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Optoacoustic Elastography for Tissue Biomechanical Property Characterization Using a Ring Transducer

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Abstract—Elastography, capable of quantitatively providing the biomechanical properties of tissue, plays a key role in clinical diagnosis, such as cancerous tumor detection and atherosclerotic plaque characterization. Phase-resolved optical coherence elastography (PR-OCE) possesses superior resolution and high imaging speed with the capability of providing point-by-point elastogram mapping. An acoustic radiation force (ARF), generated by high-intensity ultrasound bursts, offers the dynamic excitations with the benefits of directly and remotely inducing the localized displacement of tissue within the region of interest. An amplitude modulated (AM) acoustic wave can be used to generate pressure to harmonically vibrate the tissue. In this work, we successfully differentiate biological tissues with different biomechanical properties utilizing a ring transducer with AM beam geometry in a PR-OCE system, which demonstrates the feasibility and superiority to move this imaging system into clinical application.

Keywords—ultrasonic transducer, elastography, acoustic radiation force, optical coherence tomography

I. INTRODUCTION

Tissue biomechanical properties are commonly used for diseased tissue identification, which provides valuable information for medical diagnosis [1]. Elastography [2], capable of quantitatively providing the biomechanical properties of tissue by measuring the deformation of tissue under internal or external excitation, plays a key role in clinical diagnosis, such as cancerous tissue detection and atherosclerotic plaque characterization.

Among several elasticity imaging techniques being investigated, ultrasound elastography is the most commonly used method in clinic based on either speckle tracking or the Doppler velocity measurement method [2-3]. However, the major limitation of ultrasound elastography is the insufficient resolution which potentially downgrades the diagnostic accuracy in clinical application. Optical coherence elastography (OCE) [4-5], a subtype of functional Optical Coherence Tomography, is rapidly developing with the advantage of detecting nano-to-micron-scale internal local deformation of the subject. By using the Doppler velocity measurement method, phase-resolved OCE (PR-OCE) possesses superior spatial resolution and high imaging speed with the capability of providing point-by-point elastogram

mapping [6-7]. An acoustic radiation force (ARF), generated by high-intensity ultrasound bursts, offers the dynamic excitations with the benefits of directly and remotely inducing the localized displacement of tissue within the region of interest [8]. An amplitude modulated (AM) acoustic wave can be used to generate pressure to harmonically vibrate the tissue.

A phase-resolved acoustic radiation force optical coherence elastography (ARF-PR-OCE) system [9] has been previously reported capitalizing the advantage of transient elastographic imaging of tissue mechanical properties in a semi-quantitative way. In this work, we successfully differentiate biological tissues with different biomechanical properties utilizing a ring transducer featured by beam geometry in an ARF-PR-OCE system, which demonstrates the feasibility and superiority for clinical application.

II. EXPERIMENTAL ARRANGEMENT

A. Imaging System Set-up

The schematic of the confocal ARF-OCE system is shown in Fig. 1. A customized 4 MHz focused ring transducer, responsible for acoustic excitation, was arranged in a confocal configuration with the OCT detection beam. The ultrasonic transducer had a focal depth of 50 mm with a 5 mm-diameter hole in the middle allowing the fast confocal OCT light scanning on the sample through a 70 mm-focal-length objective lens. The confocal arrangement was tested before the actual experiment to confirm the focal zone of the acoustic wave and OCT beam were symmetrically overlapped.

The OCT sub-system is based on an 890 nm SD(SD for what?)-OCT system. The acquisition rate of this system is 20 kHz. The axial and lateral resolutions of the system were measured to be 3.5 and 14.8 μm , respectively. The signal-noise-ratio (SNR) of the system was 100 dB with 650 μW of sample arm power and a 50- μs A-line rate. The minimum detectable phase for this system was measured to be 1.5 mrad, which corresponded to a velocity sensitivity of 2.13 $\mu\text{m/s}$. A water cell was inserted in the reference arm in the SD-OCT system to compensate the dispersion induced by the water in the sample arm.

An amplitude modulated (AM) signal was used to generate a periodic acoustic radiation force perpendicularly onto the sample. A function generator (DS345, Stanford Research Systems, USA) generated several hundred Hz a low kHz (several hundred or a low kHz?) square wave (50% duty

cycle amplitude modulation-AM) which modulated the amplitude of the 4 MHz burst generated by another function generator (33220A, Agilent Technologies, USA). Then the modulated signal was then amplified by 46 dB using a RF power amplifier (PAS-000023-25, Spanawave, USA) ranged from 0.15 MHz to 230 MHz. Lateral scans were only made within the ultrasound focal zone where the acoustic radiation force induced particle displacement was assumed to be evenly distributed.

Fig.1. Schematic of the confocal ARF-OCE system, including a SD-OCT system with a photograph of the customized focused ring transducer.

B. Phantom and tissue sample preparation.

To test the proposed ARF-OCE system's capability of detecting local displacement induced by an acoustic radiation force and differentiating tissues of varying Young's modulus, several homogeneous-cylindrical silicone phantoms with a diameter of 35 mm and a height of 3 mm were fabricated. Phantoms were made of silicone and the associated curing agent. With different ratios of silicone to curing agent, Young's modulus of the samples can be controlled. The Young's moduli of two sets of phantoms were tested by the compression test (MTS Synergie 100) and measured to be 53.686 kPa and 75.103 kPa, respectively.

