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● *Original Contribution*

CONGRUENCE OF IMAGING ESTIMATORS AND MECHANICAL MEASUREMENTS OF VISCOELASTIC PROPERTIES OF SOFT TISSUES

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Abstract—Biomechanical properties of soft tissues are important for a wide range of medical applications, such as surgical simulation and planning and detection of lesions by elasticity imaging modalities. Currently, the data in the literature is limited and conflicting. Furthermore, to assess the biomechanical properties of living tissue *in vivo*, reliable imaging-based estimators must be developed and verified. For these reasons, we developed and compared two independent quantitative methods—crawling wave estimator (CRE) and mechanical measurement (MM) for soft tissue characterization. The CRE method images shear wave interference patterns from which the shear wave velocity can be determined and hence the Young's modulus can be obtained. The MM method provides the complex Young's modulus of the soft tissue from which both elastic and viscous behavior can be extracted. This article presents the systematic comparison between these two techniques on the measurement of gelatin phantom, veal liver, thermal-treated veal liver and human prostate. It was observed that the Young's moduli of liver and prostate tissues slightly increase with frequency. The experimental results of the two methods are highly congruent, suggesting CRE and MM methods can be reliably used to investigate viscoelastic properties of other soft tissues, with CRE having the advantages of operating in nearly real time and *in situ*. (E-mail: parker@seas.rochester.edu) © 2007 World Federation for Ultrasound in Medicine & Biology.

Key Words: **Crawling wave estimator, Stress relaxation, Kelvin-Voigt fractional derivative model, Gelatin phantom, Veal liver, Prostate, Shear wave velocity, Young's modulus.**

INTRODUCTION

The biomechanical properties of soft tissues are intrinsically related to their composition. It is well known that pathological processes typically alter the stiffness of soft tissues. Therefore, digital palpation, a qualitative clinical tool, has been used for centuries to diagnose the presence of localized tumors in accessible regions of the human body. Recently, thermal therapy techniques such as radio frequency ablation (RFA), microwave, laser and high-intensity focused ultrasound (HIFU) have been utilized to create tissue necrotic coagulation for killing tumors. Those necrotic lesions appear stiffer than surrounding tissue as well. A better understanding of the mechanical properties of soft tissues, including cancerous, thermal treated and normal tissues, is of particular importance for biomechanics and medical applications, such as biomechanical modeling, surgical simulation and planning and imaging pathologies by elasticity estimators.

Although mechanical properties of structural materials have been studied and well characterized by various mechanical testing methods for decades, little is known for most biological soft tissues. Moreover, the mechanical properties of human soft tissues, such as Young's modulus and shear modulus, vary widely. For these reasons, various techniques have been developed to image and characterize soft tissue viscoelasticity for diagnostic and/or therapeutic purposes. In the past two decades, five major elasticity imaging modalities have been established to noninvasively image hard lesions in soft tissues based on their elasticity contrast. They are either ultrasound (US)-based approaches such as vibration sonoelastography (Krouskop et al. 1987; Lerner et al. 1988; Parker et al. 1990; Yamakoshi et al. 1990), compression elastography (Ophir et al. 1991), transient elastography (Catheline et al. 1999; Sandrin et al. 2002a,

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2002b) and acoustic radiation force (ARF)-related imaging (Bercoff et al. 2004; Fatemi and Greenleaf 1998; Nightingale et al. 2001; Sarvazyan et al. 1998) or magnetic resonance (MR) imaging-based approaches such as static MR elastography (MRE) (Fowlkes et al. 1995; Plewes et al. 1995) and dynamic MRE (Bishop et al. 1998; Muthupillai et al. 1995). Some of those noninvasive techniques have also been applied to measure soft tissue mechanical parameters directly.

An early clinical evaluation of elasticity of human liver in various diffuse diseases was reported by Sanada et al. (2000) using sonoelastographic measurement. The principle of the study is the same as that of the shear wave estimation method developed by Yamakoshi et al. (1990). The propagation of low-frequency vibration (40 Hz) in the liver was observed with a conventional Doppler imaging system and the velocities related to shear elasticity were measured by vibration phase images. However, bias can be induced during measurement by refraction and reflection of the propagating vibration waves at tissue boundaries, diffraction effects (Catheline et al. 1999) and liver displacements during an acquisition time of 90 s. More recently, one-dimensional (1-D) transient elastography (FibroScan®: Echosens, Paris, France) was established for the assessment of liver stiffness (Sandrin et al. 2003). Supersonic shear imaging (SSI), an ARF-based method, was developed to characterize breast tissue *in vivo* (Bercoff et al. 2004).

