tapes. The control mechanism has ON and OFF buttons and is covered with a flexible silicone boot that prevents tissue in-growth. The boot has a port for injection of saline into the device that displaces air and creates an isotonic interior. This same port is designed for antibiotic flushing per surgeon discretion. In the ON position, the occlusive tape contracts and is designed to apply radial pressure to the urethra of 50-80 cm of water. The degree of radial pressure was chosen from clinical experience with the American Medical Systems artificial urinary sphincter AMS 800 and thought to be an appropriate pressure range to minimize urine leakage [5-9] while not causing excessive decrease in urethral perfusion. There is a low-carbon stainless steel (316L) locking clip that locks the occlusive tape to itself to form an annular occlusive ring around the urethra. This can easily be unclipped for tape removal in the event repositioning or explantation is required. Suture tabs are attached to both the control mechanism and occlusive tape. These serve as anchoring points to suture the device in place to prevent migration.

In humans we anticipate implanting the occlusive tape in an open, deactivated condition (occlusive pressure removed from urethra), allowing it to remain in that condition for 6 weeks post-operatively to permit healing. The physician would then activate the device to apply pressure to the urethra by depressing the ON button through the intact scrotal skin. The patient can then depress the control mechanism OFF button to again remove occlusive pressure from the urethra and allow for unobstructed voiding, or lock it in the deactivated position for voiding or nocturnal deactivation. To reactivate, the patient can push the ON button. Conduit lengths were adjusted in this investigation to fit the canine anatomy.

Animal models

Objectives of animal implantation included (1) evaluation of the ability to turn the device ON and OFF following the formation of a tissue capsule, (2) urethral pressure profilometry during activation in a living subject, (3) ability to sustain the occlusion pressure following the formation of the capsule, (4) assessment for complications including urethral atrophy, erosion and device infection, and (5) histologic examination of the urethra after device placement. Female canines were chosen as a model for TMOD implantation for several anatomical considerations. The male corpus spongiosum is partially encased in the corpora cavernosa and circumferential dissection might not be feasible without incorporation of the corpora into the cuff of the device. Furthermore the presence of the bony os penis may predispose the male dogs to device erosion. In addition, there is an inadequate bulbar urethra to allow for standard placement in male dogs. Appropriate anesthesia was given in accordance with an Institutional Animal Care and Use Committee (IACUC) approved protocol. The bladder was exposed and the occlusive tape was placed around the bladder neck. A subcutaneous pouch was formed in the abdominal wall and the control mechanism inserted. The device was initially placed in the OFF or deactivated mode. After 2 weeks, the TMOD was activated (ON mode) except for night time and three times a day (30 minutes each) to simulate the natural voiding pattern of the animals. At 6 and 9 weeks post-implantation, following administration of appropriate anesthetics, the urethral sphincter was temporarily paralyzed in 3 female dogs with 0.1 mg/kg succinyl choline to simulate sphincter damage [10]. Urethral pressure profilometry was then performed by the catheter based perfusion method with TMODs ON & OFF. Bard-Davol 8Fr Adult/Pediatric Feeding Tubes (REF 0036420) were modified for use in urethral pressure measurement studies. A radiopaque stripe on the catheter aided in visualizing the position of the catheter as it passed along the urethra. An iWorx 404 Recorder with a Utah Medical DPT 100 pressure transducer was used to display and record pressure tracings on a laptop computer. Saline infusion was maintained through the catheter using a 60cc syringe and a New Era Syringe Pump Model NE-300 set at 60ml/hr. The catheter position in the bladder was confirmed with fluoroscopy. It was then pulled out utilizing a mechanized catheter puller, and pressures measured at the level of the sphincter. The same procedure was repeated with the catheter rotated 90 degrees and 180 degrees, in both the OFF and ON position.

Pathology evaluation

Pathologic examination was performed by a board-certified pathologist. The animals were sacrificed 9 weeks after the TMOD was implanted; tissues and organs were harvested for histopathology. The parameters of main interest were the thickness and cell types in the capsules, the nature of the inflammatory process including the types and distribution of the reactive cells and the possible presence of mineralized tissue. Particular attention was paid to compressed and uncompressed segments of the urethra for evidence of urethral atrophy and erosion. Pathologic evaluation was also performed on multiple internal organs including lungs, heart, thymus, colon, small intestine, ovaries and liver.

