

Measurement of Tissue Mechanical Properties with Shear Wave Dispersion Ultrasound Vibrometry (SDUV)

James F. Greenleaf, *Life Fellow, IEEE*, Matthew W. Urban, *Member, IEEE*, and Shigao Chen, *Member, IEEE*

Abstract—Shear wave dispersion vibrometry (SDUV) produces motion in tissue using sequential pulses of ultrasound radiation pressure. The resulting motion of the tissue in the form of propagating shear waves can provide information about the material properties of the tissue given the appropriate equations of motion for the geometry of the tissue. An example application of the method is described to measure material properties in bovine tissue.

I. INTRODUCTION

Characterization of tissue mechanical properties, which includes hardness or elasticity, are closely linked to tissue state with respect to pathology [1]. This has elicited a large number of methods for measuring these properties. The main techniques are based on either ultrasound or magnetic resonance (MR) imaging [2-6]. Ultrasound based techniques are limited by the requirement of an acoustic window through which to “view” the region of interest. Another limitation of ultrasound is that applications in obese patients or organs deep within the body are limited by the penetration depth of ultrasound. Although MR Elastography (MRE) is not subjected to these fundamental limitations, MR based techniques are expensive and limited in availability, thus less likely to see worldwide clinical practice. MRE can be used for a variety of elasticity imaging applications, but it has been shown that ultrasound methods described here can get the same values of elasticity.

The ultrasound elasticity methods first developed, such as those proposed by the groups of Parker, Ophir, Greenleaf, and Nightingale, have typically formed a qualitative 2D image providing a *relative* mapping of tissue viscoelasticity [7-10]. These methods are useful in detecting abnormal lesions within a normal background however they are inadequate for assessing diffuse diseases such as liver fibrosis, when there is no normal background tissue to provide contrast. *Quantitative* methods are required in this case in which tissue elasticity is estimated in absolute units of Pascal. Acoustic shear wave speed is uniquely related to tissue material properties. Several groups have used shear wave propagation speed to quantify tissue stiffness [1, 11-

13]. The viscoelastic properties of a material can be described by a complex modulus where the real term is considered the storage modulus (elasticity) and the imaginary term is the loss modulus (viscosity). In many previous approaches tissue *viscosity* is neglected and this omission can cause bias in the estimation of tissue elasticity. In addition, recent studies suggest that viscosity is another useful index of tissue health [14, 15]. Recently a new method called supersonic shear imaging has been developed which has the potential to solve quantitatively both tissue elasticity and viscosity [16, 17]. However, this technique requires super fast imaging (with a frame rate up to 5000 frames per second), therefore, the method requires specialized equipment and is not compatible with current commercial ultrasound scanners. There is still a need for a simple and practical technique that can be implemented on the fleet of installed ultrasound scanners and that can *quantitatively* resolve both tissue *elasticity* and *viscosity*.

Towards this aim, we have developed a new method that quantifies both the storage and loss modulus from the frequency dispersion of shear wave propagation speed [18]. We call this method Shearwave Dispersion Ultrasound Vibrometry (SDUV). This paper reports further development of SDUV as summarized below. Pulse echo ultrasound correlation methods are used to detect propagation characteristics of the radiation pressure induced shear wave. The viability of the method is demonstrated with an *in vitro* experiment in bovine muscle. A new pulse sequence that potentially may make SDUV compatible with current ultrasound scanners is also developed. Feasibility of this pulse sequence for SDUV measurements *in vivo*, in the presence of respiratory and cardiac motions, is tested within the liver of an anesthetized swine and is reported elsewhere in this meeting. Application of SDUV to the heart of a pig *in vivo* is reported elsewhere in these proceedings. Application of SDUV to measurement of viscoelastic properties of excised swine kidney is also reported elsewhere. These results show that SDUV is a promising, quantitative method that could provide a quantitative complement to current ultrasound imaging techniques.

II. METHODS

A. Principle

The principle of SDUV has been described in our previous paper [18] and is briefly summarized here. For a homogeneous Voigt medium, the shear wave propagation

This work was supported in part by grant EB002167 and EB002640 from the National Institutes of Health.

