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Ex Vivo Measurements of Myocardial Viscoelasticity Using Shearwave Dispersion Ultrasound Vibrometry (SDUV)

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Abstract—**Stiffening of the left ventricle can compromise the ability of the heart to pump sufficient amounts of blood into the systemic circulation and could lead to heart failure. Quantifying mechanical properties of the left ventricular (LV) myocardium using a noninvasive technique would be of great benefit in clinical settings. We investigated the feasibility of using Shearwave Dispersion Ultrasound** Vibrometry **(SDUV) to measure viscoelasticity of the myocardium. A mechanical actuator was used to induce shear waves at multiple frequencies (40 – 500 Hz) in excised LV myocardium and urethane rubber samples, and a pulse echo ultrasound transducer was used to detect the motion at each frequency. An anti-symmetric Lamb wave model was fit to the shear wave dispersion curves in four orthogonal directions to obtain elastic and viscous moduli.**

I. INTRODUCTION

According to the American Heart Association report, the direct cost of treatment of heart failure in the United States in 2009 is projected to be around $34 billion [1]. Approximately 40% of heart failures are caused by diastolic dysfunction, characterized by the impaired ability of the left ventricle (LV) to relax (stiffening) [2]. Stiffening of the LV myocardium compromises the ability of the heart to pump sufficient amount of blood under the physiological pressures and could lead to heart failure if left untreated.

Currently, clinicians rely on measurements of ejection fraction as one of the means to assess the diastolic function. Studies show that patients with normal ejection fraction could still present with symptoms of heart failure [2-4], suggesting that the ejection fraction is not a reliable indicator of diastolic function. Other techniques for assessing diastolic function [5] do not estimate tissue properties directly.

Thus, a technique capable of characterizing material properties of the tissue would be highly beneficial in clinical settings.

Significant research effort has been directed towards designing an imaging method capable of noninvasive assessment of mechanical behavior of the myocardium. Tagged magnetic resonance imaging, tissue Doppler imaging, mechanical wave imaging, acoustic radiation force impulse imaging, and echocardiography based methods have shown promising results [6-11].

Our group has previously reported the use **Shearwave Dispersion Ultrasound Vibrometry** (SDUV) method for quantifying viscoelastic moduli of soft tissue [12, 13]. The method uses radiation force to induce shear wave propagation in the region of interest and a pulse echo transducer to detect the motion. Speed of propagation of shear waves at multiple frequencies (shear wave dispersion) is used to quantify mechanical properties of the tissue. Our group has investigated the feasibility of the SDUV technique in quantifying elasticity and viscosity of myocardium.

We report the results of measuring shear wave dispersion in four orthogonal directions on the surface of a urethane rubber sample and an excised pig myocardium using a modified SDUV technique with a frequency range of 40-500 Hz. An anti-symmetric Lamb wave model was fitted to the experimental data to estimate viscoelastic moduli.

II. METHODS

A. SDUV Technique

Amplitude modulated (AM) ultrasound beam from the "push" transducer is focused on the region of interest to generate harmonic shear waves and a pulse echo ("detect") transducer is used to register the motion, as shown in Figure 1 [13]. Ultrasound pulses from the detect transducer are transmitted at the motion detection site at a repetition rate of few kHz. A cross-spectral correlation method and a specialized Kalman filter are used to estimate amplitude and phase of the propagating shear wave [14, 15].

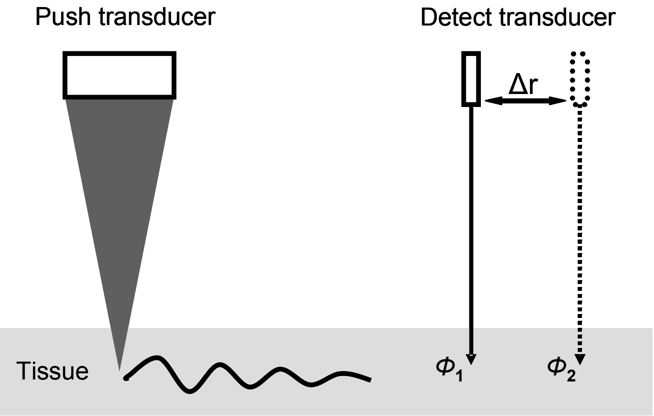

Fig. 1. Principle of SDUV: a push transducer is the source of radiation force that induces harmonic shear wave propagation in tissue; the motion is measured by a pulse echo (detect) transducer.

