Viscoelastic tissue characteristics measured by ultrasound

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Abstract

Tissue properties such as elasticity and viscosity have been shown to be related to such tissue conditions as contraction, edema, fibrosis, and fat content among others. Magnetic Resonance Elastography has shown outstanding ability to measure the elasticity and in some cases the viscosity of tissues, especially in the liver, providing the ability to stage fibrotic liver disease similarly to biopsy. We discuss ultrasound methods of measuring elasticity and viscosity in tissues. Many of these methods are becoming widely available in the extant ultrasound machines distributed throughout the world. Some of the methods to be discussed are in the developmental stage. The advantages of the ultrasound methods are that the imaging instruments are widely available and that many of the viscoelastic measurements can be made during a short addition to the normal ultrasound examination time. In addition, the measurements can be made by ultrasound repetitively and quickly allowing evaluation of dynamic physiologic function in circumstances such as muscle contraction or artery relaxation. Measurement of viscoelastic tissue mechanical properties will become a consistent part of clinical ultrasound examinations in our opinion.

1. Introduction

For numerous decades, the physical material properties of soft tissue have been an important topic of investigation. Several of the imaging techniques image fundamental attributes such as differences of mass density in x-ray computed tomography; proton density among other molecular properties in magnetic resonance imaging; and backscattering characteristics based on differences in acoustic impedance in ultrasonic imaging. The field of elastic or elasticity imaging in medical imaging modality is based on the hypothesis that alterations in tissue state are mirrored by alterations in the mechanical viscoelastic properties of soft tissues(1). Measurements of the mechanical properties of soft tissues can be done several ways, however the methods generally consist of two types – the application of a force or stress from the outside of the body and then imaging the resulting deformation (4), or applying force inside the body while measuring and imaging the deformation. Measurement of the deformation can be done using ultrasound or magnetic resonance imaging (3,7).

2. Viscoelastic parameter estimation

Quantitative elasticity imaging requires determination of the elastic or viscoelastic modulus of the tissue (2). Here, we derive some relationships between what can be measured using magnetic resonance imaging or ultrasound and fundamental properties, such as the Young's Modulus, which is the ratio of unilateral stress to strain in a sample. The Young's modulus is defined for compressional stress and the shear modulus is defined for shear stress, which is also the ratio of shear stress to shear strain. Young's modulus E and shear modulus G are related by the Possion ratio v where;

$$E = 2G(1 + v). \quad (1)$$

In the following derivations, we confine our studies to soft tissues, which are water saturated, and therefore, extremely incompressible giving a Possion ratio of about 0.5. This produces a Young's modulus equal to 3 times the shear modulus. The shear modulus can be considered complex e.g.,

$$G(\omega) = G_1(\omega) + iG_2(\omega), \quad (2)$$

where $\omega = 2\pi f$ is the angular frequency, G_1 storage modulus, G_2 is the loss modulus. Therefore, the complex shear modulus can also be written as

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$$G(\omega) = \frac{\rho\omega^2}{k^2(\omega)}, \tag{3}$$

where ρ is the mass density of the medium. In soft tissues, this is assumed to be $\rho = 1000\ kg/m^2$ and k is the complex wave number. Shear wave velocity and shear wave attenuation can be written as these two terms:

$$c_s(\omega)=\omega/\mathrm{Re}[k(\omega)]=\omega/k_1(\omega), \tag{4}$$

$$\alpha_s(\omega)=\mathrm{Im}[k(\omega)]=k_2(\omega), \tag{5}$$

Viscoelastic materials can be modeled using a rheological approach. A widely used model in elasticity imaging is the Kelvin-Voigt model, which includes an elastic spring and a viscous dashpot in parallel and provides shear elasticity μ_1 and viscosity μ_2.

Shear wave velocity and shear wave attenuation can be computed giving the next 2 equations;

$$c_s(\omega)=\sqrt{\frac{2\left(\mu_1^2+\omega^2\mu_2^2\right)}{\rho\left(\mu_1+\sqrt{\mu_1^2+\omega^2\mu_2^2}\right)}}, \tag{6}$$

$$\alpha_s(\omega)=\sqrt{\frac{\rho\omega^2\left(\sqrt{\mu_1^2+\omega^2\mu_2^2}-\mu_1\right)}{2\left(\mu_1^2+\omega^2\mu_2^2\right)}}, \tag{7}$$

The implications of these two equations are that shear wave velocities and attenuation are functions of frequency and the elastic and viscous terms of the medium. The above two equations can be solved for $\mu_1\ and\ \mu_2$ if we can measure the speed c_s and attenuation α_s over a range of frequencies.

