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● *Original Contribution*

DEVELOPMENT OF OIL-IN-GELATIN PHANTOMS FOR VISCOELASTICITY MEASUREMENT IN ULTRASOUND SHEAR WAVE ELASTOGRAPHY

MAN M. NGUYEN,[*†] SHIWEI ZHOU,[*] JEAN-LUC ROBERT,[*] VIJAY SHAMDASANI,[‡] and HUA XIE[*]
[*] Philips Research North America, Briarcliff Manor, New York, USA; [†] University of Southern California, University Park Campus, Los Angeles, California, USA; and [‡] Philips Healthcare, Bothell, Washington, USA

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Abstract—Because tissues consist of solid and fluid materials, their mechanical properties should be characterized in terms of both elasticity and viscosity. Although the elastic properties of tissue-mimicking phantoms have been extensively studied and well characterized in commercially available phantoms, their viscous properties have not been fully investigated. In this article, a set of 14 tissue-mimicking phantoms with different concentrations of gelatin and castor oil were fabricated and characterized in terms of acoustic and viscoelastic properties. The results indicate that adding castor oil to gelatin phantoms decreases shear modulus, but increases shear wave dispersion. For 3% gelatin phantoms containing 0%, 10%, 20% and 40% oil, the measured shear moduli are 2.01 ± 0.26, 1.68 ± 0.25, 1.10 ± 0.22 and 0.88 ± 0.17 kPa, and the Voigt-model coupled shear viscosities are 0.60 ± 0.11, 0.89 ± 0.07, 1.05 ± 0.11 and 1.06 ± 0.13 Pa·s, respectively. The results also confirm that increasing the gelatin concentration increases shear modulus. For phantoms containing 3%, 4%, 5%, 6% and 7% gelatin, the measured shear moduli are 2.01 ± 0.26, 3.10 ± 0.34, 4.18 ± 0.84, 8.05 ± 1.00 and 10.24 ± 1.80 kPa at 0% oil and 1.10 ± 0.22, 1.97 ± 0.20, 3.13 ± 0.63, 4.60 ± 0.60 and 8.43 ± 1.39 kPa at 20% oil, respectively. The phantom recipe developed in this study can be used in validating ultrasound shear wave elastography techniques for soft tissues. (E-mail: hua.xie@philips.com)

Key Words: **Ultrasound elastography, Shear wave elastography, Oil-in-gelatin phantom, Viscoelasticity, Shear wave dispersion, Shear modulus, Shear viscosity.**

INTRODUCTION

Elastography, a tissue stiffness measurement technique, has been used for non-invasive diagnosis in many tumors of the breasts, liver, thyroid and prostate. Among different modalities, ultrasound-based elastography stands out because of the advantages of real-time imaging, relatively low cost and absence of ionizing radiation. With the rapid advance of elastography in the last two decades, tissue elastic properties have become relevant in establishing the existence of and quantifying the severity of diseases such as cancer and systemic sclerosis (Foucher et al. 2006; Huwart et al. 2006; Madhok et al. 2013; Muller et al. 2009).

Tissue-mimicking phantoms are essential to all medical imaging modalities because they are easily accessible and convenient to handle. Among phantom materials such as polymer gels, silicone gels and agar, gelatin stands out because of its mechanical properties, which are close to those of soft tissue (Zell et al. 2007). There are a number of commercially available tissue-mimicking phantoms including those from ATS Labs (Bridgeport, CT, USA), CIRS (Norfolk, VA, USA) and Gammex-RMI (Middleton, WI, USA). The phantoms provided by these companies have been well characterized in terms of sound speed, attenuation coefficient and Young's modulus, which is an elasticity modulus. Because biologic tissues contain a mixture of solid and fluid materials, they should be described in terms of both elasticity and viscosity (Sarvazyan et al. 1995). However, as far as the authors are aware, currently no viscous phantoms are commercially available. Although researchers have investigated the stability and non-linear elastic behavior of oil-in-gelatin phantoms, the viscous properties of these phantoms have not been fully investigated (Madson et al. 2005, 2006; Pavan et al. 2010, 2012). A recent study reported on the use of tissue viscous properties in determining histologic stages of liver steatosis (Barry et al. 2012). As viscosity may become a valuable metric in addition to elasticity in disease

Address correspondence to: Hua Xie, Philips Research North America, 345 Scarborough Road, Briarcliff Manor, NY 10510, USA. E-mail: hua.xie@philips.com

diagnosis and classification, we believe that there is a need for the assessment of phantom viscosity in conjunction with elasticity.

