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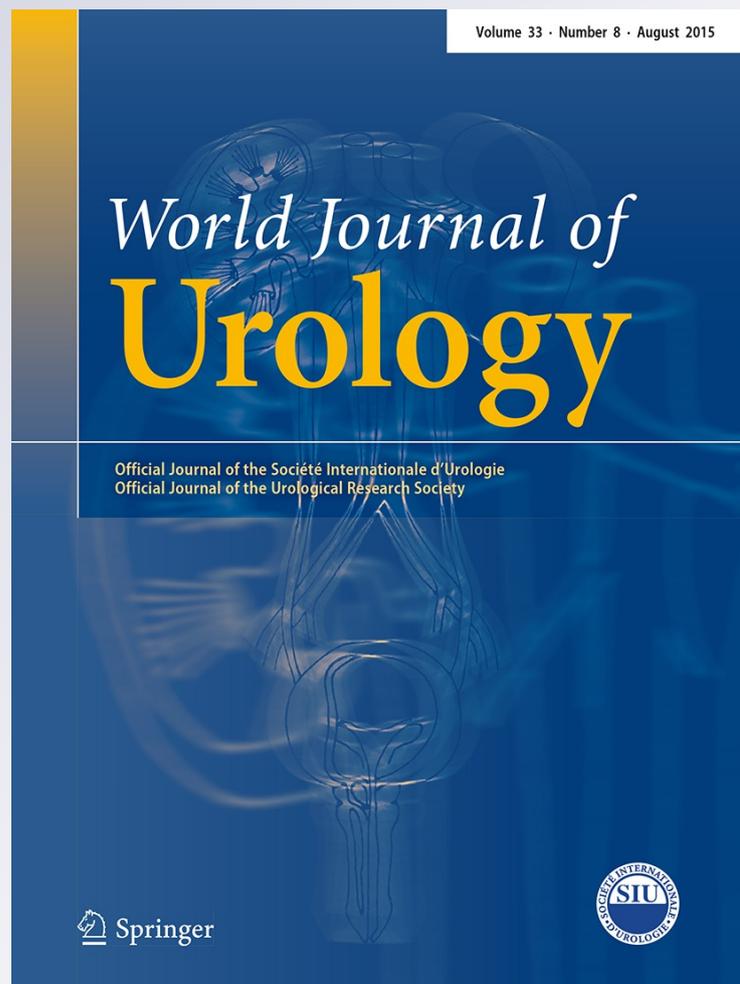
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A finite element model validates an external mechanism for opening the urethral tube prior to micturition in the female

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Abstract

Purpose Existing theories for micturition in the female mandate total relaxation of the pelvic floor while detrusor pressure pushes the urethra open. However, video X-ray and electromyogram data indicate that micturition is preceded by active outwards opening of the outflow tract by backward-/downward-acting muscle vectors. If the detrusor pressure alone is enough to expand the tube, why does the active opening take place? The aim was to model the urethral tube in detail to assess the relative importance of the active opening mechanism and detrusor pressure.

Methods Finite element methods were used to model the urethral tube in detail. Nonlinear-elastic properties similar to urethral component tissues were taken from the literature. The boundary conditions applied to the tube

model included internal pressure due to detrusor contraction (60 cm H₂O) and various displacements and constraints such as pubourethral and pubovesical ligament attachments.

Results In order to achieve opening dimensions similar to those in the lateral X-ray under the action of detrusor pressure alone, the pressure had to be increased by two orders of magnitude above normal levels.

Conclusions Normal detrusor pressure alone is not sufficient to achieve opening of the urethra against the elasticity of the constituent tissues, suggesting that normal micturition requires an active mechanism provided by backward-/downward-acting pelvic floor muscles, as predicted by the integral theory.