3. The shear wave approach

Sarvazyan et. al. suggested a method called shearwave elasticity imaging, SWEI (1). In this method radiation force produced by a focused ultrasound creates shearwaves in the tissue. This shearwave propagates out from the focal center. The speed of these shearwaves can be related through the equation $Cs = \sqrt{\mu_1/\rho}$ if there is no attenuation.

There are many methods of creating shearwaves including those by SSI (8), in which short high intensity ultrasound tone bursts are focused along a line of points in the tissue and producing shearwaves. Imaging the shearwave propagation requires high speed ultrasound to measure particle motion because the shear wave propagates in tissue at up to 5 meters per second. The most advanced modern ultrasound systems can obtain up to 10,000 frames per second and so these shearwaves can be measured rather easily. Shearwave velocity dispersion in various tissues have been reported previously in such tissues and organs as liver, kidney, brain, prostate, skeletal muscle, breast, cornea, and blood clots(10,13,14,19, 20, 22, 23).

3.1. SDUV

A new method of measuring shearwaves is to use shearwave dispersion ultrasound velocimetry, SDUV (12, 19). The speed of the shearwave is calculated by the following equation:

$$c_s(\omega) = \frac{\omega\Delta r}{\Delta\emptyset}, \tag{8}$$

where $\Delta\emptyset$ and Δr are phase difference and distance between two observation point along the shearwave path. Linear regression can be used to calculate a least square estimate of the ratio for each frequency. This measurement of course is

made over a range of frequencies because the speed of the shearwave varies if the velocity is dispersive, that is, the imaginary term $K_2(\omega)$ is not 0.

We have developed a new method of inducing many shearwaves in tissue by pushing multiple areas simultaneously, thus, shearwaves propagate in all directions at the same time. Directional filtering is used to produce sequential images of shearwaves propagating in selected directions. The speed of propagation of these shearwaves is used to calculate the material properties of the tissue. This method is called CUSE for comb-beam ultrasound shear elastography. There have been several applications of comb-beam elastography.

The following is an example clinical trial in which CUSE has been used to diagnose lymph node metastasis in patients with breast cancer. In a set of 68 patients whose suspicious lymph nodes were detected with ultrasound, half were found to be negative and half were positive by biopsy. CUSE was used to determine the speed/stiffness of the nodes as shown in Figures 1 and 2. Table 1 shows the means and standard deviations of the set of stiffness measurements in the positive and negative lymph nodes. Setting the sensitivity of the CUSE shear wave method at 100% gives a specificity of 84%. This method would have saved about 26 biopsies if it were used on the original set of 68 patients.

