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Preliminary Study on the Effect of Stiffness on Lamb Wave Propagation in Bovine Corneas

Xin-Yu Zhang, Yin Yin, Yan-Rong Guo, Xian-Fen Diao and Xin Chen

Abstract—The viscoelastic properties of human cornea could provide valuable information for various clinical applications. Particularly, it will be helpful to achieve a patient-specific biomechanical optimization in LASIK refractive surgery, early detection of corneal ecstatic disease or improved accuracy of intraocular pressure (IOP) measurement. However, there are few techniques that are capable of accurately assessing the corneal elasticity in situ in a nondestructive fashion. In order to develop a quantitative method for assessing both elasticity and viscosity of the cornea, we use ultrasound radiation force to excite Lamb waves in cornea, and a pulse echo transducer to track the tissue vibration. The fresh postmortem bovine eyes were treated via collagen cross-linking to make the cornea stiff. The effect of stiffness was studied by comparing the propagation of Lamb waves in normal and treated corneas. It was found that the waveform of generated Lamb waves changed significantly due to the increase in higher modes in treated corneas. This result indicated that the generated waveform was a complex of multiple harmonics and the varied stiffness will affect the energy distribution over different components. Therefore, it is important for assessing the viscoelastic properties of the cornea to know the components of Lamb wave and calculate the phase velocity appropriately.

I. Introduction

Characterization of viscoelastic properties of biological tissues has become an important research area over last two decades, since studies found that these properties are highly correlated with pathological statues of human tissue. In ophthalmology, the assessment of corneal viscoelastic properties could provide valuable information for various applications [1]. It may lead to a patient-specific biomechanical optimization in LASIK refractive surgery to ensure surgery safe and prevent severe complications. It is also helpful to early detection of corneal ecstatic disease or improved accuracy of intraocular pressure (IOP) measurement. Therefore, there is demand for techniques that are capable of accurately assessing the corneal elasticity in situ in a nondestructive fashion. Techniques based on static elastography [2] and surface wave elastometry [3] were proposed to assess corneal mechanical properties. Li et al proposed an all-optical method which uses OCT to record the propagation of surface acoustic wave and measure the cornea elasticity [4].

The propagation properties of shear waves were found to be closely related to the elasticity of materials and therefore several ultrasound-based techniques were proposed to excite the shear waves in a tissue region, measure their propagation properties, and estimate the tissue's viscoelasticity. Some representative techniques include Acoustic Radiation Force Imaging (ARFI)[5], supersonic shear imaging (SSI) [6], and shear-wave dispersion ultrasound vibrometry (SDUV) [7]. However, the cornea plate is thin (typically 1 mm) and there is a strong contrast in shear velocity between the cornea and surrounding media. Strong reflection and mode conversions at these interfaces generate partially guided wave propagation. The elastic waves propagating in infinite and thin elastic plates were known as Lamb waves. Tanter et al reported a high-resolution quantitative imaging of cornea elasticity estimated by Lamb wave propagation using SSI [8]. Their work shows the possibility of ultrasound-based techniques for assessing the corneal elasticity in situ. However, this method provides only the assessment of Young's modulus, which can not accurately characterize the viscoelastic nature of the cornea tissue.

Our study aims to propose a quantitative method for assessing both elasticity and viscosity of the cornea. This study used the ultrasound radiation force to excite Lamb waves in corneas, and a pulse echo transducer to track the tissue vibration. The fresh postmortem bovine eyes were treated via collagen cross-linking to increase the stiffness. By comparing the propagation of Lamb waves in normal and treated corneas, the effect of stiffness was studied and some preliminary results were reported in this paper.