The authors are with the Department of Physiology and Biomedical Engineering, Mayo Clinic College of Medicine, Rochester, MN 55905 USA (Contact information for J. F. Greenleaf; fax: 507-266-0361; e-mail: jfg@mayo.edu).

speed c_s depends on the frequency of shear wave ω_s (i.e. “dispersive”):

$$c_s(\omega_s) = \sqrt{\frac{2(\mu_1^2 + \omega_s^2 \mu_2^2)}{\rho(\mu_1 + \sqrt{\mu_1^2 + \omega_s^2 \mu_2^2})}}, \quad (1)$$

where ρ , μ_1 , and μ_2 are the density, shear elasticity, and shear viscosity of the medium, respectively [18,20]. The density of various soft tissues shows very little variance and can be assumed to be 1000 kg/m³. Therefore, the variation of c_s versus frequency (typically in the range of hundreds of Hertz) can be measured in the studied medium and fit by Eq. (1) to solve inversely for elasticity, μ_1 , and viscosity, μ_2 .

As shown in Fig. 1, SDUV uses a “push” transducer operating in amplitude modulated (AM) mode to generate harmonic vibration within the studied medium at the transducer focus. The speed of the harmonic shear waves of frequency ω_s propagating outwards from the vibration center can be monitored by the “detect” transducer operating in pulse-echo mode at two locations along the propagation path. The propagation speed of a shear wave at ω_s is estimated by tracking the phase change of the wave over the distance it has propagated

$$c_s(\omega_s) = \omega_s \Delta r / \Delta \phi_s, \quad (2)$$

where $\Delta \phi_s = \phi_1 - \phi_2$ is the phase change over the traveled distance Δr . The frequency of the shear wave is determined from the spectrum of the motion at the harmonics of the push frequency shown in Fig. 3. The dispersion characteristic of the studied tissue is fit with Eq. (1) to solve for its elasticity and viscosity. It is important to note that SDUV is not a 2D imaging method, but provides a local average of tissue viscoelasticity within the shear wave propagation path (typically a few millimeters).

B. Technical advantages of SDUV

SDUV fully resolves the frequency characteristics of shear wave propagation speed, allowing both elasticity and viscosity to be properly solved. The approach used by FibroscanTM and several other methods measures the group velocity of an *impulse* shear wave and does not resolve its frequency dependency [10, 24, 26]. As a result, a simplified version of (2) assuming zero viscosity is used

$$c_s = \sqrt{\mu_1 / \rho}. \quad (3)$$

Therefore, information about viscosity, another valuable index of tissue state, is lost. In addition, this simplification may cause significant bias to elasticity estimation because the estimate of elasticity is now forced to account for the influence of viscosity on shear wave speed. An *in vitro* MRE study on porcine livers shows that if viscosity is assumed zero and (3) is used, the value of elasticity of same

liver tissues increases about 70% merely by changing the shear wave frequency from 100 to 300 Hz [35].

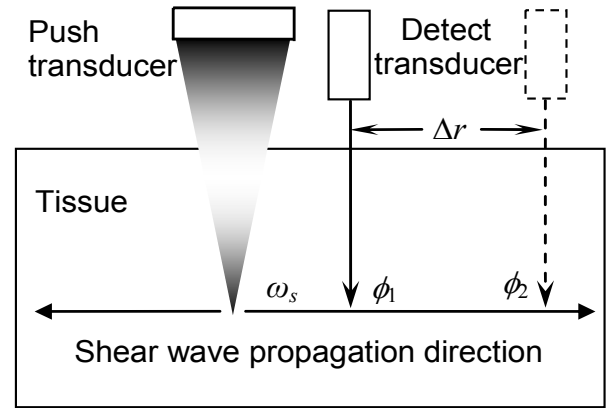


Fig. 1. Principle of SDUV. A push transducer induces a vertically polarized shear wave in the tissue which is measured by a pulse echo transducer. The push and pulse echo transducers can both be implemented with the same array transducer such as the probes on a commercial scanner.

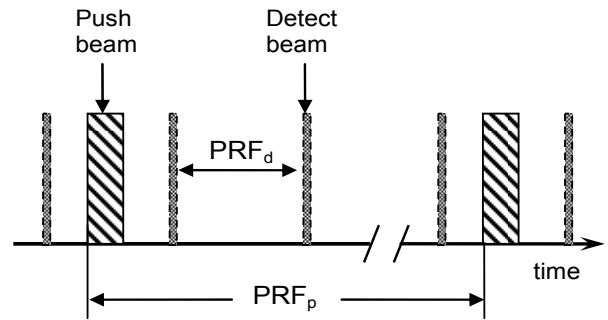


Fig. 2. Timing of the push and detect beam. The push beams are repeated at a rate of PRF_p , and the detect beam is repeated at a rate of PRF_d .

