Development of perineal noise recording as a non-invasive method for diagnosis of Bladder Outlet Obstruction

ABSTRACT. We are developing two models of the urethra to study perineal noise recording as a non-invasive method to diagnose Bladder Outlet Obstruction. In both models, a flexible model made from Polyvinyl Alcohol (PVA) and a computational model based on Computational Fluid Dynamics (CFD), we study the relation between the recorded noise and the degree of obstruction. In the PVA model we have confirmed the hypothesized relation between recorded noise and the degree of obstruction. In the CFD model we calculated that the location at which the amplitude of the noise is maximum mainly depends on the degree of obstruction.

INTRODUCTION

In ageing males, lower urinary tract symptoms (LUTS), for example a poor flow rate, possibly result from an obstructed urethra caused by an enlarged prostate. In some cases, however, a weakly contracting bladder also causes a poor flow rate. At present the International Continence Society (ICS) recommends a provisional method for diagnosing bladder outlet obstruction on the basis of the maximum flow rate and the associated detrusor pressure, graphically represented in a pressure-flow plot (1), (Fig. 1). The transurethral catheters used for such a pressure flow study induce the risk of urinary tract infection and urethral trauma (2, 3). Recently, non-invasive (and more patient-friendly) measurement techniques have been developed and tested to diagnose Bladder Outlet Obstruction (BOO) in patients with LUTS: the condom-catheter method (4), the cuff method (5) and Doppler flowmetry (6). Alternatively, a non-invasive measurement technique may be based on urethral noise recording, i.e.
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voiding with a microphone pressed against the perineum (between scrotum and anus). An example of such a noise recording is shown in Figure 2. A major advantage of such a diagnostic method is its simplicity. The patient can void freely without interruptions, there is no contact between penis and equipment and it is specifically directed towards diagnosing BOO. The development of this non-invasive technique for diagnosing LUTS started in the mid-sixties with a voiding audiograph (7). It was thought that the splashing noise of urine voided in a cup, recorded with a microphone and corrected for the voided volume, was a measure for bladder pressure. One decade later, the microphone was moved from the cup to the body at the level of the perineum and the noise produced in the urethra and the flow rate were recorded (8). It was hypothesised that urinary flow is turbulent at the bladder neck. These turbulences cause pressure fluctuations on the wall of the urethra that can be recorded as noise transmitted via the urethra to the skin. It was also hypothesised that this perineal noise is related to the degree of prostatic obstruction. In latex (9, 10) or silicone (11) test tubes it has been shown that pressure fluctuations are indeed induced by flow and that the power spectrum of the recorded noise depends, among others, on the degree of obstruction applied.

The precise relation between perineally recorded noise during voiding and the degree of obstruction is not obvious. There are many factors besides the degree of obstruction that could influence the recorded noise, e.g. viscoelastic properties and thickness of the urethral wall and tissue surrounding the urethra. This review presents the development of two models of the urethra to study how perineally recorded noise relates to the degree of prostatic obstruction. The first model is a highly flexible and extensible tube made of a 10% aqueous solution of the polymer Polyvinyl Alcohol (PVA). This cryogel behaves like rub-

Figure 1 - The provisional ICS method for definition of obstruction. Classification of bladder outlet obstruction is based on a combination of maximum flow rate and the simultaneously measured detrusor pressure value during a pressure-flow study. A voiding with low flow rate, e.g. 8 ml/s, may either be obstructed or unobstructed depending on the detrusor pressure.
ber after a freezing/thawing process that controls the viscoelastic properties. The second model is based on Computational Fluid Dynamics (CFD). In the last two decades the application of this computational technique has been extended to biological systems including the peripheral circulation (12, 13, 14, 15), the respiratory tract (16) and the male urinary tract (17, 18). It enables simulations of (urinary) flow through complexly shaped tubes.

POLYVINYL ALCOHOL MODEL URETHRA

As mentioned before, in recent decades latex and silicone tubing has been used as a model of blood vessels (9, 10) and the urethra (11). These tubes are considerably stiffer than arteries and the urethra. A more flexible and extensible tube can be made from PVA cryogel (19), (Fig. 3). This polymer-solution (liquid at room temperature) was poured in a mould; storage in a freezer overnight and thawing at room temperature during the day completed one freeze/thaw cycle and stiffened the PVA cryogel. The number of freeze/thaw cycles, the rate of freezing/thawing and the concentration of the cryogel control the viscoelastic properties of this PVA cryogel.