II. Methods

A. Principle

Some studies were done by using the propagation property of Lamb waves in the organs with plate-like geometry to estimate the tissue' elasticity [8, 9] as well as viscosity [10]. Lamb waves propagate with specific modes that have highly dispersive behaviors but in the very lows frequency range, only one symmetric (S0) and one anti-symmetric (A0) mode are found. An asymmetrical Lamb wave model was developed by Kanai [9]. Assuming that a viscoelastic plate with thickness 2h has similar density to the surrounding liquid and the wave number of compressible waves is much smaller than that of Lamb waves in it, he presented the following equation:

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$$
\begin{aligned}
f(c_L,\mu,\omega) &= 4k_L^3\beta\cosh(k_L h)\sinh(\beta_L h) \\
&-(k_s^2-2k_L^2)^2\sinh(k_L h)\times\cosh(\beta_L h) \\
&-k_s^4\cosh(k_L h)\cosh(\beta_L h)=0
\end{aligned} \quad (1)
$$

Where ω is angular frequency, c_L is the phase velocity of Lamb waves, $k_L = \omega / c_L$, $k_s = \omega\sqrt{\rho_m / \mu}$ is wave number of shear waves, ρ_m is the density of biological tissue, $\beta_L = \sqrt{k_L^2 - k_s^2}$ and $\mu = \mu_1 + i\omega\mu_2$ where μ_1 and μ_2 are the shear elasticity and viscosity, respectively. The measured Lamb wave velocity is then fitted with (1) to exact μ_1 and μ_2.

B. Experimental Setup

The experimental system setup is illustrated in Fig.1. The system mainly consisted of a transmitter to produce the ultrasound radiation force and a receiver unit using a SonixRP system (Sonix RP, Ultrasonix Medical Corporation, Richmond, BC, Canada). Two arbitrary signal generators were utilized to generate the system timing and excitation pulse. The pulse was amplified by a power amplifier having a gain of 50 dB to drive an excitation transducer, which is a 1 MHz single-element focused transducer, to induce the tissue vibration.

The SonixRP system was applied to detect the vibration using pulse-echo mode with a linear array probe. The center frequency of the probe was 5 MHz and the sampling frequency of SonixRP was 40MHz. As shown in Fig. 2, the excitation transducer and detection probe were fixed on multi-degree adjustable brackets and controlled by three-axis motion stages. During the experiment, an intact eyeball was embedded in gel phantom and placed in water tank while the cornea was kept above the phantom.

C. Experiment Design

The experiment was carried out on 10 fresh excised postmortem bovine eyes obtained from slaughterhouse (Nanshan District, Shenzhen, China). Before the experiment, half of the eyes were treated to increase their stiffness using the procedure similar to previously described techniques [11]. First, after careful removal of the epithelium, the corneas were coated with a Dextran solution (20%, Detran T 500, Pharmacia-Biotech, Freiburg, Germany). The corneas were immersed into 1% glutaraldehyde solution for 10 min and then stored in a moist chamber in dark space for another 45 min. Another half of the eyes were untreated as control group. During the experiment, all eyeballs were embedded in gel phantom and placed in a water tank.

The corneal responses to excitation were investigated in two different ways. Firstly, 10 excitation pulses were applied to the apex of cornea at every 5 ms. Each pulse lasted for 200 μs. Secondly, a single excitation pulse with the duration of 200 μs was used to hit the apex of corneas.

To measure the propagation of the generated waves, 10 points spaced by 0.475 mm were investigated with the linear array transducer using pulse-echo method. Computer programs based on software development kit (SDK) of SonixRP were developed for detecting the tissue vibrations and Lamb wave propagation. The programs defined a specific detection sequencing and timing that repeatedly transmit pulses to a single scan line and receive the echoes with a PRF of 4 kHz. The vibration of Lamb waves at a location was extracted from I and Q channels using the I/Q estimation algorithm described in the paper by Zheng [12].

