The ARTUS device: the first feasibility study in human cadavers

Tim A. Ludwig, MD,[1*] Philip Reiss, MD,[1*] Marco Wieland,[2] Andreas Becker, MD,[1] Margit Fisch, MD,[1] Felix K. Chun, MD,[1] Roland Dahlem, MD[1]

[1]Department of Urology, University Hospital Hamburg-Eppendorf, Germany

[2]Myopowers Medical Technologies SA, Lausanne, Switzerland

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Introduction: *The aim was to perform a feasibility study of the new artificial sphincter device ARTUS in human cadavers. ARTUS is a new electro-mechanical device, which may prevent urethral damage due to a new working principle which is to perform only sequential pressure on successive parts of the urethra.*

Material and methods: *The implantation of the ARTUS device was performed in six cadavers (3 males, 3 females) with different body mass indices. Subsequently the basic operation data (operation time, cuff size, length of wires, complication) were assessed.*

Results: *The implantation of the ARTUS device is performed easily by the same technique which is commonly used for the AMS 800 implantation. The mean operation time was 20 minutes. The mean cuff size was 4.5 cm in male and 6 cm in female cadavers. The average length of the wires was 12 cm. The necessary subcutaneous pouch had to be bigger than the space used for the tubes of the AMS 800 device. The study is limited by its preclinical setting.*

Conclusions: *Our results demonstrate that this new artificial urinary sphincter device can be easily implanted. The technical and surgical approaches are similar to those which are applied in the case of the AMS 800 device. Therefore experienced surgeons will be able to adapt their technique easily.*

Key Words: **a**rtificial urinary sphincter, cadaver study, intrinsic sphincter deficiency, micro-electrical-mechanical system, stress urinary incontinence

Introduction

Since 1973,[1] hydraulic artificial urinary sphincter (AUS) implantation is considered to be the gold standard in surgical treatment for severe stress urinary incontinence (SUI), providing excellent patient satisfaction.[2,3] For instance, Van der Aa et al showed that according to pad usage incontinence was improved in up to 61%-100% and total continence was regained in 4%-86%.[4] In the afore mentioned meta-analysis a reoperation rate of 14.8%-44.8% was described. Despite these excellent results, it is important to note that up to 60% of all AMS 800 devices require surgical revision within 10 years.[5] The most common complications are infections and urethral erosions in 3.3%-27.8%.[4] Specifically, these complications might be directly related to the continuous pressure which is exerted on the urethra by the inflated cuffs after activation of the system.[5,6] Clearly, these complications rates are a major drawback of currently used artificial sphincter systems. Moreover, the handling of currently used devices is controlled mechanically by a pump which

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*both authors contributed equally to this work

Address correspondence to Dr. Tim A. Ludwig, Department of Urology, University Hospital Hamburg-Eppendorf, Martinistraße 52, 20246 Hamburg

TABLE 1. **Base data of the cadavers used in this study**

Cadaver	Gender	Age (years)	Height (cm)	Weight (kg)	Body mass index (kg/m^2)
1	Male	46	189	90	25.20
2	Female	66	169	77	26.96
3	Male	72	175	71.5	23.35
4	Female	51	158	63	25.24
5	Female	63	168	125	44.29
6	Male	42	176	92.8	29.96

is located in the scrotum of the patient. Thus, in order to apply the system, patients have to press the pump to release the sphincter cuffs. This requires manual dexterity. Despite reasonable clinical results in terms of system handling, one might hypothesize that a certain number of patients is not qualified for using the AMS 800 device either due to haptic inabilities or because of anticipated dexterity problems after implantation.

Addressing the afore outlined limitations of the currently used systems, a novel sphincter system has been successfully developed and described in 2013 by Valerio et al: the so-called ARTUS (ARTificial Urinary Sphincter) device.[7] In fact, animal models show a reduced rate of histological alterations of the urethra within the phase I trial. Subsequently the ARTUS aim at:

1) applying a computer-controlled modular pressure on the urethra in order to avoid or at least decrease complications such as atrophy and erosion.
2) improving and simplifying patients' comfort by a using a remote control.
3) providing a computer-based warning and feedback system based on urethral cuff pressures and prior to potential system failures.

