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The challenges in artificial muscle research to treat incontinence

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Summary

Sphincters to guarantee continence are in pricipal the simplest muscles, because only two states (closed and open) seem to be important. The healthy urinary sphincter, however, provides dynamic components. During the filling phase the increase in tonus prevents urinary loss. The sphincter rapidly responds to pressure pulses caused, for example, by coughing. Contemporary artificial sphincters, however, merely generate two states and often induce atrophy and erosion. Hence the success of commercially available, continually improved implants is still limited. This communication reviews two physical principles, shape memory alloys and electrically activated polymer nanostructures, for applications in artificial sphincters which adapt the pressure acting on the urethra and react to stress situations such as coughing. The application of these principles allows intermittent reduction of pressure on the urethra, thus involving significantly less atrophy. The fabrication of reliably working nanostructures, however, is ambitious and will need time-consuming, high-level engineering.

Key words: artificial muscle; urinary sphincter; shape memory alloy; electrically activated polymer; nanotechnology

Introduction

From an engineering point of view the urinary sphincter belongs to the simplest muscles, since in principle only two states exist. Usually the sphincter closes the urethra. It is opened only for a restricted period of time to pass water. The anatomy of the urinary sphincter and the interplay with the contraction of bladder muscle during voiding, however, is rather complex. Hence abnormalities often result in unintentional loss of urine, especially under stress situations such as coughing, sneezing or physical activities. Many people, above all the elderly, suffer from stress incontinence defined as the involuntary loss of urine during increased abdominal pressure induced by coughing etc. Stress incontinence chiefly affects women, who can often be successfully treated by rather conventional methods such as sling procedures [1]. Urge incontinence more frequently affects men. For example, some 30% of males at the age of 70 are incontinent, with serious implications for their quality of life [2], since urethral closing pressure has become inadequate. Severe incontinence in men is generally a result of pelvic surgery, such as radical prostatectomy for prostate cancer. Here the classic management is the artificial urinary sphincter.

To effectively treat patients with severe incontinence, for example after prostatectomy or trauma, the relatively simple, purely mechanically driven device AMS 800™ (American Medical Systems, Minnetonka, Minnesota, USA) is used and regarded as gold standard for the treatment of prostatectomy-induced incontinence. The clinical success, however, is limited [3], especially since the surgeon sets the pressure continuously acting on the urethral tissue. Although the implantation of the AMS 800™ has been continually improved [4], up to 50% of the implants have to be removed within the first five years [5–7]. This makes it highly desirable to have alternative, more advanced devices, as recently proposed and under development.

The present review introduces two concepts as up-and-coming alternatives to the artificial sphincters in current use. It describes the principles of shape memory alloys (SMA) and low-voltage, electrically activated polymers (EAP) for two-state artificial sphincters, together with operating modes allowing adaptation of pressure on the urethral tissue to that of healthy natural sphincters.

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Function of the currently used artificial urinary sphincter AMS 800™

The artificial urinary sphincter AMS 800™ is a rather simple, purely mechanically driven device to treat severe urinary incontinence, as illustrated in figure 1 [8]. The cuff surrounds a segment of the urethra. Usually the urethra is closed because the liquid in the elastic silicone cuff prevents urine from passing. If the patient intends to void, he or she operates the pump manually and the liquid flows into the reservoir until the urethra opens. Subsequently, within a period of three to four minutes, the fluid slowly flows back into the single (or double) cuff. In this way the urethra occludes again and the patient becomes continent.

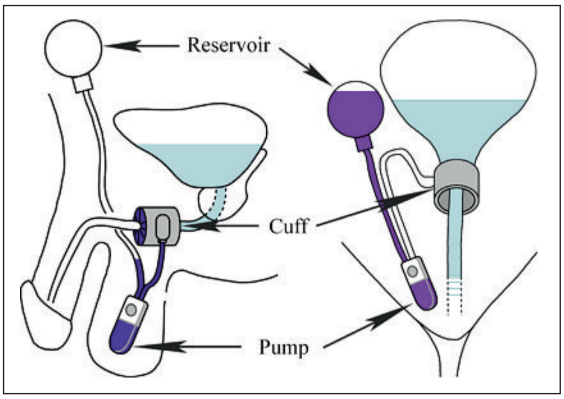

Figure 1

The AMS 800™, regarded as the gold standard for the treatment of severe urinary incontinence, consists of pump, cuff, and reservoir. The fluid-filled cuff generates a constant pressure on the urethral tissue, set by the surgeon. The male or female patient can pass water by manually operating the pump in the scrotum and labium respectively. The pump transports the fluid from the cuff to the reservoir, whereby the urethra opens.

