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In Vivo Patient Measurements of Bladder Elasticity Using Ultrasound Bladder Vibrometry (UBV)

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Abstract—**A healthy compliant bladder is capable of storing increasing volumes of urine at low pressures. The loss of bladder compliance is associated with various diseases. The urodynamic studies (*UDS*), the current clinical gold standard for measuring bladder compliance, requires catheterization and measuring intra-bladder pressure as a function of filling volumes. Ultrasound Bladder Vibrometry (*UBV*) is a noninvasive technique that uses focused ultrasound radiation force to excite Lamb waves in the bladder wall and pulse-echo techniques to track the wave motion in tissue. Cross-spectral analysis is used to calculate the wave velocity, which is directly related to the elastic properties of the bladder wall. In this study, we compare the measurements of changes in bladder elasticity as a function of bladder pressure and volume obtained using *UBV* and the pressure-volume measurements obtained using *UDS*. *UBV* and *UDS* of an excised porcine bladder are presented. Comparative studies in neurogenic and healthy patient bladders are also summarized.**

I. Introduction

An elastic bladder is important for storing increasing volumes of bladder urine at low pressures [1]. Bladder stiffens with age and various pathological processes and is associated with increase in connective tissue relative to the smooth muscle in the bladder wall [2]. Urodynamic studies (UDS) are currently considered the gold standard in clinical assessment of bladder compliance and are based on measuring the detrusor pressure as a function of catheter filling. A compliant bladder expands to accommodate the filling volume, resulting in a low detrusor pressure, while a non-compliant bladder does not expand as readily and the detrusor pressure rises during filling. The urodynamic studies last approximately 45 minutes, are uncomfortable with pain, traumas and infections reported during and after the procedure in both men and women [3].

Recently, we have developed the Ultrasound Bladder Vibrometry (UBV) to quantify the mechanical properties of the bladder wall in animals and patients. UBV used ultrasound to excite and track a Lamb wave in the bladder wall. The velocity of the wave is then related to the mechanical properties of the bladder at the point of measurement. In this study, we use UBV technique to measure bladder elasticity at various pressures and volumes in an excised pig bladder and compare the results with those obtained using UDS. UBV was then used to measure bladder elasticity as a function of bladder volume in patients with healthy and neurogenic bladders undergoing UDS examination.

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II. Methods

A. Ultrasound Bladder Vibrometry

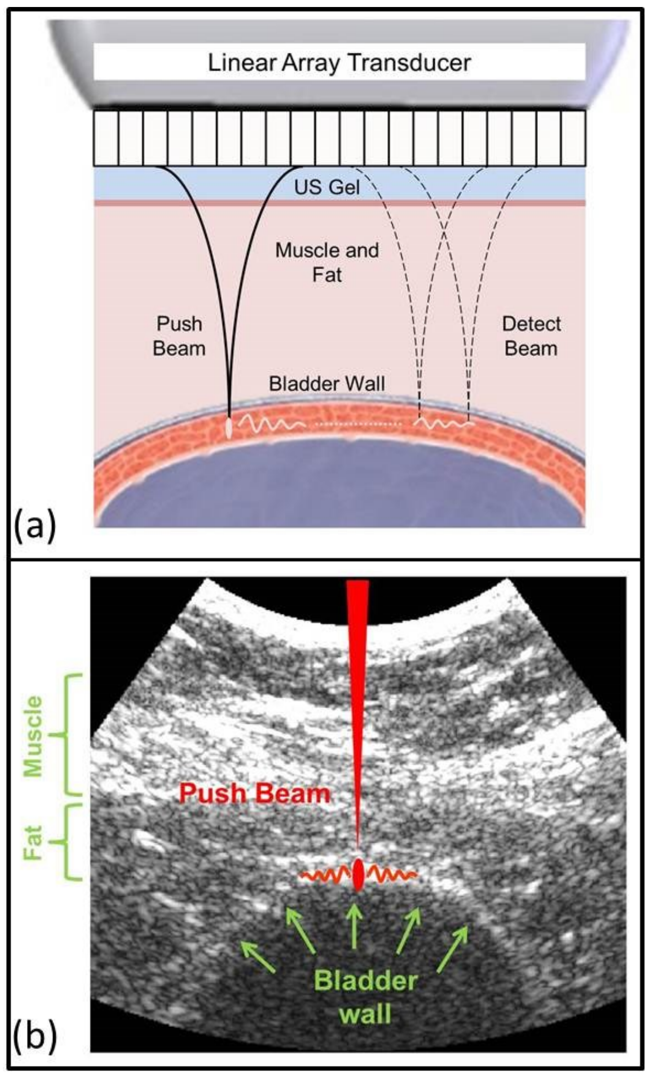

Fig. 1. Principle of UBV: (a) the push beam excites a Lamb wave in the bladder wall and the detect beams track the motion; (b) the B-mode image shows the bladder wall in its natural surroundings.

