Title: A Novel Method for Dynamic Mechanical Analysis of Soft Viscoelastic Materials and Comparison to Magnetic Resonance Elastography.

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Introduction: Magnetic Resonance Elastography (MRE) is rapidly becoming a useful clinical tool for the assessment of tissue stiffness in vivo. Currently the most prominent clinical MRE application is for noninvasively determining the extent of hepatic fibrosis due to various disease processes as an alternative to biopsy. Increasing liver fibrosis correlates with increasing liver stiffness. MRE is a quantitative MRI phase-contrast technique that measures the shear stiffness of a material (units are Pascals or Pa) by imaging the spatial deformations in an object (e.g., liver or phantom) resulting from an externally applied mechanical stress at a specific frequency. The resulting multidimensional strain field can be analyzed to produce a map of the stiffness distribution in the object. MRE has been shown to be a precise method (1), however its absolute accuracy has not been well established because there is no widely accepted method for measuring the mechanical properties of very soft viscoelastic materials or biologic tissues (< 100 KPa). We present a simple system that employs the general methods used in Dynamic Mechanical Analysis (DMA) (2) to enable these measurements to be made and the results are compared directly to those obtained using MRE.

Methods: DMA yields information about the mechanical properties of a specimen subjected to minor, usually sinusoidal, externally applied forces (stresses). The applied mechanical stress (σ_A) elicits a corresponding strain (ε_A) (deformation) whose amplitude (A) and phase shift (δ) can be determined. The complex modulus (E*) is the ratio of the stress to the strain and represents the stiffness of the material. The magnitude of the complex modulus is $|E^*| = |\sigma_A|/|\varepsilon_A|$. The complex modulus of the material at frequency ω is composed of the storage modulus $E'(\omega) = (E^*\cos\delta)$ and the loss modulus $E''(\omega) = (E^*\sin\delta)$. These are dynamic elastic characteristics and are material specific. MRE of the liver typically reports only $|E^*| = [E'(\omega)^2 \times E''(\omega)^2]^{1/2}$. Our DMA system consists of a stiff plate (much higher $|E^*|$ than the material being tested) connected to a liner motor. The sample rests on the plate. A mass is placed on top of the sample which covers the entire sample surface (Fig. 1).

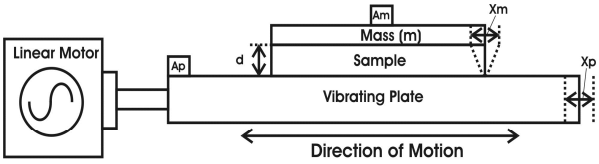

Fig. 1: A_p = Plate acceleration [$|A_p| \sin(\omega t)$], X_p = Plate displacement [$(|A_p| / \omega^2) \sin(\omega t)$]
A_m = Mass acceleration [$|A_m| \sin(\omega t+\delta)$], X_m = Mass displacement [$(|A_m| / \omega^2) \sin(\omega t+\delta)$]
δ = Phase angle between A_p and A_m, Dx = $(X_m - X_p)$, d = Sample thickness

Motion of the plate induces motion in the sample which in turn induces motion in the mass. The dyamic motions of both the vibrating plate and the vibrating mass are measured (either directly using accelerometers mounted to each or indirectly using a optical device such as a laser vibrometer). The stress on the sample resulting from the motion of the mass can be calculated (mass x acceleration / surface area = F/S) as can the strain ((plate displacement - mass displacement)/sample thickness = Dx/d). The complex modulus of the material can then be calculated as F·d/S·Dx. The viscoelastic properties of most materials are affected by temperature, therefore all measurements were conducted at ambient room temperature (~22 ºC).