Keywords Micturition · Pelvic muscle contraction · Active opening · Female urethra · Finite element model

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Introduction

The traditional conservative opinion for micturition is that the opening of the female urethra is only caused by the bladder pressure, generated by the detrusor following ‘relaxation of the pelvic floor’ [1]. In 1990, the integral theory of female incontinence [2] hypothesised that the opening of the urethra during micturition is mainly caused by the action of directional muscle forces on the surrounding tissues, relaxation of the forward vector and contraction of the posterior vectors (levator plate and the conjoint longitudinal muscle of the anus). This mechanism is, in its reverse action, important for continence, and its introduction into clinical medicine caused a paradigm shift which led to the widespread development and acceptance of suburethral tapes for surgical treatment of urinary incontinence [3–6].

The active opening mechanism causes the urethra to funnel, lowering the resistance to flow by the expulsive action of the detrusor.

No proof was offered at the time, but these predictions were partly validated in 1993 by X-ray data [7] (Fig. 1), which shows active opening of the outflow tract by backward/downward vectors. Electromyogram data [8, 9] demonstrated that a pelvic floor contraction preceded the commencement of micturition. Experimental data and mathematical simulations on the flow through the human urethra demonstrated an inverse exponential relationship between the urethral diameter and the detrusor pressure required for bladder evacuation [10]. Specifically, the pressure is found to be inversely proportional to the diameter raised to the fifth power, so if the urethra can be opened out to twice the diameter by the backward vectors (arrows, Fig. 1), the internal resistance to flow decreases by a factor of 32. This explains female 'obstructive micturition' in fundamental terms: the urethra cannot be opened out if the activating muscles have loose ligamentous insertion points.

Although these data strongly supported the concept of an external mechanism, it still did not finally disprove the traditional theory that detrusor contraction by itself was responsible for the funnelling observed in Fig. 1b. While Fig. 1 is of a particular patient, the general shape of the urethra in this patient is typical of the shape that was observed in X-ray studies of 20 patients and a further study of 12 patients involving electromyograms and the use of vascular clips in addition to X-ray [8, 9].

In order to investigate the behaviour of the urethra in detail, we created a finite element model using known anatomy, bladder pressures and stiffness of the tissue components of the urethra. If our modelling showed that there was no significant opening of the urethra at normal detrusor pressure, one could regard that as an important step towards confirmation of the integral theory. An essential practical consequence of the theory is that the downward opening vector (white arrow, Fig. 1b) contracts against the uterosacral ligament (USL), so that if the USL is loose, the vector force weakens and the patient will have bladder emptying difficulties. Furthermore, this condition is correctible by strengthening the USL [11, 12].

Some basic steps in the development of the model were reported in brief form at biomechanics conferences [13, 14], where the focus was on the finite element modelling rather than the clinical significance of the work. In this more developed and extended paper we include detail of the work that has not been published before. Most importantly, we discuss for the first time the clinical significance of the results of the modelling in the context of the integral theory of Petros and Ulmsten [2], which asserts that the urethral tube must be opened by an external mechanism.