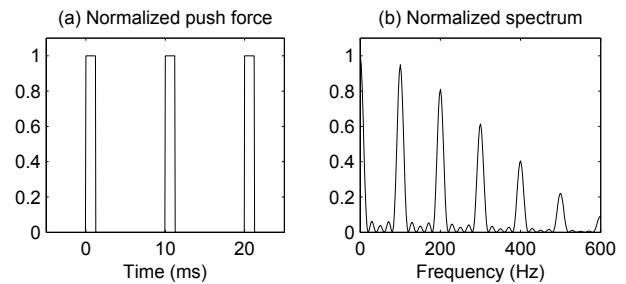


Fig. 3. Force is exerted on tissue by the ON/OFF push sequence in (a) time- and (b) frequency-domain. The push force has duration of 1.0 ms and is repeated with a frequency of 100 Hz.

Another important advantage of this method is that the propagation of the shear wave is solely governed by the local tissue properties once the shear wave is launched. That is, if there are no reflections from tissue boundaries during the measurement then the equations governing the motion of the shear wave are local. Therefore, SDUV measurements

are not affected by the characteristics of the ultrasound push beam (e.g., its beam shape or intensity) or overlying tissue properties (e.g., its ultrasound attenuation coefficient), which are typically unknown. This feature produces very clean quantification of tissue elasticity and viscosity by separating the effects of the instrument (ultrasound transducer generating the push beam) from measurements. The ultrasound push beam is therefore used to generate shear waves locally within tissue, which due to high attenuation of shear waves in tissues are confined to several millimeters from the push beam focus. This eliminates interference from reverberation of shear wave as opposed to methods that use mechanical excitation from the body surface to “probe” inner tissues.

C. Measurement of the motion

The intermittent pulse sequence for SDUV has both spatial and temporal features. As indicated Fig. 1, the push beam and the detect beam are focused at different locations. Current commercial array transducers are capable of electronically steering the ultrasound beam without the need to mechanically move the transducer. The push beam is used to generate a shear wave within the studied tissue. The detect beam is in pulse echo mode to monitor and record the shear wave propagation. The detect beam is steered to at least two different locations to detect the shear wave phase. The timing of the pulse sequence is shown in Fig. 2. The push beam has a pulse repetition frequency of $PRF_p = 100$ Hz and exerts a pushing force of constant amplitude, every 10 ms, to the same tissue region at the transducer focus Fig. 1. The Fourier transform of the simulated plot in Fig. 3(a) is shown in Fig. 3(b) and indicates that the spectrum of such repeated ON/OFF push force contains not only the fundamental ON/OFF frequency at 100 Hz, but also its harmonics at 200, 300, and 400 Hz, etc. Therefore, shear wave dispersion information at multiple frequencies is intrinsically available with this push sequence and repeating the push pulses at different frequencies is not required. As a result, SDUV measurement time is reduced and heating by ultrasound to tissue is also minimized. The force duration shown in Fig. 3(a) is 1.0 ms for illustrative purposes whereas in conventional practice the duration of a push pulse is typically 100-200 μ s.

Experiments in tissues indicate that shear waves above 500 Hz generated by such ON/OFF push sequence are very weak. There are several reasons: A) The force at higher frequencies has lower magnitude, as shown in Fig. b. B) Tissue vibration in response to a push force of fixed amplitude decreases when frequency increases. C) Higher frequency shear waves attenuate more quickly when propagating in tissue. The combined result is that shear waves above 500 Hz are negligible with this push sequence. Therefore, as far as the multi-frequency shear waves are sampled by the ultrasound detect beam at a pulse repetition frequency (PRF_d) higher than 1 kHz, there should be no aliasing. In current practice, we typically use a PRF_d greater than 1.6 kHz and limit the dispersion analysis up to about 400 Hz.

D. Results in excised Bovine muscle

Figure 4 shows the shear wave propagation speed as a function of frequency measured along (circles) and across (crosses) the fibers of a sample of fresh excised bovine muscle. The solid lines are the Least Mean Square (LMS) fits from Eq. (1) that give a shear elasticity of $\mu_1 = 29$ kPa and a viscosity of $\mu_2 = 9.9$ Pa·s along the fibers; and $\mu_1 = 12$ kPa and $\mu_2 = 5.7$ Pa·s across the fibers.

