The expanding frontier of optical elastography and diagnostic biomechanics

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ABSTRACT

The term "elastography" covers a dynamic and expanding set of diagnostic imaging techniques which probe the biomechanical properties of tissues. This overview covers some of the major approaches that have evolved and their role in improving clinical diagnoses. A deeper level of study is also emerging linking our estimates of viscoelasticity to the multiscale structure and composition of living tissue in normal and diseased states. These studies can be undertaken at the highest spatial resolution with optical techniques, and examples in cornea, brain, and skin will be covered.

Keywords: OCT, elastography, rheology, biomechanics, shear waves, biomarkers

1. INTRODUCTION

The field of elastography can be broadly defined as imaging the elastic properties of tissues. This has evolved over the past three decades from laboratory imaging of phantoms and tissue specimens with ultrasound to include magnetic resonance (MR) imaging and optical imaging systems. The first published images [1, 2], to our knowledge, were developed by Robert Lerner and Kevin Parker at the University of Rochester using ultrasound imaging with Doppler signal processing of the motion of the internal tissues and materials. By 1990, they had modified clinical Doppler imaging scanners to produce “sonoelastography” images in real time which could demonstrate hard tumors in soft surrounding tissues [1-6]. A robust development of approaches rapidly evolved in different laboratories. The ever-growing “family tree” of techniques can generally be classified within three groups according to the stress applied to the body during the elastography scan. These are quasi-static, transient, and continuous methods [7]. Quasi-static methods apply a slow and steady increase in displacement at a boundary and typically track the induced strain. Transient methods apply a relatively short burst of force or displacement to a boundary and then the response of tissue is imaged following the stimulus. Continuous methods apply longer sinusoidal excitations that excite shear waves, for example at 50 Hz in MR elastography for the whole adult liver or at 2000 Hz in optical coherence tomography (OCT) elastography in smaller specimens. An overview of the historical development of these techniques, along with established clinical applications and mathematical approaches to estimating the viscoelastic parameters from the tissue displacements is given in Ormachea and Parker [8]. The development of optical techniques has a close parallel to those in ultrasound and MR elastography, albeit at a much higher spatial resolution and with the application of higher frequency shear waves. Excellent overviews of the rapid development of optical elastography are found in [9-11].

2. RESULTS

As an example of high resolution elastography in living tissue, Figure 1 shows a study of elastography within a mouse brain, revealing the changes from awake to sleep states associated with diurnal changes in the glymphatic system. Reverberant shear wave activation was applied at 2000 Hz and internal shear wave propagation was scanned in 3D by an OCT system described in detail previously [12, 13].