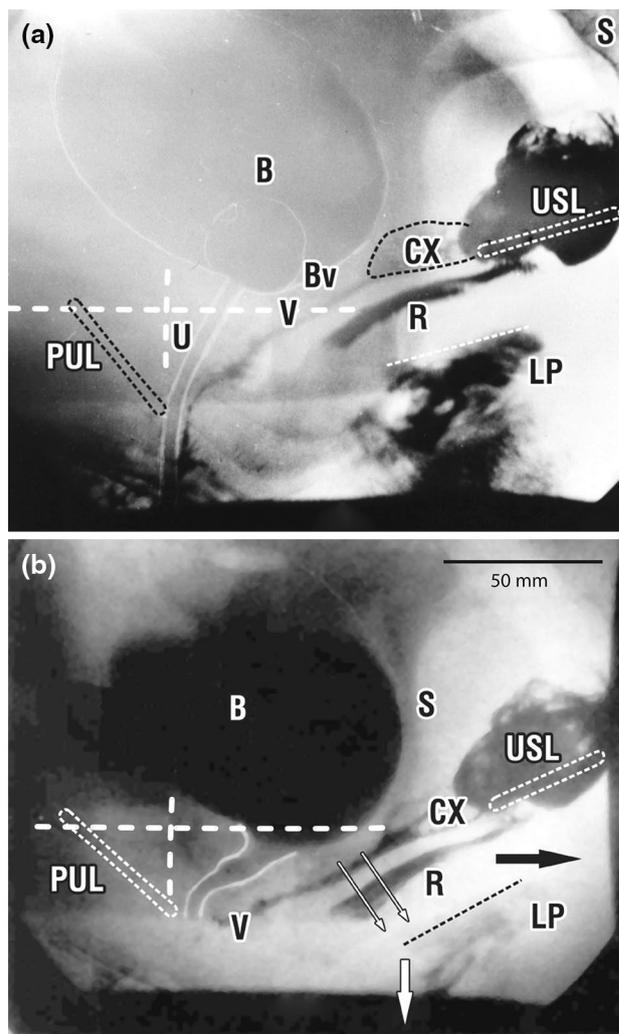


Fig. 1 Female patient, sitting lateral X-ray [7]: **a** resting urethra closed. Slow twitch muscle fibres stretch the vagina against pubourethral ligaments (PUL) anteriorly, and USLs posteriorly, like a suspension bridge. **b** Micturition—same patient. The urethra and bladder neck appear to have been opened out by the downward angulation of levator plate (LP) causing downward stretching of the vagina (V) and rectum (R). Note how the urethra is now well behind the vertical white line, consistent with m.puboccygeus (PCM) relaxation. The *white arrow* represents the effective downward opening vector. The *black arrow* represents the backward (stretching) vector, a prerequisite for optimum effect of the downward (opening) vector. The backward stretching is made possible by the fascial attachment 'Bv' between bladder base and anterior vaginal wall. LP levator plate, U urethra, B bladder, CX cervix and S sacrum

The structure of the human female urethra

The urethra is a complex structure consisting of several different types of tissue [15–18]. The main features are illustrated in Fig. 2a, b. The submucosa is composed primarily of longitudinally arranged collagen fibres and is filled with a rich vascular plexus along the entire urethral length. This layer plays a role in closing off the urethra, but is not expected to

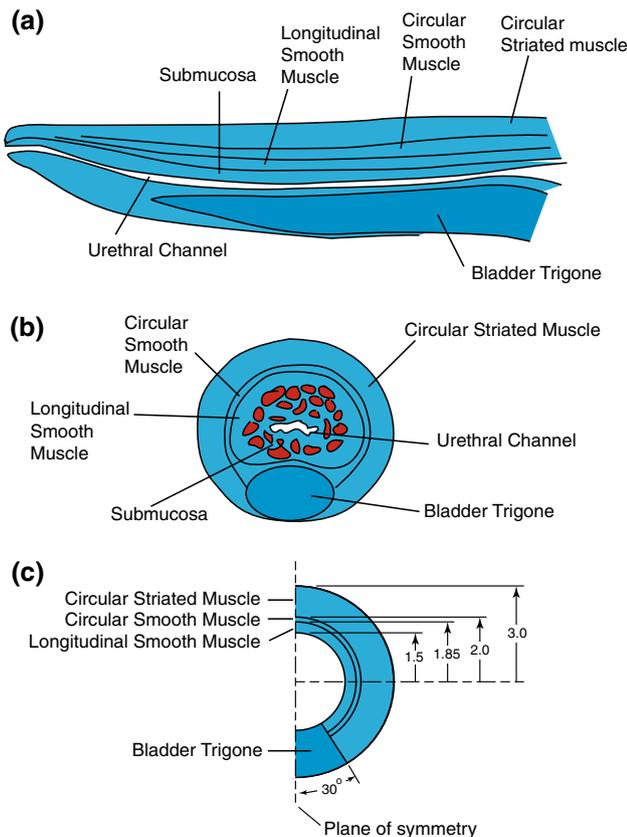


Fig. 2 Lateral (a) and cross-sectional (b) views of the human female urethra (after [17]). The lower diagram (c) shows the simplified geometry adopted for the finite element model, together with radial dimensions of the sections in mm

provide significant resistance to opening. Surrounding the submucosa is a longitudinally arranged layer of smooth muscle. Outside this layer there is a thin, circumferential layer of smooth muscle. The thickness of this circular layer is almost the same throughout the entire length of the urethra, although it may be slightly thicker in the proximal third. A relatively thick striated muscle layer encircles the inner urethral layers with its thickest part at the middle two-thirds of the urethra. Any detailed model of the urethra needs to take into account the geometry of the different components of the tube and the various properties of those components.