Furthermore, a section of formalin-fixed human cancerous kidney provided by the pathology department at the University of California Irvine, was used to test the feasibility of the imaging system to measure the mechanical properties of biological tissues. The kidney with tumor was preserved in the phosphate buffered saline solution prior to the experiment to keep it well hydrated. During the experiment, the sample was also immersed in the phosphate buffered saline solution to maintain the osmolarity of the cells.

III. RESULTS AND DISCUSSIONS

A. Concept validation and phantom study

The acoustic induced vibration in the longitudinal direction and the Young's modulus of the sample could be obtained by the OCE system from the phase shift information, for which a detailed explanation is in the previous paper [9]. The instantaneous axial velocity can be expressed as equation 1,

$$v(x, z, t) = \Delta\phi(x, z, t)\lambda_0/4\pi n\tau \quad (1)$$

where x and z are the lateral and axial location, respectively, $\Delta\phi$ represents the phase shift between two adjacent A-lines, λ_0 is the center wavelength of the light source, n is the tissue refraction index which is assumed to be 1.4 in this paper and τ is the time interval between adjacent A-lines. The displacement Δd and the axial strain ε of the sample are expressed as

$$\Delta d = \int_{t_1}^{t_2} \frac{\Delta\phi(x, z, t)\lambda_0}{4\pi n\tau} dt \quad (2)$$

$$\varepsilon = \int_{t_1}^{t_2} \frac{\Delta\phi(x, z, t)\lambda_0}{4\pi n\tau z_0} dt \quad (3)$$

where z_0 is the original thickness of the sample prior to the ultrasonic stimulation. Finally, Young's modulus can be characterized by

$$E = \frac{\sigma}{\varepsilon} = \frac{F/A}{\varepsilon} \quad (4)$$

where σ is the axial (or normal) stress (force per area) acting on the sample, F is the acoustic radiation force out of the ultrasonic transducer, and A is the sample surface area.

A homogenous silicone phantom was first imaged by ARF-OCE imaging system under an 800 Hz square wave modulation. The OCT intensity image [Fig.2 (a)] provided the structural information of the phantom. The ARF-OCE image [Fig.2 (b)] associated with phase map indicates displacements of the particle in the sample that can be characterized through Equation 2. The results confirm that the displacements within the confocal region of acoustic excitation and OCT detection were evenly distributed.

Fig. 2. (a) OCT intensity image of the homogenous silicone phantom (b) ARF-OCE image of the phantom under 800Hz AM excitation.

To prove the concept that ARF-OCE was capable of differentiating phantoms by calculating the Young's modulus ratio of different phantoms, the displacements of two phantoms were plotted in Fig. 3. The silicone cured with 1.05 g curing agent and 1.15 g curing agent experienced displacements of 0.20 μ m and 0.28 μ m, and the corresponding strain of the 3 mm thickness is 0.0067% and 0.0093%, respectively. Thus, the Young's Modulus ratio of the two phantoms was calculated to be 1:1.40 from our ARF-OCE

system, which accurately agreed with the compression test of a 1:1.41 Young's Modulus ratio.

Fig. 3. Axial displacement of silicone phantoms with different stiffness.

B. In vitro imaging of cancerous human kidney tissue

To demonstrate the potential of this technology in cancer detection, imaging of a section of cancerous human kidney tissue was performed with a PR-OCE system (Fig. 4). The 2D ARF-OCE image [Fig.4 (a)] displayed strong vibrational phase contrast in the middle represented by green color, and relatively low vibration on both sides represented by red color. This indicated that the tissue in the middle is softer (smaller Young's Modulus) than the tissue on both sides. The H&E histology results in Fig.4 (e) shows a normal adipose tissue structure in the middle, which is intrinsically soft and cancerous cells with abnormally large nuclei had diffused to both sides, which renders a high stiffness region. The OCE result is consistent with the H&E. Moreover, the abnormal cancerous cells are more densely packed on the right side in histology, which agreed with a 2D ARF-OCE image that the right portion of tissue was stiffer with less vibration than the left portion of tissue. The 3D OCT image [Fig.4 (b)] offered a general morphological view of the tissue; however, no further information was provided to distinguish the tissue with different stiffness. As shown in 3D ARF-OCE image [Fig. 4 (c)], normal adipose tissue in the middle with the triangle shape and cancerous tissue diffused on both sides were clearly distinguished. The point-to-point elastic map with high resolution structural image was achieved in the fused image [Fig.4 (d)]. This preliminary result demonstrated that our ARF-OCE's potential capability of quantitatively characterizing tissue biomechanical properties to achieve margin detection for cancerous tissue.

Fig. 4. (a) 2D ARF-OCE image, (b) 3D OCT image, (c) 3D ARF-OCE image, (d) fused image and (e) histology image of cancerous human kidney tissue.

IV. CONCLUSIONS

We have developed an ARF-OCE system featured on the confocal alignment of dynamic ultrasound excitation and OCE detection to achieve high spatial resolution, high speed and high motion sensitive point-to-point elastic imaging. The concept of quantitative tissue biomechanical characterization has been validated on both phantom and human tissue studies. The results demonstrated that our confocal ARF-OCE is a promising technique for delineating diseased tissue, with a high potential for clinical application.

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