In UBV, ultrasound radiation force (push beam) is focused at the bladder wall to excite impulsive anti-symmetric Lamb waves 200–600 µs in length (Figure 1a). Pulse-echo ultrasound (detect beam) tracks tissue motion through successive B-modes .

Cross-spectral analysis of the received echoes is used to calculate wall motion as a function of time [4]. Fourier-space analysis [5] of the motion is used to calculate the change of Lamb wave velocity as a function of frequency, or the Lamb wave dispersion. The Lamb wave dispersion equation is fit to the dispersion data to estimate bladder viscoelasticity. The use of the Lamb wave dispersion equation for the given geometry has been extensively validated in our previous work [6-8]. Assuming that the bulk modulus is much larger than the shear modulus, the elasticity is estimated by fitting the anti-symmetric Lamb wave dispersion equation (1) to the Lamb wave dispersion data:

$$4k_L^3\beta_L \tanh(\beta_L h) - (k_s^2 - 2k_L^2)^2 \tanh(k_L h) = k_s^4 \qquad (1)$$

where $k_L = \omega / c_L$ is the frequency dependent Lamb wave number, c_L is the frequency dependent Lamb wave velocity, $\beta = \sqrt{k_L^2 - k_s^2}$, $k_s = \omega\sqrt{\rho_m/\mu}$ is the shear wave number, μ is the shear modulus of elasticity, ω is the angular frequency, ρ_m is the density of the sample and h is the half-thickness of the sample [6, 9].

B. Ex Vivo Studies

An excised pig bladder was filled with water until the surface was taut and placed inside a water tank. The inside of the urethra was covered with industrial glue and attached to rubber tubing. A column of water and a syringe were used to control the pressure inside the water-filled bladder by injecting water into or drawing water out of the system with the syringe (Figure 2).

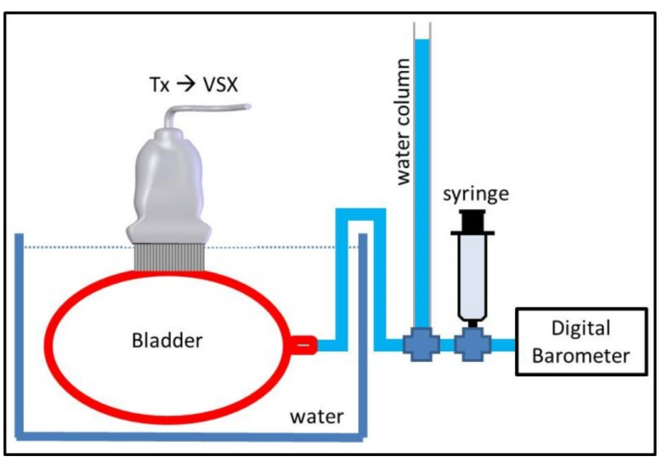

Fig. 2. Experimental setup for the *ex vivo* porcine bladder measurements.

A pressure gauge was used to measure the pressure inside the bladder. A programmable ultrasound imaging platform (Verasonics, Inc. Redmond, WA, USA) operating an L7-4 transducer (center frequency of 5 MHz and made by Philips Healthcare, Andover, MA) was used to excite 400 µs impulse in the bladder wall and track the motion. Plane wave imaging detection pulses were transmitted at a pulse repetition frequency of 4 kHz. Fourier-space analysis was used to calculate the shear elastic modulus at several pressures and volumes.

C. In Vivo Patient Studies

Several patients with healthy and neurogenic bladders undergoing routine UDS evaluations at the Mayo Clinic were recruited for our study. All the patients signed the patient consent form consistent with our Institutional Review Board (IRB) protocol. The Verasonics system (Verasonics, Inc. Redmond, WA, USA) operating a C4-2 transducer (center frequency of 3.3 MHz and made by Philips Healthcare, Andover, MA) was used to excite 400 µs impulse in the bladder wall and track the motion. Plane wave imaging detection pulses were transmitted at a pulse repetition frequency of 2 kHz.

III. Results

The *ex vivo* experimental setup was used to measure the elasticity of an excised pig bladder. A sample result at the pressure and volume of 27 mmHg and 400 ml of water inside the bladder is shown in Figure 3. The B-mode of the bladder wall is shown in 3(a). A red line showing the bladder wall boundary was obtained by fitting a parabolic curve to the maxima of the B-mode image along the vertical axis.