Figure 2 - An example of simultaneously measured urine flow rate (top panel) and perineal noise (lowest panel). The noise was recorded using a microphone pressed against the perineum. The peaks in the noise recording before voiding and at the end of voiding are probably caused by a contraction of the pelvic floor muscles.

Figure 3 - Cross section and side-view of a PVA model urethra (reproduced from Neurourol. Urodyn. 24: 381-388, 2005, with kind permission of John Wiley & Sons, Inc.).
In a number of model urethras we studied the relation between the recorded noise and the degree of obstruction of the urethra (20). We constructed three models with different viscoelastic properties; we applied three degrees of obstruction by inflating a blood pressure cuff placed around the urethral model and recorded the noise at three positions distal to the applied obstruction (Fig. 4). The flow rate was kept constant and was identical in all recordings. We analysed the recordings by calculating the average noise-amplitude of the recorded noise signals and the average weighted frequency of its power spectrum (the essential frequency). We found that both depended significantly (ANOVA, p<0.05) on the degree of obstruction (Fig. 5). Both increased with increasing degree of obstruction. This result supports the hypothesis that there is a relation between the recorded noise and the degree of obstruction. It also supports the hypothesis that a non-invasive method for diagnosing bladder outlet obstruction might be based on perineal noise recording. However, we found that the two studied parameters of the recorded noise also depended on the distance between microphone and obstruction and on the viscoelastic properties of the model urethra. The three factors were found to be independent of each other.

In order to relate the recorded noise unambiguously to the degree of obstruction, despite differences in viscoelastic properties and position of the microphone, we have fine-tuned the model urethra to match the viscoelastic properties of the human male urethra. As a model for the viscoelastic properties of the human male urethra we used the pig urethra because of the similarities between pig and human physiology (21). We made bladder/urethra preparations from 8 male and 10 female pigs sacrificed at the department of Experimental Cardiology (Erasmus MC, Rotterdam, the Netherlands). The part of the urethra closest to the bladder was selected for the measurements (distal to the prostate for the male pigs). An example of a cross-section of the male and female pig urethra is shown in Figure 5.
Figure 5 - Mean (±1 standard error of the mean) average amplitude and essential frequency of five noise recordings done at nine different combinations of degree of obstruction and microphone position in three PVA-urethras with different wall stiffness (PVA1, PVA2 and PVA3). The degrees of obstruction are separated by dotted lines and displayed on the X-axis. Within each degree of obstruction the distance from the obstruction increases from left to right (3, 5 and 7 cm). This graph is reproduced from Neurourol. Urodyn. 24: 381-388, 2005, with kind permission of John Wiley & Sons, Inc.

Figure 6 - Cross-section of the proximal part of the male (top) and the female (bottom) pig urethra. We stained elastin, collagen (purple) and muscle tissue (green) using Elastic von Gieson staining. In the male cross-section the lamina propria is surrounded by muscular tissue with a horseshoe-like shape. In the female cross-section the lamina propria is surrounded by muscular tissue with a circular shape. The top part of this figure is reproduced from Neurourol. Urodyn. 25: 451-460, 2006, with kind permission of John Wiley & Sons, Inc.

Figure 6 is shown in Figure 6. We used Elastic von Gieson staining (22) to mark elastin, collagen and muscle tissue in these cross-sections, which show a difference in tissue composition of the urethral wall between male and female pig urethras. We also made 12 different model urethras (21). Half of the model urethras had a circular-shaped flow-channel and the other half a Y-shaped channel. Within each group four model urethras were freeze-thawed 1, 2, 3, and 4 times and two consisted of a once or twice freeze-thawed cylinder in a separate shell that was freeze-thawed 3 times. Each model was placed in a water-filled container (approx. 1 cm below the water-surface) at room temperature and each pig urethra was placed in a container (approx. 1 cm below the solution-surface) filled with a cold (10°C) modified Krebs solution. One side of the model or pig urethra was connected to a 5 ml syringe to manually inject a known volume of water in a very short time. The pressure response was recorded using a disposable pres-
sure transducer connected to the other side of the urethra. Increasing volumes were injected and the pressure response was recorded. In order to derive the viscoelastic properties, the simplified analytical solution of the step-response of a mechanical model was fitted to 1000 samples (equivalent of 1 sec.) of the pressure signal. The fit-procedure resulted in 6 coefficients, three coefficients accounted for the amount of stress in the urethral wall, two accounted for the relaxation of the urethral wall in time and one accounted for vibration of the wall upon stepwise-applied strain.