In this paper we report the first clinical feasibility study in which the new device was implanted in male and female cadavers of different body mass indices (BMI).

Materials and methods

Study design

The current study represents a prospective, phase I, ex vivo study evaluating the feasibility of the surgical technique as well as refinements of the surgical approach to the novel ARTUS device compared to the currently applied surgical technique. The study was performed according to the principles of the Declaration of Helsinki and was approved by our institutional review board. In addition informed consent of patient's relatives was acquired.

Between May and June 2011, the ARTUS prototype device was implanted in six cadavers of different genders.

Study cohort/surgical team

The study cohort consisted of three recently deceased male and female cadavers, respectively. Baseline characteristics of all patients are displayed in Table 1. All procedures were performed by the same team: a senior reconstructive surgeon, assisted by a resident in training (R4).

The ARTUS device

The device consists of three units: specifically, the contractile units (cuffs), Figure 1a, a control unit, Figure 1b, and a battery, Figure 1c. A maximum number of up to five contractile units (cuffs) can be implanted. Available cuff sizes are comparable to those of the AMS 800 device. The applied prototype was designed for two cuffs. All parts of the system are insulated with

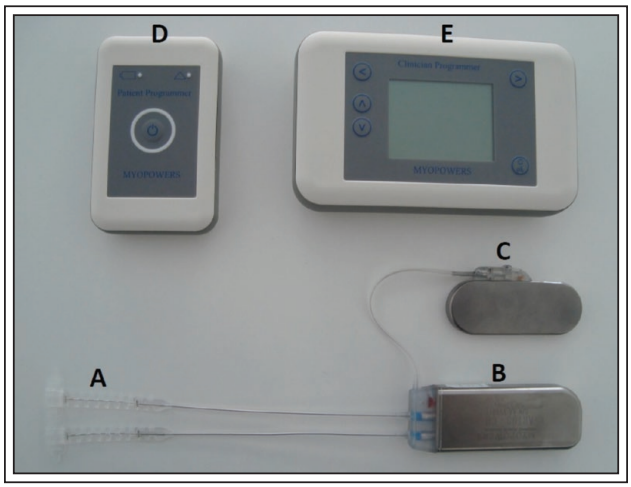

Figure 1. The device with two contractile units (cuffs). **A)** control-unit, **B)** battery, **C)** the patient's remote control, **D)** and **E)** physicians remote control.

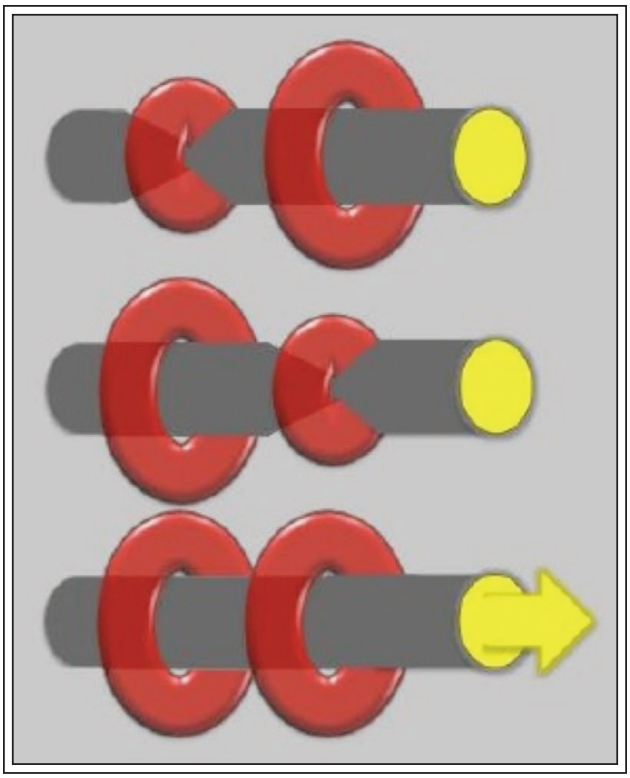

Figure 2. Working principle of the ARTUS-System. System set up is meant to perform a sequential pressure on successive parts of the urethra.

medical grade silicon. There are two versions of the remote control: one simple shutdown remote control for the patient giving additional information about power status of the device, Figure 1d, and a second more complex remote control allowing a setup of the device for physicians, Figure 1e. Since there was only a prototype applied in this study, reliable information concerning battery life time and definite size of the device cannot be given up to now.