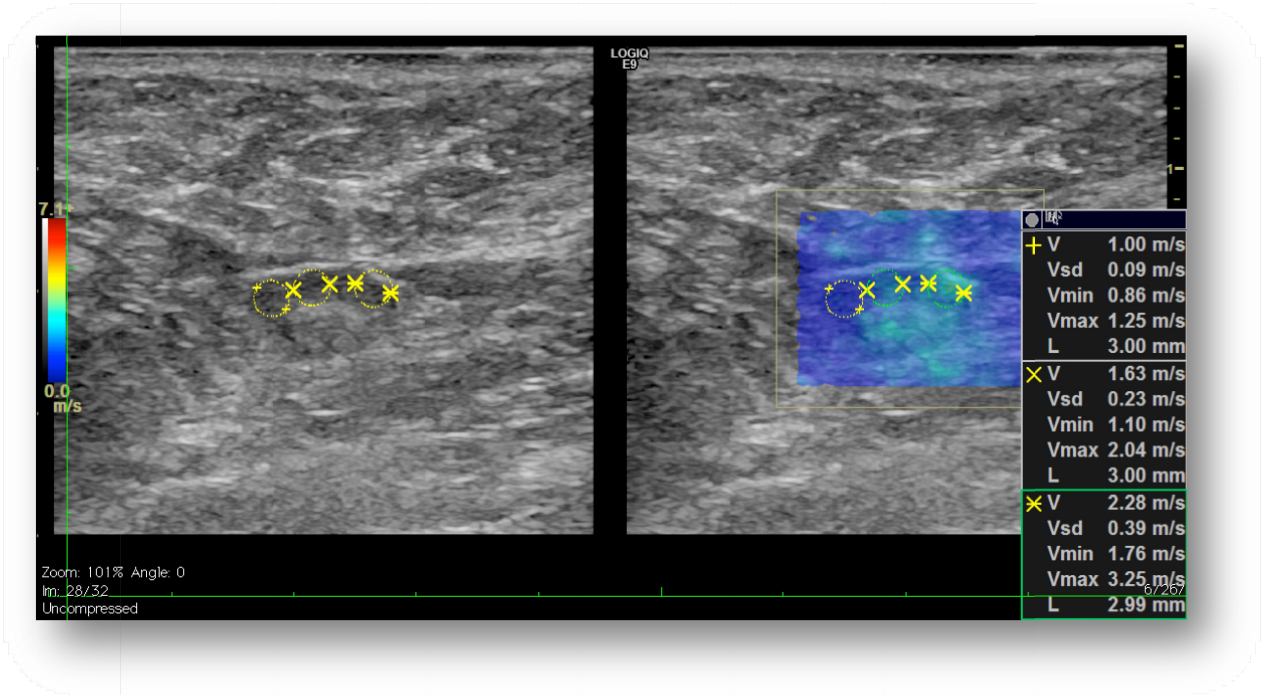

Figure 1. B-scan, left, and tissue stiffness scan, right, of breast lesions biopsied as reactive lymph node. The speed of shear wave ranges from 3.25 to 0.86 m/s.

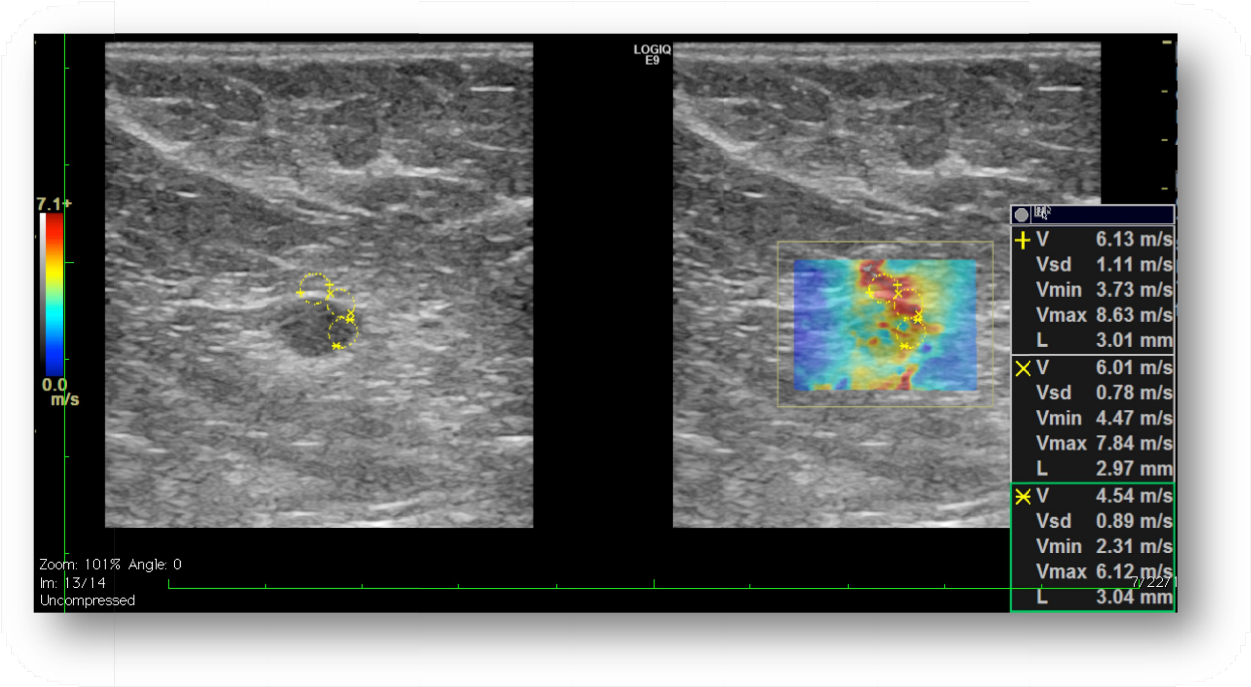

Figure 2. B-scan of lymph gland, left, and stiffness scan, right, of biopsied proven adenocarcinoma. Speed of shear wave ranges from 8.6 to 2.3 m/s.

Table 1 shows the effect of malignancy on stiffness for the 68 patients.

Pathology	Number	Mean (kPa)	Std. Dev. (kPa)	p-value
Benign (B)	34	16.21	14.94	<0.0001*
Malignant (M)	34	55.71	30.06	

4. Conclusion

Measurements of tissue mechanical properties using ultrasound can be used to diagnose metastatic lymph nodes in patients with breast cancer. After detection of suspicious lymph nodes with ultrasound imaging, quantitative measurements of stiffness using the CUSE method can diagnose biopsy proven cancerous/benign nodes with 100% sensitivity and 84% specificity possibly saving many biopsies if used in practice. The wide availability of ultrasound methods and their ubiquitous use in breast ultrasound examinations provides a universal basis for the application of this method in the diagnosis of malignant metastasis in lymph nodes of these patients.

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