We found a difference in viscoelastic properties between male and female pigs (23). In female pig urethras the same stress-values could be achieved as in male pig urethras but at significantly higher strain than in male pig urethras (Fig. 7). This difference in viscoelastic properties was supported by the difference in muscular tissue surrounding the lamina propria in male and female pig urethra, as shown in Figure 6. Based on the comparison between the model urethras and the male pig urethra (21), a model urethra with a Y-shaped flow channel that was uniformly freeze-thawed three times was chosen as the best model of the human male urethra for studying the relation between noise recording during urine flow and the degree of bladder outlet obstruction.

To further test how well this model urethra represents the male urethra, we have done urethral pressure measurements (to be published). We created three different continence zones in the model urethra by applying three different blood-pressure cuffs around the model and inflated them to different pressures using a water column. At each cuff pressure we measured a quasi-static approximation of the Valsalva Leak-Point-Pressure (VLPP). We also recorded a Urethral Pressure Profile (UPP) by withdrawing a fluid perfused catheter at different withdrawal rates and with different perfusion rates through the urethral model. From each UPP, corrected for the pressure loss in the catheter, the maximum was denoted as the Maximum Urethral Closure Pressure (MUCP). We found that with increasing cuff pressure the measured VLPP as well as the MUCP increased. VLPP, however, was found to be a more accurate measure than MUCP. We also found that MUCP depended significantly on the perfusion and withdrawal rate of the catheter and on the type of continence zone. In Figure 8

![Figure 7 - Stress in the urethral wall of male (●) and female (○) pig urethras as a function of the applied strain with fitted exponential functions (solid lines) and 95% CI of these functions (dashed lines). The stress-strain relation for the selected model urethra (Y-shaped channel, freeze-thawed 3 times) is plotted in this graph as ★. This graph is reproduced from Neurourol. Urodyn. 25: 451-460, 2006, with kind permission of John Wiley & Sons, Inc.](image-url)
examples of recorded pressure profiles are presented that demonstrate the dependence we found. Similarities between the urethral pressure profiles in a model urethra and those in a male urethra support the model urethra as a good representation of the human male urethra.

Our next aim in development of perineal noise recording as a non-invasive technique is studying the relation between recorded noise and obstruction in detail. This will be done in the three times freeze-thawed model urethra by varying the degree of obstruction and record the noise between 1 and 12 cm, at intervals of 1 cm, downstream of the obstruction. Inflating a blood pressure cuff around the model urethra will create the obstruction and by connecting a water-column to one side of the model urethra a bladder will be simulated. Varying the pressure in the cuff and in the “bladder” will result in a flow rate between 0 and 35 ml/s and a bladder pressure ranging from 45 to 130 cm H₂O.