Although the three-component system is quite simple in its design, patients need a certain period of time to learn how to operate it correctly, since the pump to be activated is located in the scrotum and labium respectively. Note that many patients are elderly people with extended learning curves.

Even more important, the surgeon sets the pressure acting on the urethral tissue. Since only one constant value can be chosen, the surgeon must find the right balance: low pressures reduce the risk of tissue atrophy but fail to establish reasonable continence. High pressures give rise to better continence but are associated with tissue atrophy and possibly erosion. The constantly acting pressure often results in fibrosis or atrophy of the urethra, so that even in centres with many cases and experienced surgeons the revision rates lie between 11% and 28% [3].

The geometry of the cuff can be optimised, as recently described in a quantitative manner by means of the urethra compression model [9]. The geometry of the AMS 800™ cuff, however, is set reasonably and only marginal improvements to the device can be expected for the future.

Shape memory alloys for urinary sphincters

An SMA relies on the crystal structure transition from martensite to austenite in several metallic alloys at characteristic temperatures. Besides the well-known nickel-titanium alloys, copper-aluminium-nickel, copper-zinc-aluminium, and iron-manganese-silicon combinations also exhibit temperature-dependent shape changes [10]. The transition temperature of the nickel-titanium alloys depends on their composition and varies accordingly from approx. –50 to 166 °C [11], a range that covers the physiological temperature of 37 °C. In its martensite phase, the alloy can be deformed to the desired shape, termed parent shape, and heated to a temperature of around 550 °C. At this temperature the atoms within the pre-shaped alloy rearrange to a regular and compact cubic pattern (austenite phase) [12]. The SMA reverts reversibly from the austenite phase at higher temperatures to the martensite phase at low temperatures for millions of cycles [11], as schematically illustrated in the upper part of figure 2. The lower part of figure 2 contains three experimental hysteresis loops obtained for a commercially available nickel-titanium alloy (BioMetal Fiber, Toki Cooperation, Japan) used for medical purposes [13, 14]. The SMA wire with a diameter of 0.1 mm was loaded with 5.17 g in water. The water bath allowed precise temperature control between 15 and 90 °C. The first loop exhibits a larger hysteresis than the subsequent ones, which shows the typical fatigue behavior of SMA materials.

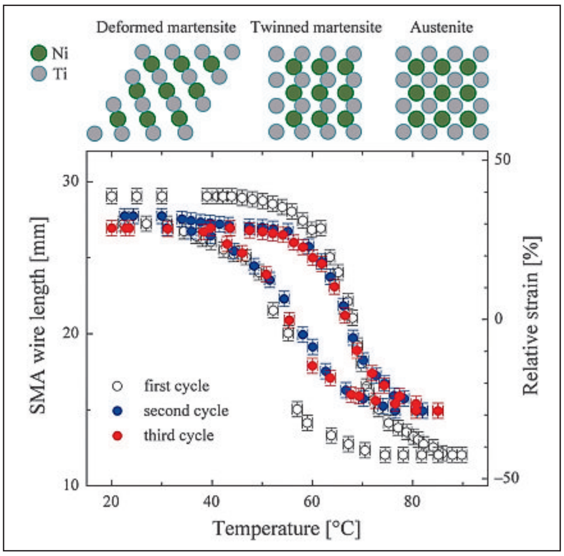

Figure 2

Shape memory alloys exhibit a thermal hysteresis loop as a result of the martensite-austenite lattice phase change.

NanoPowers S.A., a Swiss medtech company, has produced advanced artificial urinary sphincter prototypes based on SMA wires generating enough force and strain to close the human urethra. This sphincter operates in the 'piano mode', compressing and relaxing different urethra segments by three or four modules as elucidated in figure 3, patent pending. This operating mode al-

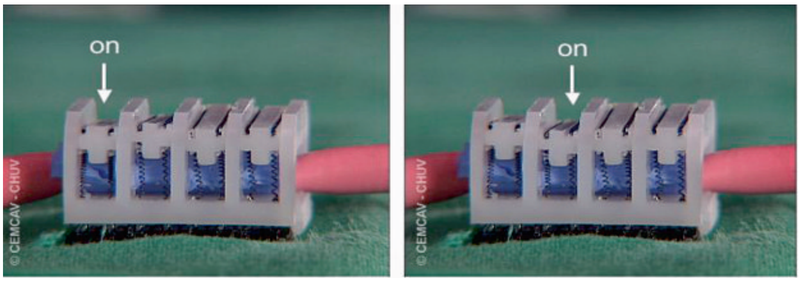

Figure 3

The 'piano' effect permits recovery of the urethral tissue segments. The modules alternately act in open and closed positions with a pre-defined time sequence. In stress situations more than one module can switch to the closed stage to increase the resistance of the device to the pressure pulses.

lows tissue recovery within the urethra segments, where the module is in open state. In particular, the surgeon can adjust the pressure of each module individually in a patient-specific manner. The power consumption during operation, however, is high, and thus high capacity batteries or sophisticated thermal isolation are required. Specific designs are under development to run the device with significantly lower power consumption.