Human cadaveric model

Surgical procedure: TMODs were inserted in 3 male cadavers in order to perform intra-operative measurement of device location and length of tape needed in the final model and to evaluate via urethral pressure profilometry the ability of the device to generate and maintain occlusive pressure. Lastly, we determined the ease of device operation in the scrotal location and the ability to activate/deactivate device through scrotal skin. For cadavers 1 and 2, a penoscrotal approach was used for dissecting the bulbar urethra circumferentially and freeing its fascial attachments. A 16 Fr Foley was used to aid in the dissection. For cadaver 3, placement of the device was performed through a perineal incision. For both approaches, the occlusive tape encircled the dissected urethra and locked

in place with the locking clip. The suture guide tab was anchored to the tunica albuginea of the corpora cavernosa on either side with non absorbable sutures. The control mechanism was placed in a scrotal pocket formed through the incision and the device was sutured to the dartos fascia with non absorbable suture through the suture tabs preventing the control mechanism from twisting or migrating (Figure 2). The device ON/OFF mechanism was manipulated to test for ability to activate and deactivate. Urethral pressure profilometry was performed using iWorx404 pressure recording system and Labscribe computer software (iWorx Systems, Inc, Dover NH). Calibration was performed according to manufacturer guidelines.

Results

Canine Model

Device operability in Canine model: Placement of the occlusive and conduit tapes around the bladder neck was surgically feasible. Lab personnel were able to activate and deactivate the TMOD using audible/palpable clicks as indicators that activation or deactivation had been accomplished. No device malfunction was registered during the test period.

Pressure studies: On weeks 6 and 9 post operatively, urethral pressure measurements showed a urethral occlusion pressure ranging between 9-42 cm H₂O for the temporarily denervated sphincters and deactivated TMOD compared to 57-82 cm H₂O with activated TMOD. The occlusive pressures were maintained at the end of the study even following the formation of the capsule.

Gross necropsy findings revealed normal healing and a thin fibrous capsule surrounding the control mechanism, the conduit tape and occlusive tape. There was no urethral atrophy and tissue capsule around the device was uniform and thin, approximately 1 mm thick and no adhesions were present.

Following explantation of the TMOD devices, each surface and component was examined under 10X magnification for wear which may have been caused through ON/OFF operation or rubbing of components through bodily movement during implantation. No evidence of wear could be found. The intended anatomical positioning of the TMOD (in human or canine model) should not allow the Occlusive Tape or Conduit Tape to contact and rub against the Control Mechanism. However, the extended Conduit Tape length used for the dog trial allowed the Conduit Tape to coil over and be pressed against the Control Mechanism in one of the subjects. Close attention was paid to this contact area, but no wear could be seen under 10X magnification.

Pathological examination revealed unremarkable pseudo-capsular tissues surrounding the silicone Control Mechanism and ePTFE Occlusive Sheath. Chronically compressed and adjacent uncompressed urethral sections were not different from one another in histologic appearance. An inflammatory reaction and areas of thin or absent transitional epithelium were observed in both compressed and uncompressed urethral sections of the dogs (figure 3). No histologic evidence of toxicity was detected in the urethra, liver, small intestine, colon, thymus, lymph node, adrenals, kidneys, lungs, right atrium, right ventricle, left atrium, left ventricle, ovaries or uterus. There was no structural evidence of systemic toxicity. Blood chemistry studies were all within normal limits.

The device was oriented around the urethra. In that site no untoward effect was detected. The control mechanism was encapsulated by mature fibrous tissue. One animal had a short (~0.8mm) area where the transitional epithelium was eroded (score of 3), but not ulcerated. Beneath that area a 'mild' number of inflammatory cells (score of 2) were present. No

histologic evidence of vascular congestion or edema was detected in the transitional epithelium, lamina propria, muscularis mucosa or tunica muscularis but some was present in the serosa. The total irritation index score was 5 which indicated a mild irritative response [10-11].

Male Cadaveric Model

The occlusive tape was successfully placed around the bulbar urethra and the ON/OFF mechanism was positioned in a dartos pouch in the scrotum and the lengths noted. The procedure was technically feasible and the pump was accessible for manipulation.

Urethral pressure profilometry performed after placement of the tape with the device in the OFF position showed a urethral occlusion pressure in the range of 24-30 cm H₂O. Following device activation the recorded occlusive pressures were 79 and 80.9 cm H₂O for cadaver #1 (urethral circumference at site of placement 3.5 cm) (figure 4), 61 cm H₂O for cadaver #2 (urethral circumference at site of placement 4.0 cm), and 105 cm H₂O for cadaver #3 (urethral circumference at site of placement 4.5 cm). The tape circumference used for the all three cadavers measured 4 cm in circumference.

Comments

The current study sheds light on the use of a spring-loaded mechanism for applying circumferential pressure. This is a novel concept for this kind of device. The TMOD offers several advantages over the currently available artificial urinary sphincter. It is a single piece device that does not require assembly reducing preparation time by operating room staff. It is non-hydraulic, and requires no pressure regulating balloon placement leading to less dissection. The reduced width of the tape minimizes the dissection around the bulbar urethra. This reduced need for dissection might reflect a lower risk of urethral injury during dissection or increased ease and comfort of practicing urologists leading to higher utilization of the artificial sphincter in treatment of urinary incontinence. The spring mechanism offers a faster activation. The ON/OFF buttons are much simpler to operate than the AMS 800 pump and deactivation button. This may allow for easier patient control and for fewer catheter-induced erosions which can occur when a catheter is placed in a man with an AMS 800 that has not been deactivated.