Near the focus of the push transducer, tissue displacement due to radiation force is mostly parallel to the beam axis, characteristic of cylindrical shear waves [12]. The phase delay of such a wave varies linearly with the distance from

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the beam axis [12]. Thus, by controlling the frequency of the excitatory harmonic wave, one can estimate the speed of propagation of the shear wave by measuring the change in phase $\Delta\phi = \phi_2 - \phi_1$ over distance from beam axis Δr:

$$c_s = \omega \frac{\Delta r}{\Delta \phi}. \qquad (1)$$

Equation 1 requires phase measurements from at least two points along the line of shear wave propagation. This can be accomplished by moving the pulse-echo transducer by Δr to a different location.

B. Anti-symmetrical Lamb Wave Model

An anti-symmetric Lamb wave model was used by Kanai [16] to represent the motion of the septal myocardium due to aortic-valve closure. The myocardium was modeled as a homogenous viscoelastic plate composed of a Voigt material so that the shear modulus $\mu = \mu_1 + i\omega\mu_2$, where μ_1 and μ_2 are the elastic and viscous moduli. Assuming that the bulk modulus is much larger than the shear modulus, the anti-symmetric Lamb wave model requires the following equation to hold:

$$\begin{aligned} &4k_L^3\beta\cosh(k_L h)\sinh(\beta h) = \\ &(k_s^2 - 2k_L^2)^2 \sinh(k_L h)\cosh(\beta h)\,, \qquad (2) \\ &+k_s^4 \cosh(k_L h)\cosh(\beta h) \end{aligned}$$

where $k_L = \omega/c_L$ is the Lamb wave number, ω is the angular frequency, 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, ρ_m is the density of the sample and h is the half-thickness of the sample.

Equation (2) is fitted to the Lamb wave dispersion curves (velocity versus frequency) to obtain elasticity and viscosity coefficients μ_1 and μ_2.

C. Experiment

Urethane rubber samples were prepared by mixing equal amounts by mass of Part A and Part B of Reoflex 20 (Smooth-On, Inc., Easton, PA), and a softener (So–Flex Flexibilizer, Smooth-On Inc., Easton, PA). In order to provide scatterers for ultrasound waves, 1% by mass of graphite shavings (Aldrich Chemical Company, Inc., Milwaukee, WI), 1-2 micrometers in diameter, was added to the mixture. The mixture was poured into an 11 cm x 8 cm x 1.2 cm plastic mold and allowed to cure for 24 hours.

Pig hearts were obtained from a local butcher shop. The hearts were obtained a few hours after the animals were sacrificed. Left ventricular free wall myocardium was excised from the pig hearts in our laboratory.

The following procedure was followed for both urethane and excised myocardium samples. The samples were embedded in a gelatin (70% water, 10% glycerol, 10% 300 Bloom gelatin, 10% potassium sorbate preservative, all by volume and all manufactured by Sigma-Aldrich, St. Louis, MO) inside a plastic container. The container was mounted on a stand in a water tank (Figure 2). A window was cut out on the bottom of the container to allow for motion detection.

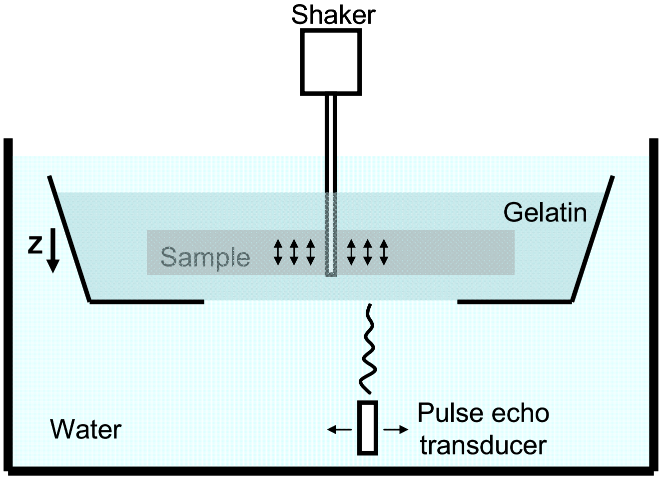

Fig. 2. Experimental set up for a modified SDUV approach: a mechanical actuator (shaker) was used to excite shear waves in the sample; pulse echo transducer was used to detect the motion. The gelatin was used as a stabilizer.

A mechanical shaker (V203, Ling Dynamic Systems Limited, Hertfordshire, UK) was used instead of a push transducer in order to ensure large motion. A glass rod coupled with the shaker was glued to the hole bored through the thickness of the sample. Four cycles of sinusoidal waves were used to drive the shaker at different frequencies ranging from 40 to 500 Hz to induce cylindrical shear waves in the sample. Motion was measured at each frequency in four orthogonal directions (x-y plane) using 7.5 MHz pulse echo transducer with a pulse repetition rate of 4 kHz. Motion was recorded at 31 points along a line, 0.5 mm apart. Phase estimates at these points were used to fit a regression curve and calculate the shear wave speed at each frequency, as described in the SDUV method [12, 13].

