Geometric Focusing of High Frequency Shear Waves for Noninvasive High Resolution MR Elastography

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INTRODUCTION Microscopic resolution Magnetic Resonance Elastography (μMRE) would be more useful in assessing the development and differentiation of engineered tissues in vitro if it could be done without direct physical contact with the tissue or specimen of interest. Such a method would also avoid possible contamination of the tissue sample if it could be done without even having to open the sealed test tube within which the tissue is being grown. Additionally, in combination with microscopic MRI, μMRE could be useful in assessing the 3 dimensional viscoelastic properties of biopsied specimens with high resolution. However, using MRE to determine viscoelastic properties with tens of microns resolution requires that both the MR image, itself, have this resolution and that the shear waves generated have wavelengths on this scale or near to it, .e. g., hundreds of microns. Previously, the authors have conducted MRE studies on engineered tissue specimens at 11.7 T, using high performance RF coils and gradients, and direct contact compact, high frequency mechanical actuators [Othman et al. 05, 07]. While high image resolution was available (tens of microns in-plane for 500 micron image slices), due to attenuation from viscous effects that increase with increased shear wave frequency and scale with wavelength, reducing wavelengths to less than a millimeter resulted in a restricted field of view confined to the vicinity of the shear wave actuator located on the surface of the medium within which the tissue was suspended. More recently, the authors have addressed this problem with some success by replacing the surface-based shear wave actuator with an axially oscillating needle that penetrates into the material of interest and enables measurable shear wave motion up to several kHz within several mm of the needle.

In the present article, we present results of a pilot study where we combine the benefits of noninvasiveness and geometric focusing of the rapidly attenuating shear waves to extend the useful shear wave frequency range, and thus achieve very short shear wavelengths that will help in providing more localized estimates of material properties. This is accomplished by vibrating the entire test tube axially, effectively using the entire inner test tube wall as an axisymmetric shear wave source that creates waves travelling radially inward. While these waves attenuate as they travel away from the wall due to viscous effects, this is countered by the geometric focusing that occurs as they travel towards the central axis of the test tube. The basic viscoelastic wave propagation theory supporting this approach is reviewed followed by a description of our experimental setup and pilot results.

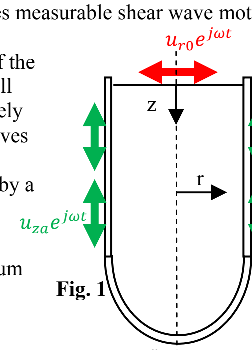

Fig. 1

THEORY Referring to **Fig. 1**, considering axisymmetric vertical motion of the test tube undergoing steady state harmonic motion $u_z(r = a, t) = u_{za}e^{j\omega t}$, and assuming a welded contact of the test tube wall with the media inside it, for an isotropic viscoelastic medium far enough away from the free surface at the top of the medium and from the bottom of the test tube, we have [Beltzer 88]:

$$u_z(r,t) = u_{za}\frac{J_0(k_\beta r)}{J_0(k_\beta a)}e^{j\omega t}, \qquad k_\beta = \omega\sqrt{\frac{\rho}{\mu_R + j\mu_I}},$$

where $j = \sqrt{-1}$, J_0 denotes a zeroth order Bessel function of the first kind, ρ is the medium density, and the real and imaginary parts of the shear modulus, μ_R and μ_I, will depend on the type of viscoelastic model that is assumed. For values of $\rho = 1{,}000\ kg/m^3$, $\mu_R = 8\ kPa$ and $\mu_I = 1.5\ kPa$, **Fig. 2** compares the shear wave amplitude generated in a 4.2 mm inner diameter test tube from a surface source at the top of the test tube oscillating at 5 kHz with an amplitude of 100 microns parallel and in contact with the surface (Fig. 2a: consider the test tube on its side with the shear wave actuator as indicated by the red arrow) versus from axial vibration of the entire test tube at 5 kHz with an amplitude of 100 microns as indicated by the green arrows (Fig. 2b). Clearly, the geometrically focused shear waves result in a more uniform amplitude of shear waves throughout the entire region within the test tube as compared to application of shear waves from the medium surface, which attenuate in amplitude exponentially losing an order of magnitude every 2 mm for the values used in this simulation.