**COMPUTATIONAL FLUID DYNAMICS MODEL URETHRA**

The second model we have developed to study perineal noise recording as a non-invasive diagnostic method for BOO is based on Computational Fluid Dynamics (CFD). Theoretical and experimental fluid dynamics studies have shown that flow passing an obstruction starts recirculating in vortices and further downstream restores to forward flow (24, 25, 26). The point at which flow restores is called the reattachment point. Since at this point the maximum r.m.s. wall pressure and thus the maximum urethral noise amplitude is found (9, 12, 27, 28), the reattachment point may be the best location to non-invasively record perineal noise. We studied some of the parameters that influence the location of this point in a simple two-dimensional computational model of the prostatic urethra (29). Figure 9, top panel, shows the computational model,
consisting of the bladder, the bladder neck, the prostatic urethra and a posterior part of the urethra. Each model was divided in ~2200 fluid elements (second panel). Some boundary conditions were applied to the model, and the fluid was given the properties of water. Calculations were carried out at 4 different bladder pressures, 5 degrees of obstruction and 3 obstruction shapes. In each simulation, the velocity (third panel) and pressure (lowest panel) distributions and the wall shear stresses were calculated (Fig. 10). The model calculations showed that recirculation of urine may occur above a certain degree of obstruction. This recirculation is related to decreased pressure (below atmospheric level) at the obstruction outlet. The location of the reattachment point depended primarily on the degree and secondarily on the shape of the obstruction and it was independent of the applied bladder pressure. This finding led us to the hypothesis that two diagnostic parameters may be derived from perineal noise. The first is the location of the maximum noise amplitude as a
measure for the degree of prostatic obstruction. The higher the degree of obstruction, the more distal this point is located. Since the noise amplitude is highest at the reattachment point, perineal noise should simultaneously be recorded at a number of locations along the urethral wall to identify this location. The second diagnostic parameter, the frequency of the perineal noise, may be a measure for the bladder pressure. The dominant mechanism generating noise at the reattachment point is the frequency of passing fluid vortices traveling from the obstruction to the reattachment point via streamlines. The frequency of newly developed vortices depends on the fluid velocity (12). Based on physical principles, it may be expected that the obstruction diameter and the bladder pressure influence the maximum fluid velocity the most. The model calculations showed that with varying degree of obstruction from low \( d_{\text{obs}} = 14 \text{ mm} \) to severe \( d_{\text{obs}} = 4 \text{ mm} \) at any bladder pressure value, the maximum fluid velocity increased with only 20%. Varying the bladder pressure from 60 to 180 cmH\(_2\)O at any obstruction diameter, led to an increase in the fluid velocity with 75%. We therefore hypothesise that the frequency of noise (i.e. frequency of passing fluid vortices) depends primarily on the bladder pressure.

**DISCUSSION**

At present the International Continence Society (ICS) recommends a provisional invasive method for diagnosing bladder outlet obstruction on the basis of the maximum flow rate and the associated detrusor pressure. Recently, non-invasive techniques are developed to diagnose BOO. In this review the development of a non-invasive technique based on perineal noise recording is described. Based on differences in spectral intensities, it was shown that the recorded noise correlated with flow rate (8). Experimental (11, 30) and clinical studies (30, 31) were published on the relation between noise recordings and BOO. The test tubes used in these experiments were rather stiff compared to the more flexible and distensible blood vessel or urethra. In the same period of time studies were done on vascular murmurs caused by stenoses, a method referred to as phonoangiography (9, 10, 32, 33, 34, 35). It was shown that based on either the mean power frequency (11), the break frequency of the noise spectrum (9, 10, 35), the shape of the recorded noise signal (30) or a combination of the average power amplitude in a specific frequency range.

Figure 10 - Each panel shows wall shear stress along the urethral wall with a total length of 150 mm, starting from the obstruction outlet to the end of the urethra, (Fig. 3, top panel). The location of the reattachment point did not depend on bladder pressure (top panel), but depended on the degree of obstruction (middle panel) and on the obstruction shape (lowest panel).
quency band with the simultaneously measured flow rate (31) diagnosing arterial stenosis and BOO could be possible.

In a review on bio-acoustic signals it was noted that the phonoangiographic methods might be non-invasive and inexpensive, but that clinical application of these methods has been overtaken by large-scale application of ultrasound Doppler (36). Nevertheless, over the years attempts have been made to relate noise recordings from biological fluids (e.g. blood, urine) to the obstruction passed (stenosis or prostatic obstruction). And despite encouraging results, a non-invasive measurement device based on noise recordings is not yet available.

In this review we have presented two models of the human male urethra for studying perineal noise recording as a non-invasive technique for diagnosing males with LUTS, caused by an enlarged prostate. We have shown in the Polyvinyl Alcohol (PVA) model urethra that the recorded noise indeed depends on the degree of obstruction, but also on the viscoelastic properties of the model wall. Therefore, we have developed a PVA model urethra with viscoelastic properties comparable to the male pig urethra. The advantage of such a model is the ability to physically control the various factors that influence the recorded noise, e.g. the viscoelastic properties and the degree of obstruction. The PVA model can be used to record noise that is presumably produced by the flow through an obstructed urethra. We also developed a model urethra based on Computational Fluid Dynamics (CFD). In the CFD model urethra the various factors can be controlled mathematically and it can be used to visualize the flow through the obstruction and urethra.

Future aims are to study the relation between noise and the degree of obstruction in more detail, as mentioned, and the development of a measurement-setup for validating the perineal noise recording technique in male volunteers. This measurement-setup is then to be used to test the developed diagnostic method in a patient population. Eventually this method is intended to diagnose obstruction in patients with impaired voiding.

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REFERENCES