Materials and methods

The finite element model

The initial (relaxed) cross-sectional shape of the urethra was taken to be circular. During micturition, the submucosa is compressed into a thin layer. It is therefore ignored in this analysis. The length of the urethra was taken to be

40 mm, while representative diameters of the tissue layers in a typical urethral tube have been determined by examining various cross-sectional views [15–18]. In order to further simplify the analysis, while still retaining sufficient complexity to capture the main features of the behaviour, the structure and the dimensions of the cross section were taken to be uniform along the length of the tube and equivalent to the mid-cross section. The simplified model's cross section and its dimensions are shown in Fig. 2c. Although the structure is three-dimensional, the vertical plane of symmetry evident in Fig. 2c means that only half the structure (as illustrated) needed to be modelled.

The model analysis was carried out using ABAQUS/Explicit V6.3-1 (Simulia, Providence, RI, USA) with three-dimensional, 8 node, 'reduced integration' trapezoidal elements and an explicit (time step) algorithm. The problem was treated as a pseudo-time dependent analysis while the load (i.e. internal pressure) was applied incrementally. The solution presented in this paper was obtained using 5,850 elements, which was found to provide excellent accuracy at reasonable cost. Further increases in element number made no detectable difference to the computed geometry.

Material properties

No direct measurements of the properties of the tissue layers in the urethra are available. Instead, nonlinear-elastic ('hyper-elastic') properties of similar tissues were adopted from the literature [19, 20]. Each material was assumed to have uniform properties.

In typical hyper-elastic material models, the strain energy function, or potential, W , is used to relate stresses to strains in differential form:

$$\sigma = \partial W / \partial \epsilon, \tag{1}$$

where σ and ϵ denote stress and strain tensors, respectively. Many forms of the strain energy function W have been devised [21]. In this study, a range of established functional forms of W were tested to gauge their effectiveness in representing the material property data available for the biological materials of interest. The best general behaviour was obtained by using a 'quadratic polynomial' form of W suitable for representation of typical soft tissues (incompressible and hyper-elastic). This can be written as

$$W = C_{10}(I_1 - 3) + C_{01}(I_2 - 3) + C_{20}(I_1 - 3)^2 + C_{11}(I_1 - 3)(I_2 - 3) + C_{02}(I_2 - 3)^2, \tag{2}$$

where I_1 and I_2 are the 'strain invariants', which are related to the strains in the material. The coefficients C_{ij} are determined by fitting the model to mechanical test data for the material of interest. Such data are available in the literature for a range of

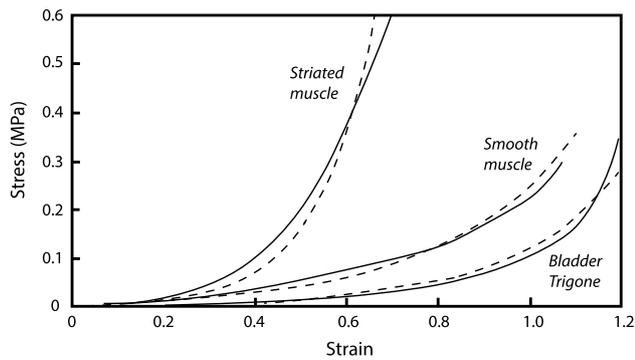


Fig. 3 Comparison between the measured uniaxial stress–strain relationship for smooth muscle, striated muscle and bladder trigone [19, 20] (solid lines) and the best fit of the quadratic material model (broken line) over the range of strains indicated

human soft tissues, such as striated and smooth muscle, and trigone of the human bladder. Although we have chosen to utilise the specific data reported by Abe et al. [19] for muscle tissues and Yamada [20] for the trigone of the bladder, we note that these data are not inconsistent with other measurements of the properties of such tissues [22–24].