In our canine model, we expected that the simpler female anatomy is more appropriate for the initial evaluation of the device feasibility, operability and biocompatibility. Further testing is to be conducted on male canine models. This allows for potentially two different positions for placement of the tape, at the membranous urethra distal to the prostate apex, or around the penile urethra distal to the insertion of the crus. Placement of the occluding tape around the membranous urethra by the apex of the prostate is being evaluated in an alternative male canine model. This could better approximate the implantation site in human males, and would allow for placement of the control mechanism in the scrotum.

All three devices implanted in the cadavers had 4 cm occlusive tape. Cadaver #3 had a larger urethral circumference at the site of implantation of the device which translated to higher occlusion pressures as noted on the urethral pressure profilometry. The use of a 4.5 cm length tape might have provided occlusive pressures in the desired target range of 50-80 cm H₂O. Further evaluation with 4.5 cm tapes of urethral circumferences of 3.5 and 4.0 cm would help identify the possibility of a one-size-fits-all device.

The erosions in the luminal urothelium noted on pathologic examination are most likely consistent with catheter trauma induced during urethral pressure profilometry performed at 6

& 9 weeks post-implantation. It must be realized the device was not in direct contact with the transitional epithelium and that an effect on it occurred in only one of three animals.

Conclusions

Activation of the implanted Tape Mechanical Occlusive Device resulted in intra-urethral pressures within the desired range of 50-80 cm H₂O. The device has proven to have no evidence of systemic toxicity. It has met the requirements for reliability and biocompatibility. Further testing in male canines is warranted. Early human clinical trials should follow given the proof of technical feasibility, biocompatibility and lack of systemic toxicity of TMOD.

Acknowledgments

This research was performed with government support under SBIR Grant Number 1R43DK076397-01A1 awarded by the National Institutes of Health.

References

1. Ficarra V, Novara G, Fracalanza S, D'Elia C, Secco S, Iafrate M, Cavalleri S, Artibani W. A prospective, non-randomized trial comparing robot-assisted laparoscopic and retropubic radical prostatectomy in one European institution. *BJU Int* 2009;104.4:534–9. [PubMed: 19281468]
2. Kundu SD, Roehl KA, Eggener SE, et al. Potency, continence and complications in 3,477 consecutive radical retropubic prostatectomies. *J Urol* 2004;172:2227–31. [PubMed: 15538237]
3. Menon M, Shrivastava A, Kaul S, et al. Vattikuti institute prostatectomy: Contemporary technique and analysis of results. *Eur Urol* 2007;51:648–58. [PubMed: 17097214]
4. Reynolds WS, Patel R, Msezane L, Lucioni A, Rapp DE, Bales GT. Current use of artificial urinary sphincters in the United states. *J Urol* 2007 Aug;178(2):578–83. [PubMed: 17570407]
5. Elliott DS, Timm GW, Barrett DM. An implantable mechanical urinary sphincter: a new non hydraulic design concept. *Urology* 1998 Dec;52(6):1151–4. [PubMed: 9836575]
6. Wein, AJ.; Kavoussi, LR.; Novick, AC.; Partin, AW.; Peters, CA. *Campbell-Walsh Urology*. 9. Philadelphia: WB Saunders; 2007.
7. Elliott DS, Barrett DM. Mayo Clinic long-term analysis of the functional durability of the AMS 800 artificial urinary sphincter: a review of 323 cases. *J Urol* 1998;159:1206–1208. [PubMed: 9507835]
8. Swenson O. Internal devices for control of urinary incontinence. *J Pediatr Surg* 1972;7:542–545. [PubMed: 4673372]
9. Scott FB, Bradley WE, Timm GW. Treatment of urinary incontinence by implantable prosthetic sphincter. *Urology* 1973;1:252–259. [PubMed: 4802066]
10. Ali-el-dein B, El-demerdash R, Kock NG, Ghoneim MA. A magnetic device for increasing the urethral resistance to flow: an experimental study in female dogs. *BJU Int* 2000;85:150–154. [PubMed: 10619964]
11. Medical device and diagnostic industry 20, no. 1, 2, 4-12, and 21, no.1. A practical guide to ISO 10993, January 1998-January 1999.
12. Biological evaluation of medical devices, ISO 10993, parts 1-12. Geneva: International Organization for Standardization, various dates;

Figure 1.
GT Urological Tape Mechanical Occlusive Device

Figure 2.
Surgical placement of TMOD in a human cadaveric model, A: diagrammatic representation,
B: Cadaver #1

Figure 3.
Cross sections of urethra showed no evidence of erosion. A fibrous tissue (pseudo-capsular) formed around the silicone-coated mechanism.

Figure 4.
Urethral pressure profilometry: A: TMOD in OFF position (deactivated), B and C: TMOD in ON position (activated).