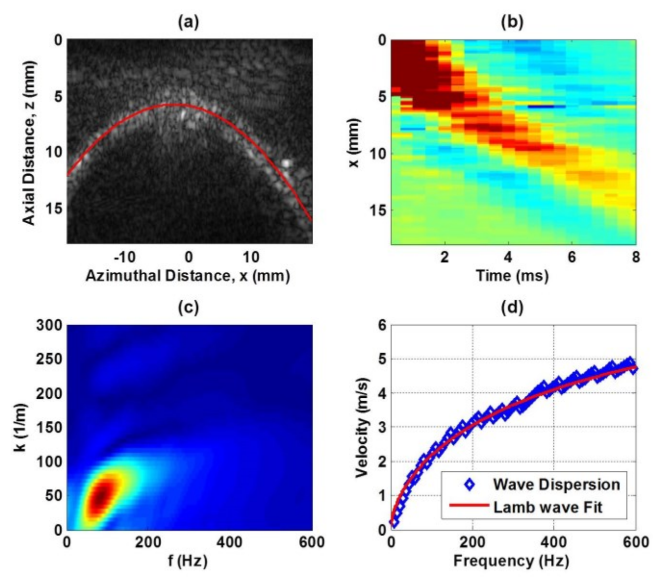

Fig. 3. Ex vivo measurements of porcine elasticity.

The knowledge of the curvature of the bladder is necessary in order to correct the displacement vector for the k-space analysis [10]. Figure 3(b) shows the impulse propagation on the surface of the bladder. The radiation force excites an impulse at (x, t) = (0, 0) and the impulse propagates with respect to time and distance (x). 2D-FFT of the displacement field in Figure 3(b) gives the k-space of the displacement (Figure 3(c)) where the horizontal axis represents frequency, *f*, in Hz and the vertical axis the wave number, *k*, in 1/m. The A_0-mode Lamb wave phase velocity dispersion is calculated by finding the pixel with the maximum magnitude for each frequency and, since the wave velocity $c = f/k$, dividing the frequency coordinates by the wavenumber coordinates of the k-space [5]. Thus obtained dispersion data are shown in blue in Figure 3(d). The Lamb wave dispersion equation (1) (red) was fit to the dispersion data (blue) to estimate bladder elasticity. The estimated thickness of the bladder from the B-mode was 2.2 mm. The estimated excised bladder elasticity was 17.4 kPa.

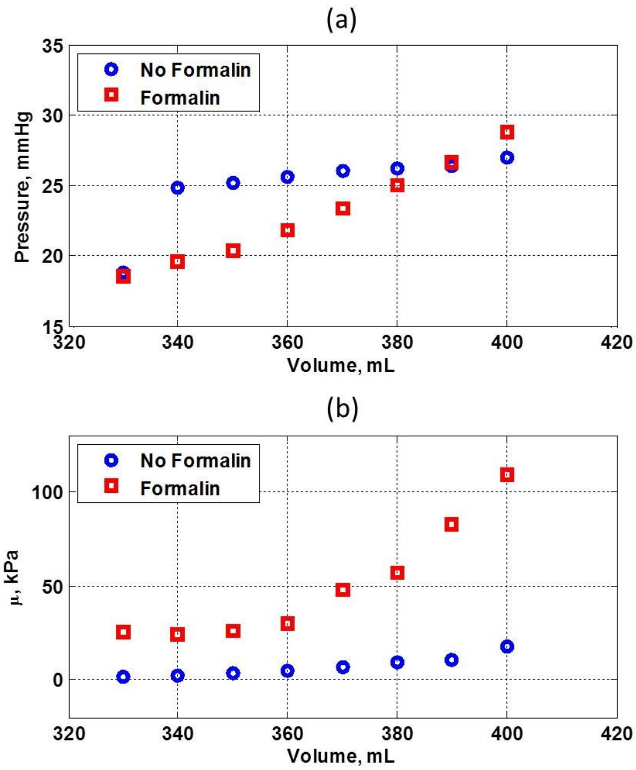

Fig. 4. Pressure versus volume (a) and shear elasticity versus volume (b) curves for an excised pig bladder before and after formalin treatment are shown

To test if UBV could be used to detect mechanical property changes in the bladder wall, excised bladder was filled with saline to the resting volume of 330 ml. The bladder was injected with saline up to a volume change (ΔV) of 70 mL in small increments while measuring the pressure inside the bladder (blue circles in Figure 4). Concurrently, UBV measurements of bladder elasticity were made at each pressure-volume step. Next, the bladder was stiffened by immersing it in 10% formalin for two hours and measurements were repeated (red squares in Figure 4).

Results of UBV measurements in a neurogenic patient bladder are shown in Figure 5a. Urodynamic Studies (UDS) in the same patient are shown in Figure 5b. Figure 5 shows that UBV and UDS have the same general trend. The UDS results shown in Figure 5b are the instantaneous values of pressure versus volume from a catheterization and are reported without standard deviations.