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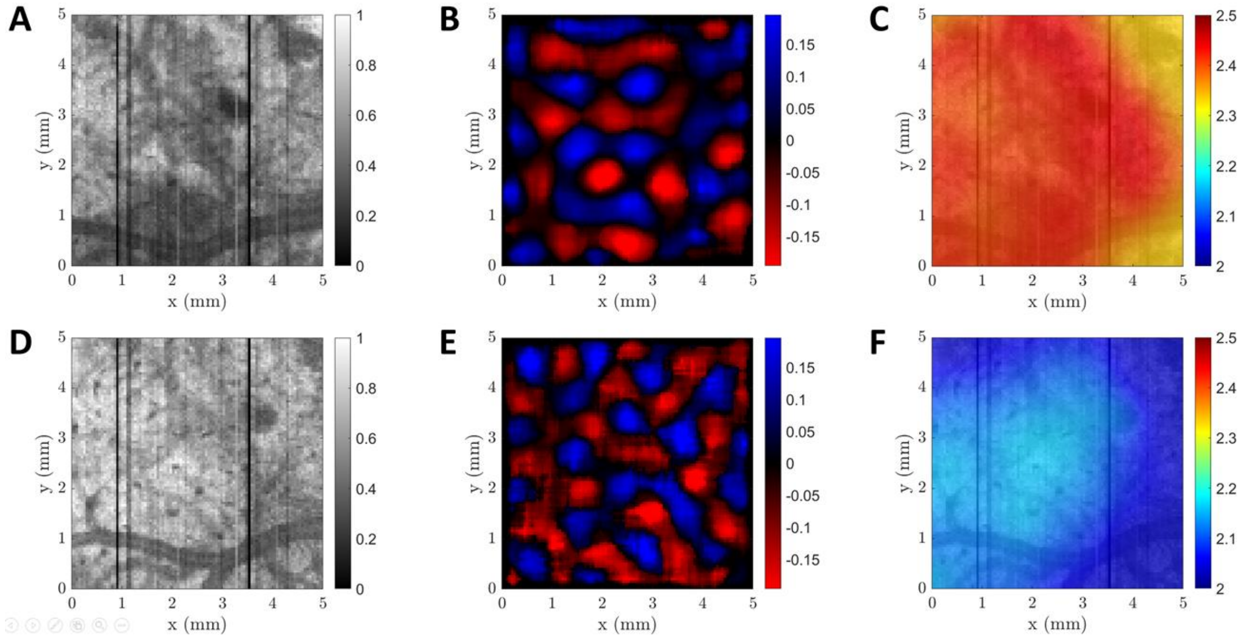

Figure 1. OCT elastography of a wild-type (C57BL/6) mouse, 9-month-old, male, cortical brain, showing measurable changes from awake to anesthesia sleep states. Top row (A, B, C): awake. Bottom row (D, E, F): asleep. Columns show (from left to right) average intensity projection of the scanned 5 mm^3 volume of the cortical grey matter; reverberant shear wave patterns at a cross sectional imaging plane within the scanned volume; and the final estimates of shear wave speed, demonstrating a marked decrease during the sleep state. (C) Top = awake, mean SWS = 2.40 +/- 0.0282 (F) Bottom = anesthetized, mean SWS = 2.12 +/- 0.0306

3. DISCUSSION

The forward direction of bio-optical elastography includes several major directions. In our opinion, the following sub-areas have a rich potential for improved diagnostic classifications of tissues and generating sensitive biomarkers for disease processes.

1) **Anisotropy.** Tissues including muscle and tendons and white matter contain oriented structures that can be modelled as a principal axis with significantly different material properties, stiffnesses, and shear wave speeds along vs. across the major axis [14]. Elastography can provide sensitive measures of these properties but at the cost of increased complexity of the scan and analyses.
2) **Nonlinear behavior.** Most tissues exhibit strain hardening, where increasing deformations result in a hardening of the response, at least within some range. Instrumentation has been devised to capture this, with the potential for enhanced differentiation of normal from pathological tissue states [15].
3) **Multimodality and multiparametric fusion.** Some platforms can now acquire elastography data along with other information such as photoacoustic or other imaging data. This opens the potential for refined differentiation of tissues given the number of uncorrelated measures that can be taken from a sample volume. This approach is developing rapidly in ultrasound systems [16-18] and can be applied to any combination of imaging measures.
4) **Change with bio/cycles and treatments.** As elastography becomes more widely available on clinical instruments, we can follow individuals as a function of time and as a function of treatments [13, 19]. This creates the opportunity to study an individual's elastic properties as a function of important changes in conditions, and to assess the effectiveness of any treatments.

In all cases, there is a parallel need for development of the corresponding clinical instruments that are ergonomic, easy for clinicians to use, and capable of rapid, accurate, and repeatable measurements of these higher order parameters.

4. CONCLUSION

After several decades of innovation, the clinical application of optical elastography is growing in applications and in specific, tailored technologies. However, beyond simple linear elastic and viscoelastic measures, a number of higher order tissue measurements remain relatively unexplored with the potential for providing important diagnostic information not available today. These include tissue nonlinear and anisotropic properties, along with time-varying properties under natural cycles and treatments.

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