The resulting values of C_{ij} used in this model study are presented in Table 1. The experimental stress–strain data and the fitted model are compared graphically in Fig. 3. These material functions are used within the finite element model of the urethral tube to express the elastic behaviour of the tissues making up the tube, which contribute the main ‘passive’ closing mechanism.

Boundary conditions

The boundary conditions applied to the tube model were consistent with the mechanisms illustrated in Fig. 4 and included internal pressure due to detrusor contraction and various constraints and displacements resulting from the surrounding tissue structures. As noted earlier, the model is symmetrical across the vertical plane indicated in Fig. 2c. Symmetry boundary conditions were applied to finite element nodes on this plane (zero normal displacement and zero tangential traction). The outer surfaces of the model were allowed to move freely, except where explicit constraints were applied, as described below.

The remaining boundary conditions consisted of the following:

Internal pressure forces

Measurements of the bladder gauge pressure (pressure relative to atmospheric pressure) in healthy subjects show that pressures as high as approximately 60 cm H₂O are typical

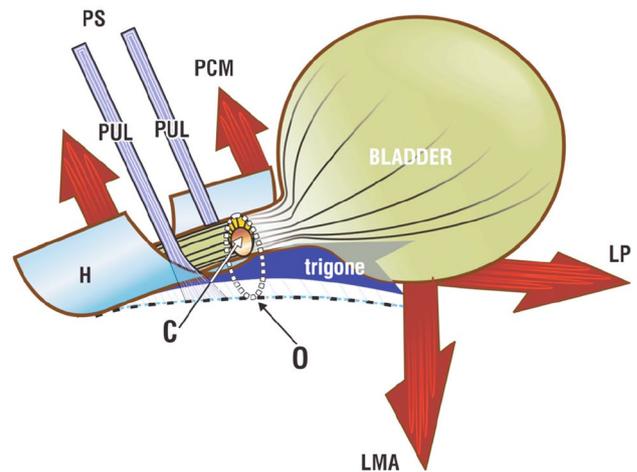


Fig. 4 Schematic model of the anatomy of micturition. The trigone of the bladder extends from bladder base to external meatus. On activation of the micturition reflex, m.pubococcygeus (PCM) relaxes. Levator plate (LP) contraction stretches the bladder trigone backwards, while the conjoint longitudinal muscle of the anus (LMA) stretches the anterior vaginal wall and the posterior urethral wall downwards to open out the urethra from ‘C’ (closed) to ‘O’ (open). The smooth muscle of the pubourethral ligament (PUL) also relaxes, facilitating the downward motion. H, suburethral vaginal hammock; PS, pubic symphysis

[25, 26]. The variation of pressure along the urethral tube is determined by the wall friction and the changes in cross-sectional area. In this study the gauge pressure was assumed to vary linearly along the length of the tube, from 60 cm H₂O in the bladder to zero at the exit.

External constraints

The movement of the distal region of the urethra is relatively confined due to firm connections to the pubic bone by connective tissue and ligaments [2, 7]. This was modelled by constraining axial movement of the distal half of the urethra.

The anchoring effects of the pubourethral ligaments (PUL) and anterior pubococcygeus muscle (PCM) ligaments were included explicitly in the model by preventing movement of the urethra along the line of the ligament at the ligament connection points. Finally, the effects of the applied forces resulting from movement of the vagina and other muscles (LMA) were modelled by applying a displacement to the trigone of the bladder according to the displacement seen in Fig. 1b. We found the bladder trigone to be the key factor in transmitting the posterior vector forces to the posterior urethral wall.

These boundary conditions are obviously a simplification of the complexity of the actual interactions between the urethra and surrounding tissues, but capture the main features of the constraints and applied loads.