The time response of the SMA sphincter is closely related to the power supply and the thermal isolation of the device. Better isolation leads to a slow actuator unable to respond appropriately to stress situations similar to the natural muscles. Consequently, the time response of the SMA-based devices will not be rapid enough to close the urethra during pressure pulses generated, for example, by coughing. Hence the system will rather be a sophisticated static one.

The overall size and placement of the SMA-sphincter should resemble the AMS 800™ cuff. Unlike the AMS 800™, the degree of continence can be adapted by activating a different number of segments. The pressure generated by the individual module must be pre-defined, but may be set to values larger than in the conventional cuff with identical risk of atrophy, since the pressure does not act constantly on the urethral tissue.

Electrically activated polymers for urinary sphincters

The basic function of electrically activated polymers (EAP) relates to a capacitor for electrical energy consisting of two electrodes and an electrically isolating, elastically deformable but incompressible polymer in-between. As demonstrated in figure 4, the positive and negative charges attract the contact layers, and thus the polymer is squeezed, leading to a remarkable shape change of the deformable device which can be used for efficient artificial muscles. These kinds of muscle were the most successful during the world contest in arm wrestling at Caltec in 2006 [15]. Unfortunately, this successful development cannot be easily transferred to the human being, since the necessary voltages applied to the microstructures correspond to kilovolts, and the related power would involve unjustifiable danger for the patient.

In summary, EAPs such as silicone exhibit superior properties, since they can provide actuation pressures suitable for artificial sphincters, an efficiency of more than 80% for the conversion of electrical to mechanical energy, low electrical leakage and, finally, an adequate response time below a millisecond [16]. To realise strains meaningful for artificial muscles, electrical fields of the order of 100 V/μm are needed. Consequently, the elastomers for medical applications must be sub-micrometer- or nanometer-thin to avoid voltages above ~24 V. The creation of low-voltage devices requires homogeneous and reliable sandwich structures of more than a thousand alternating nanometer-thin insulating and conducting layers for electrically activated actuators, as shown in the righthand scheme of figure 4. The challenge here lies in realisation of stable thin-film nanostructures allowing reversible switching between two or more states to close and open the human urethra.

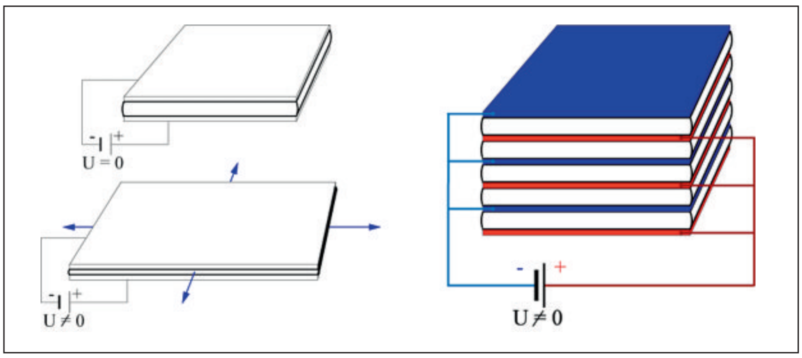

Figure 4

The application of an electrical field leads to shape changes in electrically activated polymer microstructures, since the positive and negative charges attract each other, deforming the incompressible elastomer in-between. For multi-layers, enough strain should be produced even if applying comparably low voltages.

The success of this approach depends on the production of reliable devices using nanotechnology permitting the production of thousands of nanometer-thin layers, an extremely time-consuming and expensive process. Such nanotech sphincters will not only provide constant pressure to close the urethra but should also act against pressure pulses from coughing or any other physical exertion. The aim is to achieve continence and reduce the pressure on the urethra whenever possible, to avoid the tissue damage from atrophy and erosion frequently observed in present treatments. Nanotechnology will provide the necessary tools to produce materials and medical devices with physical properties tailored to those of healthy natural sphincters and thus revolutionise patient treatment. The challenges, however, are huge, and it will take a decade or more to make EAP-based sphincters commercially available.

EAP-based sphincters will yield a more dynamic solution than the sphincters discussed above, since the patient or a pressure sensor-based feedback loop can adapt the pressure on the urethra to the specific situation. Such situations include rapid changes such as are known from coughing.