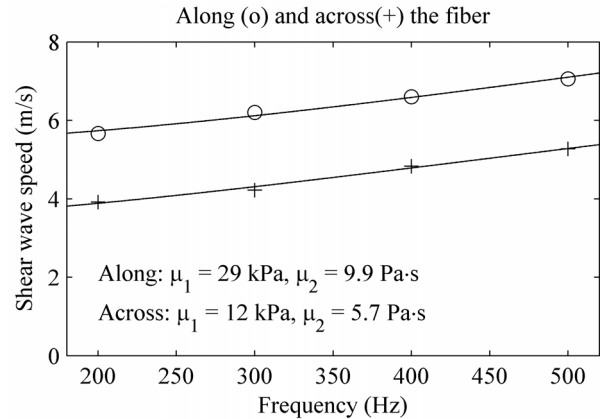


Fig. 4. Shear wave speed measured along (circles) and across (pluses) the bovine muscle tested. Solid lines are LMS fits from the Voigt dispersion model which gives estimates of stiffness and viscosity shown at the bottom of this figure.

III. CONCLUSION

SDUV provides a simple method of producing wide band shear waves that can be analyzed for their propagation characteristics as a function of frequency. Installation on the installed base of ultrasound scanners will provide worldwide access to quantitative mechanical property measurements of most tissues.

ACKNOWLEDGMENT

The authors thank Randy Kinnick for experimental support and Tom Kinter for computer support. We thank Jennifer Milliken for secretarial assistance.

REFERENCES

- [1] A. P. Sarvazyan, O. V. Rudenko, S. D. Swanson, J. B. Fowlkes, and S. Y. Emelianov, "Shear wave elasticity imaging: A new ultrasonic technology of medical diagnostics," *Ultrasound in Medicine and Biology*, vol. 24, pp. 1419-1435, 1998.
- [2] L. Gao, K. J. Parker, R. M. Lerner, and S. F. Levinson, "Imaging of the elastic properties of tissue - A review," *Ultrasound in Medicine and Biology*, vol. 22, pp. 959-977, 1996.
- [3] J. Ophir, S. K. Alam, B. Garra, F. Kallel, E. Konofagou, T. Krouskop, and T. Varghese, "Elastography: ultrasonic estimation and imaging of the elastic properties of tissues," *Proceedings of the Institution of Mechanical Engineers Part H-Journal of Engineering in Medicine*, vol. 213, pp. 203-233, 1999.
- [4] J. F. Greenleaf, M. Fatemi, and M. Insana, "Selected methods for imaging elastic properties of biological tissues," *Annual Review of Biomedical Engineering*, vol. 5, pp. 57-78, 2003.