The major principle of the ARTUS device is to exert a sequential pressure on successive parts of the urethra and therefore to avoid permanent pressure on single parts of the urethra. It is possible to control these cuffs in a so called "piano mode" Figure 2. The alternating "piano mode" activates different cuffs sequentially and thereby avoids continuous pressure on only one location of the urethra. Clearly, the "piano mode" reduces the rate of urethral tissue damage, see Figure 2.[7] The possibility to control these sequential contractions is based on the concept of having a specific contractile unit for each cuff. These contractile units rely on the principle of Shape Memory Alloys. They are composed of nitinol. Nitinol is composed of nickel and titanium, thereby exhibiting good shape memory characteristics combined with pseudoelasticity. As there is no forward current, the material is "relaxed" and applies no pressure on the urethra. Controlled by a microprocessor, the contractile units can be energized separately, thereby exerting a precisely controlled pressure on the urethra. In case of a power loss the contractile units relax, which in turn leads to incontinence. When extended, the central controlling unit allows to dynamically adapt the properties of the sphincter to physical activities (e.g. "sports mode"). A patient remote control simplifies handling of the ARTUS device. Thus, patients that were previously excluded from receiving an AUS due to haptic inability are now able to undergo a surgical solution. Furthermore, the next generation of ARTUS devices will incorporate some special applications for physicians such as an early warning system (measurement of urethral elasticity). Thereby, the potential risk of acute sphincter explantations due to erosion and atrophy will be reduced significantly.

Surgical technique

All procedures were performed under identical surgical conditions in accordance to the established OR scenario. Specifically, the patients were placed in lithotomy position. Skin disinfection, including the lower abdomen, genital area, the perineum and thighs was performed, followed by sterile draping in order to achieve comparable conditions to those in an operation theater.

In male patients the cuffs were implanted by a perineal midline incision. In this step a strict midline preparation of the urethra was performed. When reaching the bulbospongiosus muscle, the urethra was dissected distally. In female patients a suprasymphysary

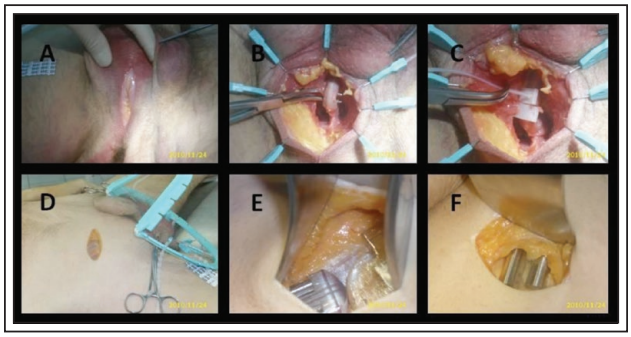

Figure 3. Operation steps. **A)** Midline perineal incision. **B)** Preparation of the urethra. **C)** Placement of the cuffs. **D)** Guiding of the wires to the subcutaneous pouch. **E)** Placement of the control unit and connecting the transmission wires. **F)** Closing of the subcutaneous pouch.

TABLE 2. **Operative data of the cadavers used in this study**

Cadaver	Operating time (min)	Cuff-size (cm)	Length of the wires used (cm)	Distance between control unit and power supply (cm)
1	17	4.5	11	2
2	28	6	12	0
3	18	4.5	9	0
4	20	6	11	1
5	20	6	15	2
6	17	4.5	13	1

incision was performed and the bladder neck was dissected without opening the peritoneum. Afterwards the cuffs were positioned around the penobulbar urethra in male, and around the proximal urethra in female cadavers. The power supply and the control units were implanted in the right lower abdomen in a subcutaneous pouch. The guiding wires were passed lateral to the spermatic cord to the cuffs in males. After this step the system was connected via guiding wires, see Figure 3 for operation steps. During every single surgical procedure, operating time, size of implanted nitinol cuffs (4.5 cm in male and 6 cm in female patients), length of the wires and position of control as well as power supply units were documented, see Table 2.