Discussion

Although artificial urinary sphincters have been implanted for more than 30 years [17], the results obtained are still unsatisfactory and restricted to a segment of patients with severe incontinence. Consequently, research activities have been initiated to determine precisely the requirements for an artificial urinary sphincter. The urethra compression model uses three parameters to predict correctly the pressures necessary to close the urethra as a function of the sphincter's geometry [9]. This model has verified that porcine urethras closely resemble human ones and can be applied for in vitro studies [9]. Such in vitro studies include stress incontinence simulated by means of universal testing machines [18].

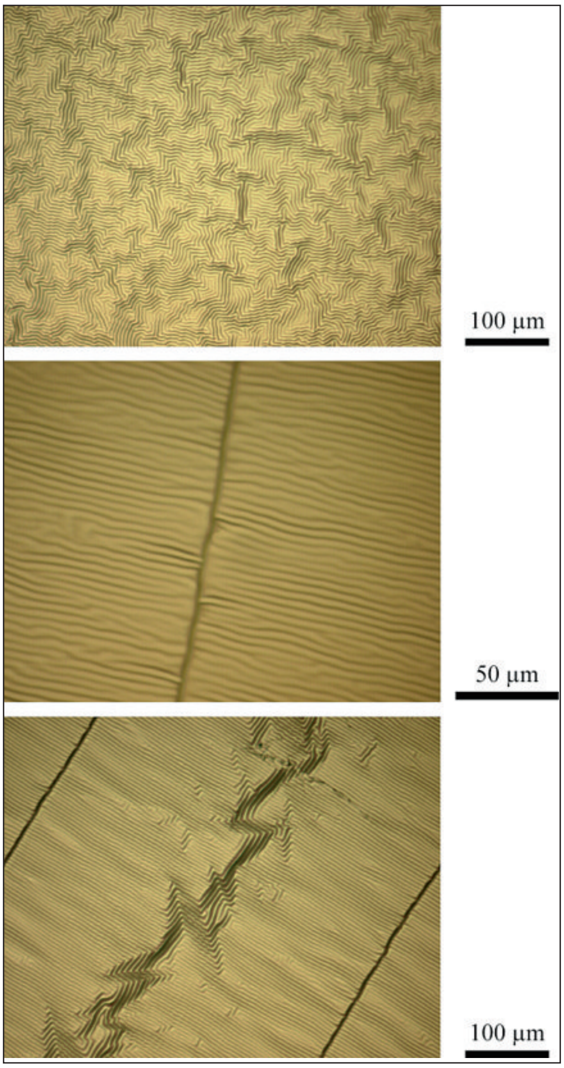

Figure 5

The evaporation of metals such as titanium onto silicone often results in the formation of well-defined ripple structures that prevent the generation of a homogeneous electrical field along the micro- or nanostructures. The periodicity of the ripples originates from the different thermal expansion coefficients of elastomer and metallic contact layer materials.

Besides the necessary forces and pressures respectively, the artificial muscle must generate enough strain on the urethra with its specific liquid-like properties [19]. Here, the recently measured visco-elastic properties of the urethral tissue yield the direct relationship between applied stress and associated strain [20, 21]. Hence, all vital parameters for the development of artificial urinary sphincters are known.

The work of the engineers to build effective artificial urinary sphincters should concentrate at this point on the use of physical principles such as SMA and EAP, with the goal of producing a medical implant which becomes similar to healthy human muscles driven by the different external and internal stimuli. Although at first glance this final step seems to be straightforward, the realisation of such simple muscles based on EAPs will take a long time.

Figure 5 shows one of the problems to be mastered in the preparation of EAP micro- and nanostructures. The evaporation of titanium contact layers onto silicone thin films under high vacuum conditions gives rise to well-defined corrugations [22]. These ripples, caused by the radiation transfer from the source, have a periodicity reflecting the difference in thermal expansion coefficients between silicone and titanium [23]. Such corrugations, associated with substantial materials transport, are not tolerated because they inhibit the formation of a constant electrical field within the elastomer and thus the proper device function. It should be noted that the fascinating corrugations are usually isotropic (upper image), but perpendicularly arrange at cracks (central image) (cf. [22]). Approx. 200 µm from the crack the ripples change direction towards isotropic distributions (lower image).

Conclusions

In summary, the commercially available artificial sphincters do not mimic natural muscle function and therefore have met with only limited success. Advanced prototypes of SMA-based sphincters are available for animal experiments. Pigs, and especially mini-pigs, are the right animal model for short- and long-term testing. Once the animal experiments have shown proven reliability, only a few further improvements are required before these devices can prove their clinical relevance.

EAP micro- and nanostructures yield additional degrees of freedom and are, therefore, important alternatives for the treatment of stress incontinence. Production of reliable EAP-based sphincters, however, calls for substantial effort at the highest engineering level and, consequently, it will be several years before EAP-based artificial sphincters are commercially marketed.

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