III. RESULTS

Shear wave propagation speeds at multiple frequencies in four orthogonal directions on the surface of an excised LV free-wall myocardium are shown in Figure 3. The open circles represent the experimental data obtained using the previously described method.

Figure 4 shows phase maps at 100, 150 and 200 Hz excitation frequencies in the +X direction of the LV myocardium sample. It is important to note that the phase is relatively preserved throughout the thickness of the sample (z-direction) and changes in a linear fashion in the x-direction as predicted by (1). Phase maps at other excitation frequencies are similar to the ones shown in Figure 4. This trend persists in all four directions and throughout experiments on different samples of LV myocardium (and urethane rubber), and is characteristic of an anti-symmetric Lamb wave motion. Continuous line in Figure 3 represents the anti-symmetric Lamb wave model fit to the experimental data. The Lamb wave model dispersion curve was fit for viscoelastic coefficients μ_1 and μ_2.

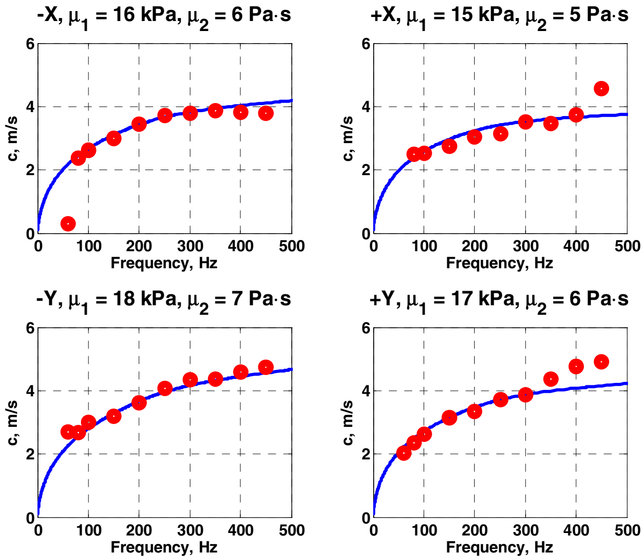

Fig. 3. Excised myocardium: experimentally obtained shear wave dispersion curves are shown as open circles. Lamb wave model (full line) was fitted to the data to obtain the values of elasticity and viscosity μ_1 and μ_2.

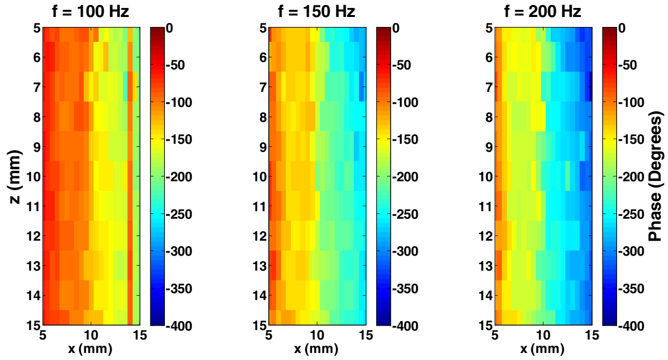

Fig. 4. Phase map of the excised myocardium sample for the given excitation frequencies. Shear wave propagates in the x-direction. The phase is relative conserved in the z-direction (thickness), characteristic of an anti-symmetric Lamb wave.

Estimated values of elasticity and viscosity in four directions are shown above the plots in Figure 3. Measurements made on this and other two samples of excised LV myocardium from different pigs are reported in Table I.

TABLE I
LEFT VENTRICULAR MYOCARDIUM ELASTICITY AND VISCOSITY RESULTS

Experiment #	Elasticity (μ_1) (kPa)	Viscosity (μ_2) (Pa·s)
1	16.5 ± 1.3	6.0 ± 0.8
2	13.8 ± 1.0	5.9 ± 0.8
3	7.8 ± 1.0	8.3 ± 0.7

Table I. Results of measuring elastic and viscous moduli of excised left ventricular myocardium using a modified SDUV approach. In each experiment, measurements were made in four orthogonal directions. The results are reported as average of the four measurements with standard deviations.

The approach used to measure elasticity and viscosity of excised myocardium samples was applied to a sample of urethane rubber. Due to lack of a "gold standard" technique for measuring mechanical properties of soft tissue and unavailability of another method at our institution, we were not able to validate our results. Thus, we used the modified SDUV technique to measure material properties of a rubber sample. Dispersion curves for a urethane rubber sample are shown in Figure 5. The experimental data and fitting results are denoted as in Figure 3. The mean and standard deviation of the elastic and viscous moduli, assuming a Voigt model, are $\mu_1 = 83.8 \pm 7.5$ kPa and $\mu_2 = 23.5 \pm 1.9$ Pa·s.