Results: Motion measurements of the plate and mass were made using a laser Doppler vibrometer (VibroMet 500, MetroLaser, Inc., Irvine, CA). This allowed for the easy changing of masses without remounting accelerometers. It also preserved the integrity of the motion system by detecting the motion without coming in contact with any of the moving parts. Samples of four synthetic materials were tested. The softest was a polyvinyl chloride polymer gel (#502 with softening agent, LureCraft Industries, Inc., LaGrange, IN). A moderately stiffer sample was a 3-part silicone elastomer (TC-5005 A/B/C, BJB Enterprises, Inc., Tustin, CA). An even stiffer sample was a 2-part silicone (same as the 3-part without the thinning agent). The stiffest sample was comprised of a 2-part silicone elastomer (Wirosil, BEGO USA, Lincoln, RI). Each sample was molded into a 2.5-cm diameter disc of uniform thickness (1.2 or 1.8 mm). Masses were chosen based on the relative stiffness of the material. The mass must be heavy enough to insure that the strain magnitude is detectable but not so heavy as to cause a mechanical resonance of the system within the frequency range of interest. Typically masses ranged from 5 to 50 grams. Figure 2 shows a graph of the |E*| values vs. frequency for the 4samples.

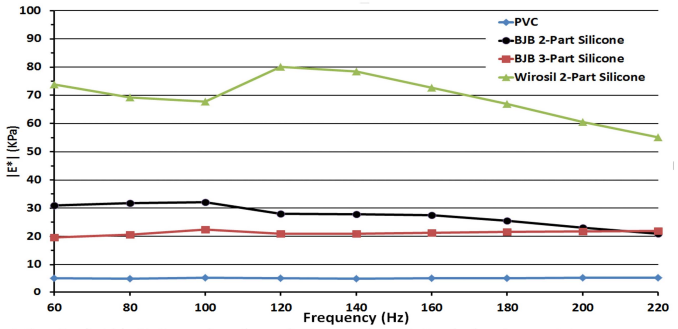

Fig 2: |E*| (Magnitude of Complex Modulus) vs. Frequency

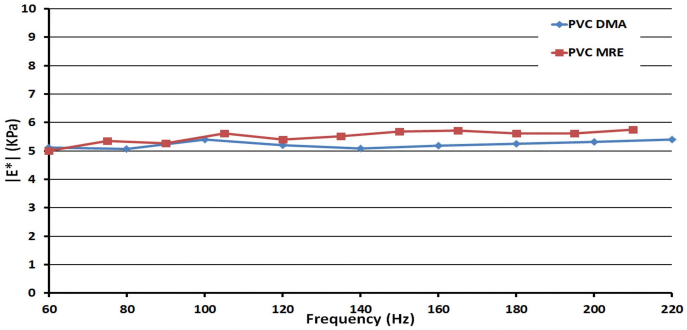

Fig 3: Comparison of DMA and MRE values of |E*| for PVC gel

MRE was performed on a large volume sample of the PVC gel over the same range of frequencies. Figure 3 shows a comparison between the MRE and DMA results.

Discussion: Standard DMA systems are designed to measure the mechanical properties of materials over a wide range of stiffnesses. However they often do a poor job with very soft materials (biological tissues and soft gels) for a variety of reasons. A system for performing DMA on soft viscoelastic materials has been previously demonstrated (3). Results showed good correlation between their system and standard rheometry DMA, but no comparison to MRE was performed. Our system uses essentially the same DMA principles described in (2) but is significantly different in that it does not require the measuring device to come in contact with the sample being tested. Inertial effects resulting from the moving mass and the sample can be mitigated by monitoring the level of strain produced for a given applied stress. The theoretical upper test frequency is limited only by the experimental setup (sample thickness, area and the mass used) and the frequency response of the laser vibrometer (1Hz to 20KHz for the Vibromet 500). In reality this system is best suited for measuring materials with |E*| values < 50-100KPa due to sample thickness, shear wavelength, and inertial mass constraints. The results show that our method can determine |E*| values in samples of varying stiffness. In addition, the results compare favorably with those obtained using MRE. Further comparisons between MRE and DMA are needed to establish the correlation of the two methods over a wide range of stiffness values.

References: 1) Shire, N. J., M. Yin, et al. (2011). Journal of Magnetic Resonance Imaging 34: 947-955.
2) ISO 6721-1 and ASTM D 4092
3) Arbogast, K, Thiabault, K, Pinheiro, BS, Winey, K, Margulies, S, J. Biomechanics, 30:757-759, 1997