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Simulation of stress urinary incontinence for *in-vitro* studies

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Abstract. A simulation system that generates dynamic bladder pressures for the use of testing and examining artificial urinary sphincters is designed, implemented, and compared to *in-vivo* measurements of Valsalva and coughing profiles. Cylinder and piston, which are integrated into the universal testing machine, simulating the bladder are connected with explanted sow urethras. The AMS 800$^{\mathrm{TM}}$ artificial urinary sphincter closes the urethra with well-defined external pressures. In order to select appropriate profiles for the bladder pressure, 34 Valsalva and coughing profiles of 6 patients were evaluated with respect to amplitude, pressure raise, dwell time, and half width.

Keywords: Artificial urinary sphincter, bladder simulation, cough profiles, cough profiles simulation, valsalva pressure, valsalva profiles simulation

1. Introduction

Stress urinary incontinence (SUI) belongs to the prevalent and costly health conditions with physical, psychological, and economical components [7,16,20]. The number of cases of severe SUI is noteworthy increasing [2]. The present treatments do only provide limited success, which is also the result of the available implant devices [3,10,17]. The most commonly used implant is the urinary control system AMS 800$^{\mathrm{TM}}$ (American Medical Systems, Minnetonka, Minnesota, USA). This mechanically driven device allows actively opening the urethra to pass urine. In the passive state it should act as the closed sphincter to prevent any loss of urine. The success, however, is limited. Up to 50% of the implants have to be revised within the first 5 years because of urethral atrophy and erosion [6,8,12]. Note, the techniques to implant the AMS 800$^{\mathrm{TM}}$ are constantly improved, refined, and revised [15].

Therefore, it is worth searching for alternative concepts mastering the present deficiencies including the restricted geometry and pre-selected, constant sphincter pressure. Several artificial urinary sphincter systems have been proposed and developed to a more or less sophisticated level [10,17]. In order to compare the efficacy of the implants itself, the rather expensive and time-consuming clinical trials should be postponed in favour of well-defined *in-vitro* studies. These *in-vitro* experiments require reproducible testing procedures that necessitate an appropriate experimental set-up. The set-up has to simulate the

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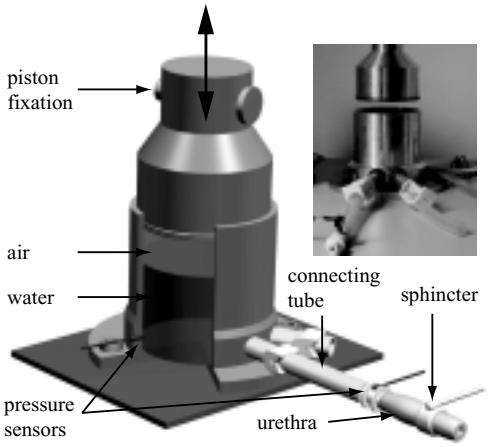

Fig. 1. Scheme of the bladder model system. The pressure impulse is lead through the connecting tube to the urethra. Two pressure sensors are fixed at the cylinder and at the end of the connecting tube, respectively.

profiles of clinically relevant bladder pressures and the possible pressure changes resulting from different kinds of physical exertion. For the experiments artificial and/or explanted animal or human urethras are required and to be connected to the simulation system and the pressure sensors.

In this communication, we present 9 profiles of Valsalva manoeuvres and 25 coughing profiles of 6 patients to define the specifications of the simulator. Based on the *in-vitro* model for static conditions [13], we have developed the simulator taking advantage of a universal testing machine. The comparison of the recorded *in-vitro* and *in-vivo* pressure profiles should permit drawing conclusions to what extent the *in-vitro* experiments fit the *in-vivo*, patient-specific situations.

2. Methods

The stress manoeuvre generator should act during simulation of SUI as the lower urinary tract *in-vivo*. The generator is composed of four main parts. The mechanical testing machine Zwick 1456 (Zwick GmbH Ulm, Germany) reproduces well-defined stress manoeuvres, arisen in the lung or in the abdomen. The piston together with the cylinder (Fig. 1) represents the bladder, in which the related pressures for the stress situations are generated. The piston compresses the pre-defined volume of air above the water in the cylinder, a mechanism raising the pressure of the water that is guided to the urethra. Here, the pressure impulse pushes against the inner urethra wall in the similar manner to coughing when leakage occurs in stress incontinent people. Finally, an artificial sphincter around the urethra inhibits or lessens the water flow through the urethra as done *in-vivo* by muscles or implants.