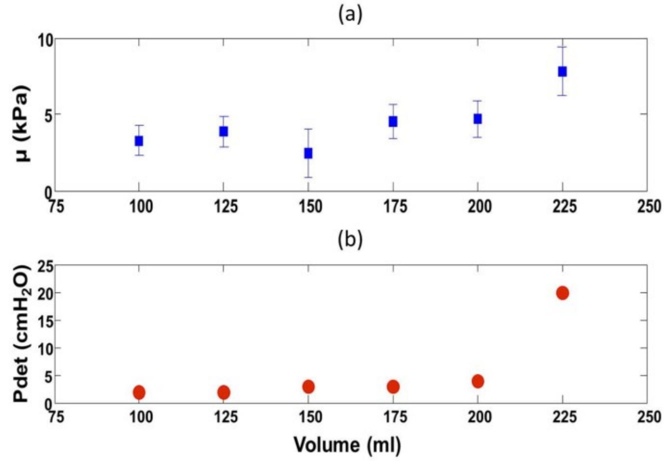

Fig. 5. Comparison between the UBV and UDS measurements in a neurogenic patient.

Figure 6 shows the UBV estimates of elasticity (μ) for three patients with normal bladders and three patients with neurogenic bladders. The neurogenic bladders' elasticity show a higher increase as a function of volume.

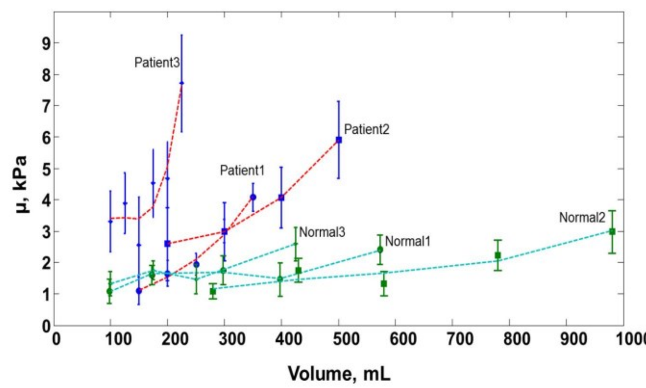

Fig. 6. UBV measurements in three patients with healthy bladders are shown in green. UBV measurements in three patients with neuoregenic bladders are shown in blue and red.

IV. DISCUSSION

The Ultrasound Bladder Vibrometry (UBV) technique was used to measure changes in bladder elasticity as a function of pressure and volume in an excised setting and *in vivo*. Assessment of bladder compliance using UBV and Urodynamic Studies (UDS) before and after formalin treatment of an excised pig bladder is reported in Figure 4. The bladder became stiffer and less compliant following the formalin submersion as is evidenced by the upward shift of the UBV curve (Figure 4b) and slight increase in the slope of the of the UDS curve (Figure 4a). The purpose of the formalin study is to demonstrate that UBV is capable of detecting changes in bladder stiffness similar to UDS.

Figure 5 shows a comparison between UBV and UDS measurements in a neurogenic patient. Both methods show that the bladder compliance does not change significantly until 225 mL at which point both the UDS and UBV curve show a significant increase in detrusor pressure and elasticity, respectively.

Figure 6 summarizes the results of measuring changes in bladder elasticity as a function of volume in three patients with healthy bladder and three patients with neurogenic bladders. Healthy bladders seem to be more compliant than the neurogenic bladders as their bladder elasticity does not increase as quickly as a function of volume.

The studies presented in this paper demonstrate the potential of UBV serving as a surrogate to UDS studies. A major advantage of UBV is that it is noninvasive. It is important to note that the mechanical index (MI) of the focused radiation force in UBV measurements is below Food and Drug Administration (FDA) limit of 1.9. Both bladder elasticity and estimates of volume can be made using a single ultrasound probe. To the best of our knowledge, these are the first *in vivo* measurements of bladder elasticity.

V. Conclusions

A comparison between Ultrasound Bladder Vibrometry (UBV) and Urodynamic Studies (UDS) techniques for assessing bladder compliance are presented. Comparative studies in excised porcine bladder before and after formalin treatment are in very good agreement. *In vivo* neurogenic patient studies comparing the UBV and UDS results show similar trends in elasticity (UBV) and pressure (UDS) increase as a function of volume. UBV measurements in three patients with normal bladder and three patients with neurogenic bladders show that the normal bladders' elasticity changes less due to increase in bladder volume. This finding is consistent with the notion to that neurogenic bladders are less compliant. The results presented in this study suggest that UBV can be used as a surrogate for UDS measurements with the major advantage of being noninvasive.

Acknowledgment

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