Table 1 Values of the hyper-elastic material model coefficients (Eq. 2) determined by fitting to experimentally determined uniaxial stress–strain data [19, 20]

Coefficient (MPa)	Smooth muscle	Striated muscle	Bladder trigone
C_{10}	-0.3812	-0.7960	-0.1600
C_{01}	0.4290	0.8428	0.1756
C_{20}	0.3048	4.351	0.1952
C_{11}	-0.9657	-11.74	-0.6060
C_{02}	0.9535	8.475	0.5527

Results

The calculated urethral tube geometry is shown in Fig. 5a. The lateral X-ray of Fig. 1b is also reproduced here for convenience. It is most important to note that in order to achieve opening dimensions similar to those in the lateral X-ray, the material properties had to be reduced by two orders of magnitude from the values reported in the literature. Conversely, with the original properties the detrusor pressure would need to be increased by two orders of

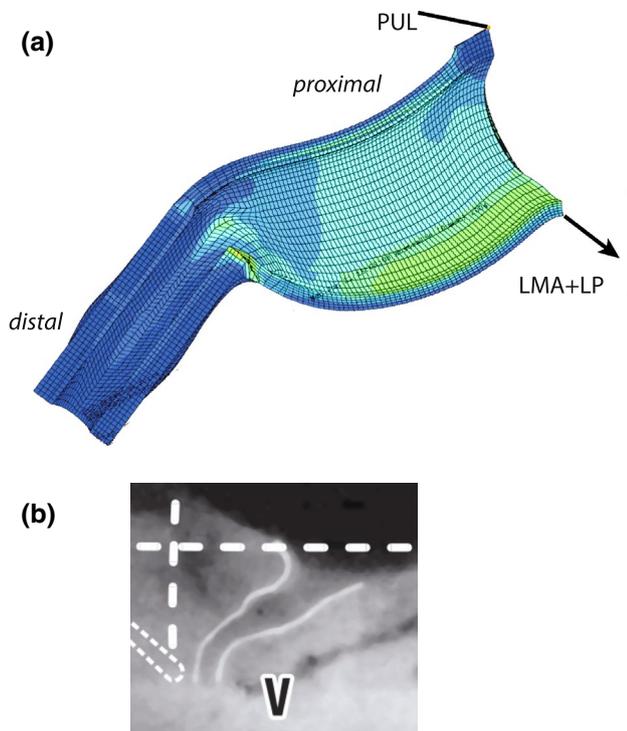


Fig. 5 Calculated urethral tube geometry (a) compared with the actual X-ray of Fig. 1b (b). The colours in (a) indicate maximum principle stress levels in the tissues, ranging from 10 (blue) to 40 kPa (green). The constraints on the boundaries of the model reflect the effects of the connective tissues and ligaments illustrated in Fig. 4, including the anchoring effect of the anterior ligament (PUL)

magnitude, from 60 cm H₂O to 6,000 cm H₂O, in order to achieve opening of the urethral tube. Without this alteration the tube was barely able to open against the natural elasticity of the tissues under the action of typical detrusor pressures alone. Figure 5a also illustrates a typical finite element mesh pattern.

Discussion

The conventional theory assumes that the female urethra opens uniquely because of the pressure of the bladder. However, we have shown that if the properties of the tissues reported in the literature are applied to the model, then the tube is unable to open to the extent seen in X-ray photographs. A similar conclusion was reached by Holecek et al. [27] after modelling the expansion of a uniform tube based on these properties.

Active opening of the urethra prior to detrusor contraction by ‘a single muscle unit’ was recently demonstrated by Watanabe et al. [28] in two patients, one male and one female, using intravaginal or trans rectal ultrasound. We presume that the ‘single muscle unit’ was the downward vector (Fig. 1), which is also evident in the video accompanying this paper (Online Resource 1). The video confirms Watanabe’s findings [28], and previous EMG and video X-ray data [2, 7–9], which indicate that the urethral tract is opened out prior to detrusor contraction and urine flow. The video shows active opening of the posterior urethral wall; the levator plate is angulated downwards by a vector force; this action pulls down the rectum, vagina and posterior urethral wall; the bladder contracts; and the levator plate continues its contraction during micturition.