The Zwick testing machine with the 20 kN force sensor installed produces pre-selected mechanical forces and displacements, controlled by the PC, which also records the data, i.e. displacements and forces, respectively, using the software (testXpert V10.11). The software operates the mechanical unit that may produce different manoeuvres, including single and multiple displacements or movements with desired force profiles. The maximal forces are far above those needed for simulating SUI. The displacement velocity of the movable lifting stage is limited to (20.8 ± 0.1) mm/s. The minimal duration of the reversal point between pressure raise and release is about 0.6 s.

The cylinder with the inner diameter of 100 mm and the height of 110 mm is mounted on its bottom on the lower, fixed part of the mechanical frame of the testing machine. The piston with the outer diameter of 99 mm is mounted on the movable stage of the testing machine. Both parts are made of V4A steel. A gasket, nitrilium o-ring with a hardness grade of 70–75 shore, serves for sealing between piston and cylinder. The cylinder is filled with water until the pre-defined level is reached. Subsequently, the piston is introduced to the selected level fixing the air volume. The pressure of the air above the water is equalized to the ambient pressure by opening the clamp on the 15 cm-long silicone tube with inner and outer diameter 12 mm and 16 mm, respectively, on the lower part of the cylinder. During operation, the testing machine compresses the air, which increases the water pressure as *in-vivo* the urine compression caused by coughing or Valsalva manoeuvres. The pressure impulses are transmitted to the urethra using a water-filled silicone tube, 30 cm long, with an inner and outer diameter of 12 mm and 16 mm, respectively, also fixed on the lower part of the cylinder (Fig. 1).

For the experiments, the water height in the cylinder was set to 70 mm. The volume of air above the water corresponds to the height of 40 mm. After introducing the piston by 5 mm and pressure equalisation the water and air height became 65 mm and 40 mm, respectively. The lower the air volume, the faster is the pressure raise and the larger is the pressure decay due to water losses.

Two sensors (26PC0250G6A sensortechnics, Germany) are implemented for pressure measurements in the cylinder and near the urethra (Fig. 1). These sensors are designed for pressure ranges between 0 and 250 mbar. The error provided by the supplier is 0.5%. The LabView 5.0 (National Instruments, TX, USA) software records the data using the measuring bridges (SCM 90I, Soclair Electronic, Steiner Technik, Switzerland).

The pressure impulses act on the urethra-sphincter system. The experiments are based on explanted sow urethras, which can be used likewise human ones because of very similar mechanical behaviour [13]. The urethras from sows (weight of about 100 kg) were freshly explanted after slaughtering and used for the experiments within 24 h. Two different sphincters were applied. One was the specially designed experimental aluminium sphincter [13] with variable lengths and well-defined pressure profile along the sphincter-urethra interface. The other one was the AMS 800$^{\mathrm{TM}}$ (American Medical Systems, Minnetonka, MN, USA) urinary sphincter with a 4.5 cm circumference cuff. The cuff was connected to a water reservoir hold on the height necessary to realize the desired hydrostatic pressure. Note that this procedure is in contrast to clinical practice [1].

In order to quantify the *in-vitro* stress incontinence, the leak-point pressure (*LPP*) was analysed. It is defined as the minimal sphincter pressure needed to avoid urine loss [18]. For the present *in-vitro* study, we applied this concept like-wise.

To perform simulations, which correspond to the *in-vivo* situation, cough and Valsalva profiles were recorded from patients. A set of 34 intra-vesical pressure profiles (25 cough, 9 Valsalva) of 6 patients (median age 60 years ranging from 13 to 79 years) was evaluated. The profiles were recorded with the Andromeda Software (Andromeda AUDACT Pro, Version 5.02, Germany) within the scope of a clinical standard cystometry. The sampling rate was set to a frequency of 20 Hz. The parameters to characterize the pressure profiles were extracted using a specifically developed Matlab algorithm (MathWorks, Inc., Version 6.0.0.88, 2000). The pressure raise dp/dt, i.e. the mean slope of the pressure profile, was extracted from the data at 20% and 80% of the maximum amplitude.

3. Results

Figure 2 shows a sequence of idealized, trapezoidal Valsalva profiles generated by the simulation system. Several parameters characterize such a profile, namely intra-vesical amplitude $p_{\max}$, slope

Table 1
Parameters of *in-vivo* cough and Valsalva manoeuvres obtained from 25 cough profiles of 6 patients and 9 Valsalva profiles of 2 patients

	$p_{\max}$ [cmH_2O]	dp/dt [cmH_2O/s]	FWHM [ms]
Cough			
maximal	197 ± 9	1630 ± 130	520 ± 20
minimal	36 ± 2	102 ± 8	120 ± 20
median	87 ± 4	560 ± 45	250 ± 20
Valsalva			
maximal	196 ± 10	88 ± 7	8360 ± 20
minimal	31 ± 2	4 ± 1	710 ± 20
median	58 ± 3	42 ± 3	1560 ± 20

The error ranges are estimated by the related standard deviation.