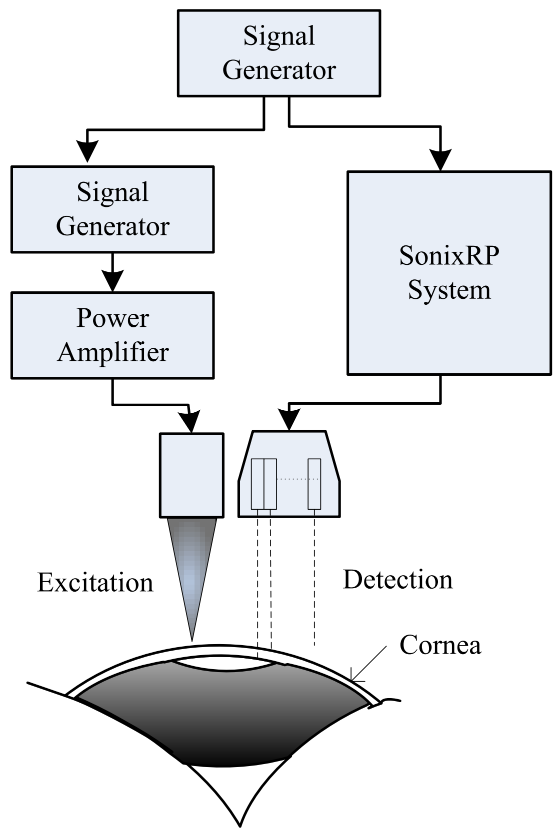

Figure 1 Diagram of the experimental system setup

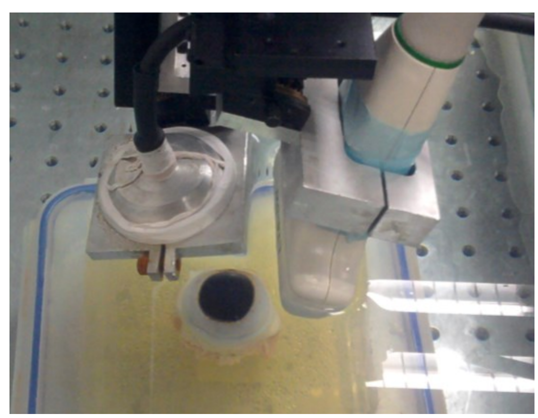

Figure 2 Picture of the transducers and an eyeball embedded in gel phantom.

III. RESULTS

Fig. 3 gives a representative plot of Lamb waves generated by radiation force excitation in a normal cornea (untreated one) and a treated cornea. The *x*-axis represents the time of propagation, and the *y*-axis is the displacement (in μm). The vibration signals at two different points were presented in this figure. The red solid line and blue dash line, respectively, refer to the point 0.95 mm and 3.33 mm away from the excitation point. As shown in Fig. 3, the waveform in a treated cornea is clearly different with that in a normal cornea. The waveform in a treated cornea shows a steep rising edge and a second peak in the falling edge. Fig. 4 gives the spectral distribution of vibration signal at the point 0.95 mm away from the excitation point. It is found that in a treated cornea the energy of the 2nd and 3rd harmonic frequency is comparable to that of the fundamental frequency while in a normal cornea the energy concentrate mainly in fundamental frequency. Fig. 5 shows the propagation of generated vibration in response to a single excitation pulse. Similarly, it was shown that the normal cornea vibrated slowly in comparison with the treated one. In another words, the vibration of the treated one had more high frequency components.

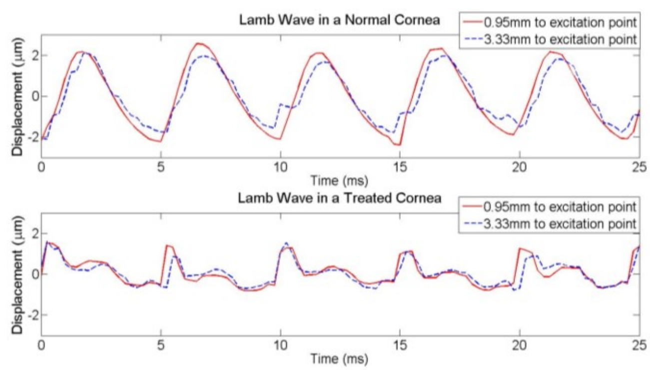

Figure 3 The waveform of Lamb waves in a normal and a treated cornea, respectively, in response to 200 Hz excitation