We contend that the observations of Watanabe et al. [28], the video and the conclusions of this study validate the core postulate of the integral theory for micturition [2] and that an active external muscle force is being applied to open the female urethra. Using intra-anal ultrasound, Watanabe et al. [28] demonstrated that a similar active opening mechanism operates in the male. We also contend that such a mechanism not only occurs, but that it is absolutely necessary in order to overcome the exponential resistance to flow of a narrow urethral tube [10]. We need to look no further than what happens with spinal cord transection. The neurological component of this mechanism is inactivated, resulting in inability of such patients to voluntarily pass urine.

This is not to say that the detrusor pressure is unimportant. The detrusor pressure is necessary to at least partially open the inner channel of the urethra by compressing the submucosa. Once the channel is open, the flow rate is dependent on the geometry of the channel (i.e. the effective diameter) and the pressure in the bladder produced by detrusor contraction.

This external opening mechanism is of more than theoretical importance. The downward-acting opening vectors contract against the USLs, the anchoring point of these vectors [2, 7–9], Fig. 1; a loose USL effectively lengthens the muscle vector, weakening its contractile force [29]; this would lead to symptoms of ‘obstructive micturition’ and residual urine. Surgical reinforcement of loose USLs has been shown to objectively improve emptying and to lower residual urine [12].

Limitations of our study

The stiffness of materials is generally determined using material obtained from cadavers, which may vary from the living tissue [30]. Ligaments muscles and ‘fascial’ tissues in the pelvis are neurologically innervated and so contract and relax according to cortical and subcortical control.

The structural components of the urethra consist of collagen, elastin and smooth muscle. Collagen and elastin are not actively contractile and do not suffer rigour mortis changes as do smooth and striated muscles. We were not able to determine the stretch differential between live and dead smooth muscle tissue. We used only data from dead tissue, which may, in fact, not be so different to that of live tissue during micturition. Anatomically, the urethral smooth muscle wall forms a continuum with bladder smooth muscle. It follows that any detrusor contraction as part of micturition would also contract the urethral smooth muscle. On this basis alone, there may be little difference between live and dead tissue with regard to our model, as the smooth muscle must be modelled in the contracted state, because the posterior urethral wall needs to be contracted and semi-rigid, like a trapdoor, if it is to be opened out by external vector forces [7], Fig. 1. This does not account for a required difference in properties of two orders of magnitude.

The dimensions of the tissue layers in the urethral tube wall were taken from histological cross sections published in the literature. As a result, there is some uncertainty in the layer thicknesses used in the model. In addition, although we have accounted for the various tissue structures across the section of the urethral tube (Fig. 2b), we did not model the changes in this cross section along its length (Fig. 2a), instead using an average cross section throughout. This may have an effect on the local behaviour of the distal end of the tube where the trigone of the bladder disappears, but the bulk of the tube was modelled adequately, particularly in the all-important proximal region. Once again, while variations in these dimensions between patients may produce minor variation in the computed shape of the tube, such variation cannot plausibly explain the two orders of magnitude discrepancy noted above. Furthermore, the computed shape compares very

well with the observed X-ray images of an actual urethral tube (Fig. 5), providing confidence in the chosen dimensions for the model components.

Conclusions

Mathematical modelling confirms the X-ray imaging and electromyogram observations stating that the pressure generated by the detrusor is insufficient and that normal micturition requires an active mechanism provided by backward-/downward-acting pelvic floor muscles, as predicted by the integral theory [2].

We have utilised a representative urethral tube tissue geometry, material properties and boundary conditions in this study, taken from published studies of the urethra and X-ray images. All of these parameters will vary from patient to patient. This minor variation could not plausibly account for a difference of two orders of magnitude as regards opening pressure, and so would not affect the core conclusion of the study stated above. Nonetheless, further study of how such variations affect the required detrusor pressure and the resulting urethral geometry would be an appropriate subject for continued research.

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