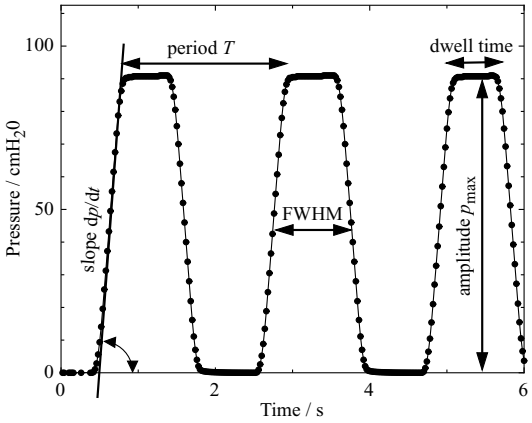

Fig. 2. A sequence of cough or Valsalva profiles are characterised by the period T between two manoeuvres, the full width at half maximum (FWHM), the maximal pressure $p_{\max}$, the dwell time and the pressure raise dp/dt.

dp/dt, half width FWHM, dwell time t_{dwell}, and period T. The parameters are not independent on each another, but linked by the relation

$$\mathrm{d}p/\mathrm{d}t = p_{\max}\,/(\mathrm{FWHM} - t_{\mathrm{dwell}}) \tag{1}$$

The maximal, minimal, and median values of $p_{\max}$, the $\mathrm{d}p/\mathrm{d}t$ and the FWHM together with their standard deviations extracted from 25 pressure profiles of coughing and 9 pressure profiles of Valsalva manoeuvres are summarized in the upper and lower part of Table 1, respectively.

Figure 3 compares one selected Valsalva pressure profile of a patient with two generated profiles from our experimental set-up. Although simulation profiles exhibit regular pressure raises and decays as well as constant $p_{\max}$, they are quite similar to the *in-vivo* Valsalva profiles. Coughing profiles cannot be simulated by the testing machine used since the minimal time to change the direction corresponds to the FWHM of about 0.8 s, which slightly depends on the values chosen for $p_{\max}$ and $\mathrm{d}p/\mathrm{d}t$.

The measurement of the *LPP* as the function of the t_{dwell} is shown for two different sow urethras in Fig. 4. Here, the *LPP*, generated by the cuff of the AMS 800^{TM} to close the urethra, is determined for selected bladder pressures. These bladder pressures, namely 65 and 85 cmH_2O, correspond to clinically relevant values. One can clearly recognize that the *LPP* does not depend on the duration of the manoeuvre for t_{dwell} between 0.6 and 5.6 s.

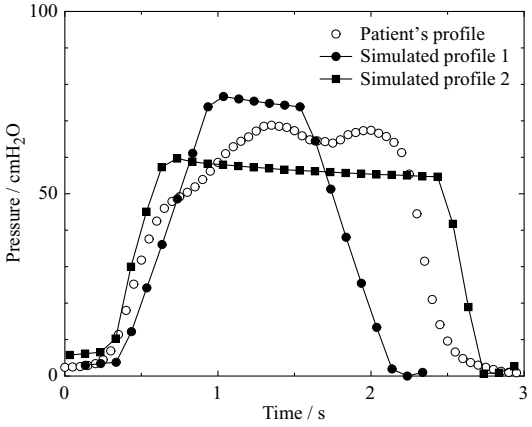

Fig. 3. A selected *in-vivo* Valsalva profile of a patient is compared with two simulated profiles.

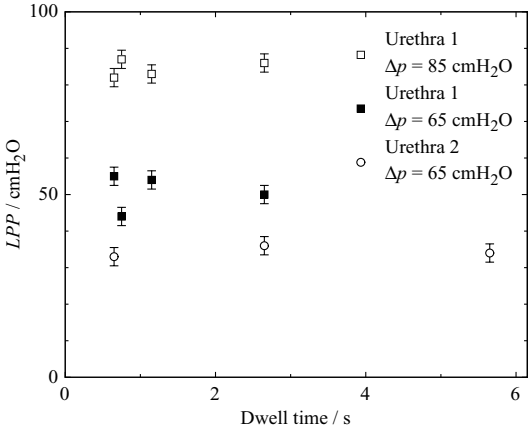

Fig. 4. *LPP* to close a sow urethra does not depend on the plateau times longer than 0.65 s. The error bars correspond to the standard deviation.