Results

The implantation of ARTUS device was performed in a similar technique and surgical approach compared to the AMS 800 device. Mean operating time was 20 min (range: 17-28 min). Mean cuff size was 4.5 cm in male and 6 cm in female cadavers. The average length of the guide wires was 12 cm (range: 10.5 cm-14 cm). Mean distance between control unit and power supply was 1 cm (range: 0 cm-2 cm). The commonly used surgical approach for the AMS 800 implantation had to be modified firstly by passing the wires from the lower right abdomen to the perineum, secondly by creating a bigger subcutaneous pouch for the control unit and the power supply. No intraoperative complication was reported during any of the procedures. With respect to the BMI of the cadavers, no significant influence on the operating time and cuff size was to be seen. Therefore one can state feasibility of the implantation of the new device in humans.

Discussion

Since artificial urinary sphincter systems were first described by Foley in 1947[8] further development of sphincter devices made implantation of the AMS 800 device being the gold standard for incontinence due to intrinsic sphincter deficiency. Although the clinical outcome, quantified by the improvement of incontinence and quality of life, is excellent, the AMS device still shows high rates of surgical revisions due to some common complications, such as infection and erosion of the urethra as well as mechanical failure of the device. If divided in mechanical and non-mechanical complications, each group represents about half of the total complication rate.[4,5] Most of the mechanical failures, such as leakages, disconnections and kinking of tubes, are due to the hydraulic working principle and hydraulic components of the AMS device. Non-mechanical failures like infection, erosion, atrophy of the urethra might be related to the compression mechanism. Continuous compression of the same part of the urethra might lead to a reduced vascularization, followed by urethral ischemia and atrophy. Garcia Montes et al showed that vascularization is an essential factor for containing continence.[9] In fact, both groups of complications are directly linked to the working principle of hydraulic sphincter devices. Although there were some trials with technically improved devices, up until today it was not possible to avoid the afore outlined complications. In order to avoid these complications, a new kind of artificial urinary sphincter should preserve urethral vascularization. Therefore it should be individually adjustable after operation. The ARTUS device relies on a dynamic pressure as well as an electromechanical principle. Therefore we believe that some of the complications that are inherent to hydraulic devices can be avoided by this new device. In an animal study Valerio et al[7] showed a proof of principle in functionality and safety for the prototype of the ARTUS device.

On the grounds of these results the transfer to humans is the next step to establish the clinical use of this new device. The technique of implantation is to a high degree comparable that of the AMS 800 device. Therefore experienced surgeons will be able to adapt

the current technique to the new ARTUS device in future clinical use. We demonstrated that the ARTUS device can be implanted easily in human cadavers.

Certainly, our study is not devoid of limitations. A major drawback is the preclinical setting of the study. We could show that the surgical technique of implantation is highly comparable to the implantation of the AMS 800 device. A multicenter clinical trial to proof the safety and functionality is planned.

Conclusion

The novel electro-mechanical urinary sphincter device ARTUS has been developed to reduce the high rate of complications in established sphincter systems like the AMS 800 device. Its electro-mechanical alternating working principle ("piano mode") represents a novel opportunity to avoid ischemia of the urethra by sequential compression of successive parts of the urethra. Our cadaver study findings clearly demonstrate its feasibility in humans. The similar surgical approach, compared to that of the AMS 800 device, makes it easy for the clinician to adopt the novel ARTUS device. Moreover, performing a strict preparation in the subcutaneous space makes the implantation even easier and more independent of the BMI. Based on our results, further clinical trials are expected to follow.

Disclosure

R. Dahlem works as a consultant for Myopowers. M. Wieland is employee of Myopowers. For all other authors there are no conflict of interest reported. □

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