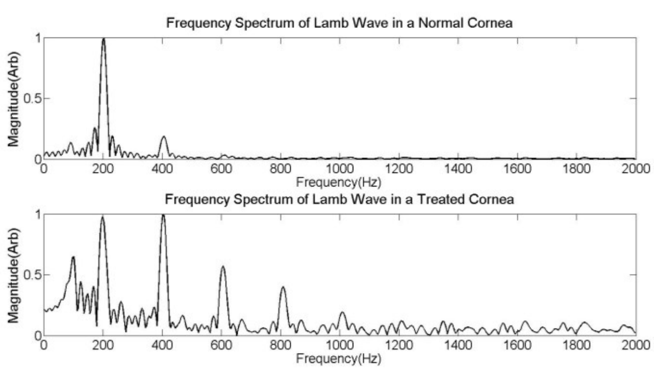

Figure 4 Frequency spectrum of Lamb wave in a normal and a treated cornea, respectively, in response to 200 Hz excitation

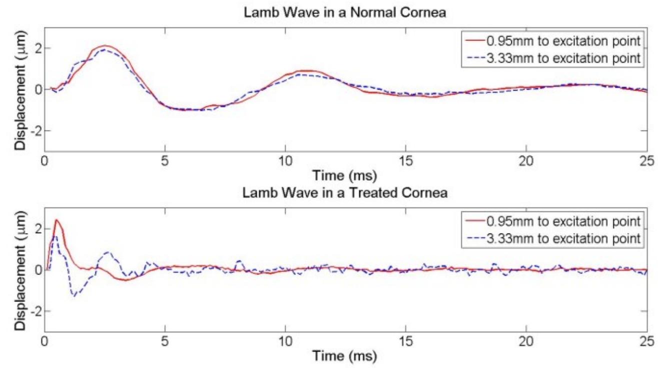

Figure 5 The waveform of Lamb waves in a normal and a treated cornea, respectively, in response to a single excitation.

IV. DISCUSSION

The vibration waveforms and their spectral distribution were compared in Figure 3 and 4. The results show that the normal and treated corneas give different responses to the same excitation. The results indicated that the higher harmonic increases when a cornea was treated to make it stiffer. This behavior is similar to higher order modes seen in Lamb wave theory where higher modes appear increases as the stiffness of the material increases.

In tissue elastography study, usually, the elastic waves were generated by external or internal excitation source and the propagation velocity of the wave were measured to estimate the viscoelastic properties of the tissue. However, an arbitrary mechanical excitation applied to the cornea will generate a complex of multiple harmonic Lamb waves carrying energy across a range of frequencies. The challenge is to recognize the multiple Lamb wave components in the received waveform and to interpret them in terms of source motion. This study shows that high frequency harmonics of Lamb wave give more contribution and affect the waveform when the stiffness of the cornea increases. In order to estimate the viscoelastic properties accurately, it is important to calculate the phase velocity appropriately if the multiple modes were presented.

The objective of our study is to propose a new method to estimate corneal elasticity and viscosity quantitatively; therefore, future work will be to develop a viscoelastic estimation model based Lamb wave propagation in a cornea.

V. CONCLUSION

Since the viscoelastic properties of cornea could provide valuable information for various clinical applications. Our study aims to develop a quantitative method for assessing both elasticity and viscosity of the cornea in situ with a nondestructive fashion. The ultrasound radiation force was used to excite Lamb waves in corneas, and a pulse echo transducer to track and measure the wave velocity. The effect of stiffness was studied by comparing the propagation of Lamb waves in normal and treated corneas. It was found that the waveform of generated Lamb waves changed significantly due to the increase in high frequency harmonics in treated corneas. This result implies that the generated waveform was a complex of multiple harmonics and the varied stiffness will affect the energy distribution over different components. Therefore, it is important for assessing the viscoelastic properties of the cornea to know the components of Lamb wave and calculate the phase velocity appropriately.

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