4. Discussion

The system for the simulation of stress urinary incontinence that is based on a universal testing machine can be used for the *in-vitro* tests of artificial urinary sphincters, for example to test the efficacy of the AMS 800$^{\mathrm{TM}}$ double cough [11]. The adaptation of the profiles generated to the *in-vivo* situation is complicated since the Valsalva and coughing pressure profiles are patient and situation dependent.

The amplitude, which can be easily controlled via path or force by the testing machine *in-vitro*, is difficult to gain exactly *in-vivo* because the base line as the reference is not well defined. As shown in the literature [4,9,14,19,21] and Table 1, the maximal values for the Valsalva and coughing manoeuvres are less than 200 cmH_2O. It is, however, also common to consider the median amplitude, which is obtained from a set of profiles. Here, the Valsalva profiles exhibit significantly lower values than coughing profiles as shown in Table 1. Based on the data given in the literature and in Table 1, the amplitude chosen for the experiments represented in Fig. 2, i.e. 100 cmH_2O, sounds reasonable from the clinical point of view.

The determination of the pressure raise dp/dt is also complex since the base line is difficult to extract and, more important, it changes during the manoeuvre. The choice of the maximal value of dp/dt does

not lead to meaningful, reproducible data that is a result of the limited frequency of data acquisition. Therefore, we used the average value obtained between 20% and 80% of the amplitude, a choice, which is somehow arbitrary, but known from empirical approaches. The median pressure raises are more than a magnitude larger for the cough, (560 ± 50) cmH_2O/s, than for the Valsalva profiles, (42 ± 3) cmH_2O/s. With the maximal stage velocity of the testing machine applied and 40 mm air height in the piston, the maximal pressure raise of the stress manoeuvre generator corresponds to 600 cmH_2O/s. Hence, Valsalva and cough raises as required for the experimental simulation can be realized. If required, one can realize higher raises either by a faster testing machine or by reducing the initial air height in the cylinder. It should be mentioned that the slopes for the pressure increases and decreases are often different but does have the same order of magnitudes. Consequently, only the pressure raises are considered for the data evaluation, here.

Half width FWHM and dwell time t_{dwell} characterize the duration of the manoeuvre. They help to differentiate between Valsalva and cough. The data often show differences in the duration of one order of magnitude (see Table 1) [4,21]. The *in-vivo* data usually do not show a constant plateau but a modulation as given in Fig. 3, which makes the quantification hard. The two alternative approaches are the duration of 80% or 90% of maximal amplitude and just the application of Eq. (1). The extraction of the half width FWHM seems to be simple at first glance, but again depends on the choice of the base line and maximal amplitude of the related profile.

The choice of the trapezoidal shape for the description of the Valsalva profiles gives rise to 3 independent parameters. One might believe that a 2-parameter model, such as a Gaussian, is sufficient. The description of the *in-vivo* data and the *in-vitro* ones, however, becomes inadequate with a 2-parameter model, as easily realized from the data reproduced in Fig. 3.

The universal testing machine used needs a certain period of time to change the direction, which results in the minimal FWHM of 0.8 s. Therefore, this study concentrates on the simulation of Valsalva manoeuvres. To simulate cough profiles, another testing machine, which allows changing the direction faster, would have to be employed.

For Valsalva manoeuvres, where the dwell times are longer than 0.6 s, which corresponds to the FWHM of 0.8 s, the *LPP* is found to be independent on the dwell time. The dwell time range used, i.e. 0.6 to 5.6 s, is shown to be characteristic for Valsalva profiles [4,21]. Our observation that the *LPP* is constant for Valsalva manoeuvres is explained by the liquid-like behaviour of the urethra [5]. The pressure impulses are relatively fast transmitted. For much smaller dwell times the visco-elastic behaviour of the urethral tissue might come into consideration. Incontinence for Valsalva manoeuvre is, therefore, mainly related to the maximal pressure amplitude. The amount of urine lost, however, depends on the duration of a certain pressure level that correlates to dwell time and half width.

Different repetition rates can be implemented but seem to be less relevant from a clinical point of view.

The close match of the *in-vivo* measured Valsalva manoeuvres and the simulated profiles of trapezoidal shape permits to test the efficacy of artificial sphincters under conditions, which are clinically relevant for the treatment of stress urinary incontinence.

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