In this study, phantoms containing different concentrations of gelatin and castor oil were developed to mimic the elastic and viscous components of soft tissues. Sound speed and attenuation coefficient, along with the shear elasticity and viscosity of these phantoms, were measured and compared with results from previous studies. This article is constructed as follows: The Background section introduces the theoretical foundations for elastography with an emphasis on shear-wave ultrasound elastography. The Methods section presents (i) the procedures for fabrication of viscoelastic tissue-mimicking phantoms and (ii) methods for quantification of the acoustic and viscoelastic properties of these phantoms. Subsequently, the Results and Discussion summarizes our experimental findings. Finally, the Conclusions are stated.

BACKGROUND

Elastography: Elasticity and viscosity measurement

Tissue mechanical properties change in many diseases. As a result, palpation, one of the oldest clinical examinations used by physicians, is an important diagnostic tool. One of the mechanical properties of tissue is elasticity, which indicates tissue hardness or compressibility. Three common elasticity moduli are Young's modulus E (longitudinal elasticity), shear modulus G and bulk or volume modulus K. For an isotropic homogeneous material, the relationships between these moduli are summarized in the equations

$$G = E/(2(1+\sigma)) \tag{1}$$

$$K = E/(3(1-2\sigma)) \tag{2}$$

where σ is Poisson's ratio, which has a value between 0.490 and 0.499 for nearly incompressible soft tissues (Rychagov et al. 2003). As a result, Young's modulus and shear modulus are related by a factor of 3, meaning $E \sim 3G$ (eqn [1]), and the ratio E/K is approximately 0 for soft tissues (eqn [2]). For different tissue types and conditions, although the variation in bulk modulus is small, shear and Young's moduli have much larger measurable variation, potentially providing better tissue differentiation and classification. In shear wave-based elastography, shear modulus can be calculated using the relationship

$$C_S = \sqrt{\frac{G}{\rho}} \tag{3}$$

where c_s is the speed at which the shear waves propagate, G is the shear modulus and ρ is the medium density, which can be assumed to be 1000 kg/m^3 for soft tissues. However, eqn (3) is accurate only when viscosity, another mechanical property of the tissue, is negligible. At high viscosity, shear wave velocity changes with the vibration frequency, and these dispersive properties reflect the viscous characteristics of the medium. Therefore, measuring shear wave phase velocity as a function of frequency can provide information about the viscoelasticity of the medium. For soft tissues, studies have indicated that the Voigt model, using a viscous damper and an elastic spring connected in parallel, well describes viscoelastic properties of soft tissue. It represents the full relationship between shear wave phase velocity C_S and shear modulus G, shear viscosity μ and angular frequency ω as depicted in the equation (Yamakoshi et al. 1990)

$$C_S(\omega) = \sqrt{\frac{2(G^2+\omega^2\mu^2)}{\rho\left(G+\sqrt{G^2+\omega^2\mu^2}\right)}} \tag{4}$$

There exist a number of ultrasound-based shear wave elastography techniques, for example, supersonic shear imaging (Bercoff et al. 2004; Tanter et al. 2008), Fibroscan (Foucher et al. 2006), acoustic radiation force impulse imaging (Nightingale et al. 2003; Palmeri et al. 2008), spatially modulated ultrasound radiation force imaging (McAleavey et al. 2009) and shear wave dispersion ultrasound vibrometry (Amador et al. 2011; Chen et al. 2009). These methods differ mainly in shear wave induction, shear wave speed measurement and shear elasticity reconstruction. In our study, we used a transient acoustic radiation force to induce broadband shear waves in tissue-mimicking phantoms and then measured the shear wave phase velocity at different frequencies and subsequently applied the Voigt model fitting to reconstruct both shear modulus and shear viscosity.

Tissue-mimicking phantoms

Several essential acoustic requirements for tissue-mimicking phantoms are used for ultrasound imaging. The International Electrotechnical Commission 1390 and American Institute of Ultrasound in Medicine Standard 1990 recommend a sound speed of 1540 m/s and frequency-dependent attenuation coefficient near 0.5 dB/cm/MHz (American Institute of Ultrasound in Medicine (AIUM), 1990; International Electrotechnical Commission (IEC), 1996). The compositions of phantoms for ultrasound elastography have been studied extensively in the last two decades. Hall et al. (1997) reported that Young's modulus is roughly proportional to the square of gelatin concentration C (g/L): $E_{gelatin} = 0.0034C^{2.09}$. The study also indicated that gelatin gels are preferable to agar gels because