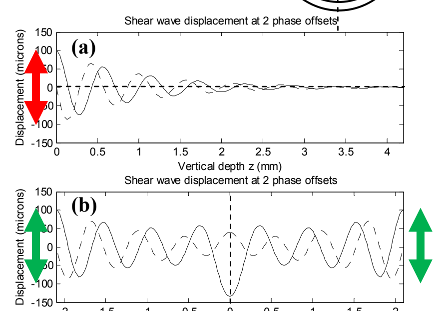

Fig. 2

EXPERIMENT Proof of concept studies were conducted in a 4.2 mm inner diameter NMR tube (5 mm o.d. New ERA, Boston, MA) in a Bruker 11.7 T (500 MHz Hydrogen) MRI system on 0.6% by wt. agarose gel. Maximum gradient field strength available was 200 G/cm. In order to avoid additional vibration, the cooling system was turned off during the MRE protocol. To avoid overheating only 60% of gradient field power was utilized and TR was kept between 1 and 2 sec. Sample results at 5 kHz are shown in **Fig. 3**. Fig. 3a shows a cross section of the axial phase image, which is shown in Fig. 3b. Here, TE = 14 msec, slice thickness = 1 mm, the FOV is 128 x 256 pixels, 8 MSG cycles are used, with 2 acquisitions averaged. The second frequency channel of the NMR system was reserved for synchronization of a signal generator and Motion Sensitizing Gradient (MSG). In the pulse program code a trigger pulse is generated in the second frequency channel 1 time period before the MSG starts. This pulse triggers an Agilent 33220A Function Generator to send N+1 sin wave cycles to the power amplifier (Yamaha Power Amplifier P3500S). One additional pulse allows time for the shear wave to propagate one cycle ahead in order to use the MSG cycles more efficiently. This number can change depending on the geometry of the sample and actuation method. The amplified signal is carried to the piezo actuation system through sufficiently thick cables, as at high frequencies and nominal voltages (100 volts peak), current requirements are on the order of amps. A piezoceramic stack actuator from Thor Labs. Inc. (6.5 x 6.5 cross section by 18 mm length) provides 11.6 micron displacement at 100 volts. It is fixed to the top of the sealed test tube via custom hard plastic fixturing. Since there is nothing to fix any part of this system to the walls of the magnet bore, a nonmagnetic hardened fiber glass weight, with 10 times the mass of the test tube, is fixed to the other side of the piezo stack actuator and is used to provide an "inertial ground" for the actuator. Results of this pilot study in Fig. 3 are similar to simulated results shown in Fig. 2b. Geometric focusing to "counterbalance" the effects of viscosity, as applied here or more generally using an array of synchronized converging shear wave sources, may enable researchers to continue to push the frequency and resolution limits of MRE.

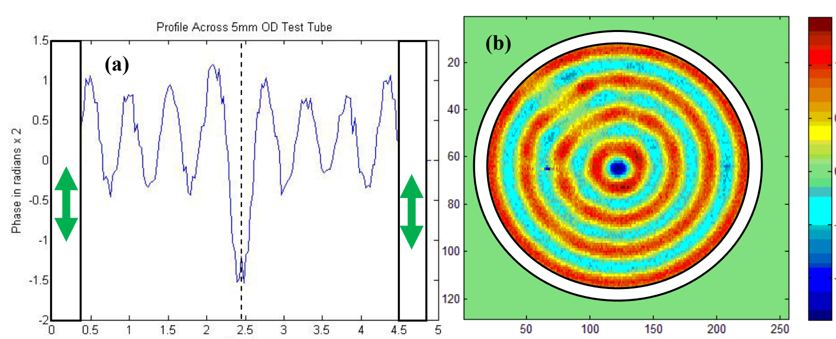

Fig. 3

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