The potential of dynamic MRE clinical implementation has been proven in preliminary human studies in which the data of human prostate, breast, brain, muscle and liver were presented (Bensamoun et al. 2006; Bishop et al. 1998; Kemper et al. 2004; Kruse et al. 2000; Papazoglou et al. 2006; Rouviere et al. 2006; Sinkus et al. 2005). In particular, Kruse et al. (2000) evaluated porcine livers with MRE at multiple shear wave frequencies and reported that the wave velocity and the shear stiffness increased with frequency. The shear stiffness measured with MRE was 3 kPa at 100 Hz. This technique provides high-resolution images, although its long acquisition time (about 20 min) and high cost are a consideration.

Independently, mechanical testing-based methods can characterize soft tissue properties and, thus, be used as a comparison to elasticity imaging methods. Several groups (Dunn and Silver 1983; Hof 2003; Huang et al. 2005; Klein et al. 2005; Kuo et al. 2001; Lally et al. 2004; Provenzano et al. 2002; Silver et al. 2001; Suki et al. 1994; Wu et al. 2003) have reported findings on mechanical properties of some soft tissues, but most of their studies were focused on tendons, ligaments, cartilage, skin, muscles, lungs or arteries, which, to some extent, have active force-generating mechanical properties. In contrast, just a few publications (Arbogast and Margulies 1998; Chen et al. 1996; Darvish and Crandall 2001; Krouskop et al. 1998; Liu and Bilston 2000; Nasseri et al. 2002; Phipps et al. 2005a, 2005b; Snedeker et al. 2005; Yang and Church 2006; Yeh et al. 2002) presented quantitative results on the viscoelastic behavior of tissues such as brain, breast, prostate, liver or kidney.

Liu and Bilston (2000) studied the viscoelastic properties of bovine liver tissue with three testing methods: shear strain sweep oscillation, shear stress relaxation and shear oscillation. In the oscillation experiments, they found the storage shear modulus in a range of 1 to 6 kPa and the loss shear modulus in a range of several hundred Pa for applied frequencies from 0.006 to 20 Hz. They also confirmed that liver tissue has fluid-like viscoelastic behavior by analyzing the relaxation response of liver. In this study, they developed a linear five-element Maxwell model and fit the experimental data to the model. The choice of tissue model seems to vary with different groups. Besides the three basic linear viscoelastic models (the Maxwell model, the Voigt model and the Kelvin model) described by Fung (1993), other linear, quasi-linear or nonlinear models were also applied to fit the mechanical testing data. In particular, Szabo and Wu (2000) derived a generalized three-parameter Kelvin-Voigt (KV) model for viscoelastic materials from the power law relationship. Taylor et al. (2002) further investigated the Kelvin-Voigt fractional derivative (KVFD) model by fitting the liver relaxation data to this model. Dynamic testing was performed by Kiss et al. (2004) on canine liver tissue and the data were fit to both the KVFD model and the KV model. The complex Young's modulus of the normal liver tissue was measured from 4 to 9 kPa over a frequency range from 0.1 to 100 Hz. By comparing the curve fitting results of the two models, they concluded that the KVFD model had better agreement with the experimental data than the KV model.

Krouskop et al. (1998) investigated the mechanical properties of normal and diseased breast and prostate tissues with a uniaxial compression indentor at low frequencies (0.1, 1 and 4 Hz). Their results showed that cancerous specimens had measurable elevated moduli compared with normal tissues in the same gland. They reported benign prostatic hyperplasia had significantly lower values (36 to 41 kPa) than normal tissue; the normal anterior and posterior tissue had elastic modulus values of 55 to 71 kPa under 2% or 4% precompression while cancer had values of 96 to 241 kPa. In addition, they noted that the storage modulus accounted for more than 90% of the complex modulus for frequencies above 1 Hz.

The biomechanical properties obtained from imaging methods such as MRE and SSI, however, were not in