- [5] K. J. Parker, L. S. Taylor, S. Gracewski, and D. J. Rubens, "A unified view of imaging the elastic properties of tissue," *Journal of the Acoustical Society of America*, vol. 117, pp. 2705-2712, 2005.
- [6] R. Muthupillai, D. J. Lomas, P. J. Rossman, J. F. Greenleaf, A. Manduca, and R. L. Ehman, "Magnetic resonance elastography by direct visualization of propagating acoustic strain waves," *Science*, vol. 269, pp. 1854-7, 1995.
- [7] R. M. Lerner, S. R. Huang, and K. J. Parker, "'Sonoelasticity' images derived from ultrasound signals in mechanically vibrated tissues," *Ultrasound Med Biol*, vol. 16, pp. 231-9, 1990.
- [8] J. Ophir, I. Cespedes, H. Ponnekanti, Y. Yazdi, and X. Li, "Elastography: a quantitative method for imaging the elasticity of biological tissues," *Ultrason Imaging*, vol. 13, pp. 111-34, 1991.
- [9] M. Fatemi and J. F. Greenleaf, "Ultrasound-stimulated vibro-acoustic spectrography," *Science*, vol. 280, pp. 82-5, 1998.
- [10] K. R. Nightingale, M. L. Palmeri, R. W. Nightingale, and G. E. Trahey, "On the feasibility of remote palpation using acoustic radiation force," *Journal of the Acoustical Society of America*, vol. 110, pp. 625-634, 2001.
- [11] L. Sandrin, M. Tanter, J. L. Gennisson, S. Catheline, and M. Fink, "Shear elasticity probe for soft tissues with 1-D transient elastography," *IEEE Transactions on Ultrasonics Ferroelectrics and Frequency Control*, vol. 49, pp. 436-446, 2002.
- [12] K. Nightingale, S. McAleavey, and G. Trahey, "Shear-wave generation using acoustic radiation force: in vivo and ex vivo results," *Ultrasound Med Biol*, vol. 29, pp. 1715-23, 2003.
- [13] Z. Wu, L. S. Taylor, D. J. Rubens, and K. J. Parker, "Sonoelastographic imaging of interference patterns for estimation of the shear velocity of homogeneous biomaterials," *Phys Med Biol*, vol. 49, pp. 911-22, 2004.
- [14] L. Huwart, F. Peeters, R. Sinkus, L. Annet, N. Salameh, L. C. ter Beek, Y. Horsmans, and B. E. Van Beers, "Liver fibrosis: non-invasive assessment with MR elastography," *NMR Biomed*, vol. 19, pp. 173-9, 2006.
- [15] N. Salameh, F. Peeters, R. Sinkus, J. Abarca-Quinones, L. Annet, L. C. Ter Beek, I. Leclercq, and B. E. Van Beers, "Hepatic viscoelastic parameters measured with MR elastography: Correlations with quantitative analysis of liver fibrosis in the rat," *J Magn Reson Imaging*, vol. 26, pp. 956-62, 2007.
- [16] J. Bercoff, M. Muller, M. Tanter, and M. Fink, "Study of viscous and elastic properties of soft tissues using supersonic shear imaging," presented at Proceedings of the IEEE Ultrasonics Symposium, 2003.
- [17] J. Bercoff, M. Tanter, and M. Fink, "Supersonic shear imaging: A new technique for soft tissue elasticity mapping," *IEEE Transactions on Ultrasonics Ferroelectrics and Frequency Control*, vol. 51, pp. 396-409, 2004.
- [18] S. Chen, M. Fatemi, and J. F. Greenleaf, "Quantifying elasticity and viscosity from measurement of shear wave speed dispersion," *J Acoust Soc Am*, vol. 115, pp. 2781-5, 2004.
- [19] Y. Zheng, S. G. Chen, W. Tan, R. Kinnick, and J. F. Greenleaf, "Detection of tissue harmonic motion induced by ultrasonic radiation force using pulse-echo ultrasound and Kalman filter," *IEEE Transactions on Ultrasonics Ferroelectrics and Frequency Control*, vol. 54, pp. 290-300, 2007.
- [20] S. Catheline, J. L. Gennisson, G. Delon, M. Fink, R. Sinkus, S. Abouelkaram, and J. Culioli, "Measurement of viscoelastic properties of homogeneous soft solid using transient elastography: An inverse problem approach," *Journal of the Acoustical Society of America*, vol. 116, pp. 3734-3741, 2004.
- [21] J. G. Abbott, "Rationale and derivation of MI and TI--a review," *Ultrasound Med Biol*, vol. 25, pp. 431-41, 1999.
- [22] K. Nightingale, M. S. Soo, R. Nightingale, and G. Trahey, "Acoustic radiation force impulse imaging: In vivo demonstration of clinical feasibility," *Ultrasound in Medicine and Biology*, vol. 28, pp. 227-235, 2002.
- [23] S. L. Friedman, "Liver fibrosis -- from bench to bedside," *J Hepatol*, vol. 38 Suppl 1, pp. S38-53, 2003.
- [24] L. Sandrin, B. Fourquet, J. M. Hasquenoph, S. Yon, C. Fournier, F. Mal, C. Christidis, M. Ziol, B. Poulet, F. Kazemi, M. Beaugrand, and R. Palau, "Transient elastography: a new noninvasive method for assessment of hepatic fibrosis," *Ultrasound Med Biol*, vol. 29, pp. 1705-13, 2003.
- [25] M. Yin, J. A. Talwalkar, K. J. Glaser, A. Manduca, R. C. Grimm, P. J. Rossman, J. L. Fidler, and R. L. Ehman, "Assessment of hepatic fibrosis with magnetic resonance elastography," *Clin Gastroenterol Hepatol*, vol. 5, pp. 1207-1213 e2, 2007.
- [26] M. W. Urban, S. Chen, and J. F. Greenleaf, "Harmonic motion detection in a vibrating scattering medium," *IEEE Transactions on Ultrasonics Ferroelectrics and Frequency Control*, vol. 55, pp. 1956-1974, 2008.