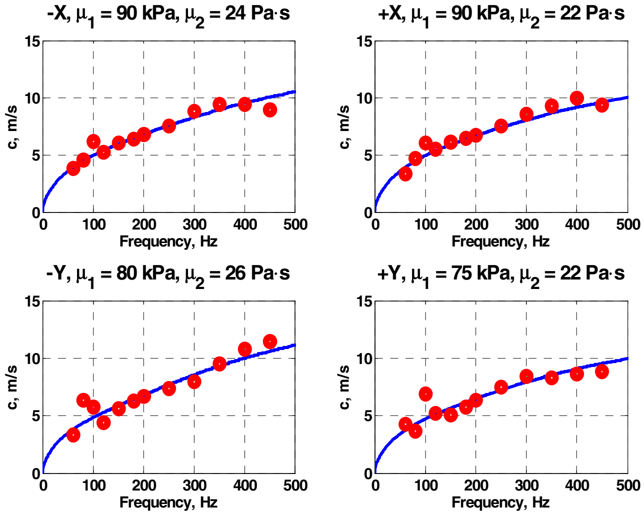

Fig. 5. Urethane rubber: experimentally obtained shear wave dispersion curves are shown as open circles. Lamb wave model (full line) was fitted to the data to obtain the values of elasticity and viscosity μ_1 and μ_2.

IV. DISCUSSION

The results suggest that the application of the anti-symmetric Lamb wave model is appropriate for characterization of tissue motion (Figure 4) and that the model fits the experimental data well.

The shear wave dispersion speeds and estimated values of μ_1 and μ_2 in four orthogonal surface directions are similar. This result suggests that the fiber orientation does not affect the shear wave speed and that the myocardial tissue behaves like a bulk material at the given frequency range. This property could prove advantageous for *in vivo* measurements and clinical applications, as the shear wave speed and viscoelastic moduli in one direction are enough to characterize regional mechanical properties.

The results of the urethane rubber experiment show that the dispersion speeds are fairly similar in different surface directions, which is to be expected because the rubber sample was isotropic. The values of μ_1 and μ_2 reflect isotropic nature of the urethane rubber and are similar to those obtained using an embedded sphere method by Chen *et al.* [17].

It is important to note that the use of the mechanical actuator could violate some of our assumptions. We assumed that the excited waves are purely cylindrical throughout the samples, but it is possible that the shear wave speed estimates are influenced by a near-field effect. This could explain the “bumps” in the dispersion curves of the rubber sample at and up to 100 Hz. Catherine *et al.* [18] reported a similar effect and argue that it can be explained by diffraction effects caused by the size of the glass rod imprint on the sample. The near-field effect is influenced by plate thickness and material properties and is likely to influence the rubber samples more than the heart samples since the heart samples are almost twice as thick as the rubber ones. To our best knowledge, the appropriateness of the Voigt model in urethane rubber has not yet been confirmed. In the future, we may have to use a different viscoelastic material model.

Our method is similar to that of Kanai [16] used to measure dispersion velocities in the heart septum due to closure of the aortic valve, frequency range 10 – 90 Hz. We report measurements made in the LV free wall due to radiation force in the frequency range 40 – 500 Hz. It is important to note that our method has the potential to make measurements at any point in the myocardium accessible to radiation force.

Elasticity and viscosity of the LV myocardium vary during a heart cycle. While we are reporting ex-vivo results, we expect our method to be capable of detecting variations in myocardial viscoelasticity periodic with a heart cycle. At this point, we are unsure of the affect a region of ischemic or necrotic tissue would have on myocardial viscoelasticity. This question will be addressed in future research.

In the future, we plan to test the use of radiation force for shear wave excitation. This approach would mimic the SDUV method and would be necessary for clinical use.

V. CONCLUSIONS

We used a modified Shearwave Dispersion Ultrasound Vibrometry (SDUV) method to make *ex vivo* measurements of propagation speeds of shear waves at different frequencies in urethane rubber samples and excised left ventricular free-wall myocardium. An anti-symmetric Lamb wave model was fitted to the dispersion curves in to estimate elasticity and viscosity of the material in four orthogonal surface directions. The shear wave speeds and elasticity and viscosity of the excised myocardium was similar in the four directions suggesting that the myocardium acts as a transversely isotropic bulk at the excitation frequencies 40-500 Hz. The confirmation of the Lamb wave model and ability to measure shear wave dispersion using the SDUV principle is an encouraging step toward *in vivo* measurements and future clinical application of the method.

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