Published in final edited form as:

Phys Med Biol. 2011 October 7; 56(19): 6379–6400. doi:10.1088/0031-9155/56/19/014.

Viscoelastic properties of soft gels: a comparison of magnetic resonance elastography and dynamic shear testing in the shear wave regime

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Abstract

Magnetic resonance elastography (MRE) is used to quantify the viscoelastic shear modulus, G^* , of human and animal tissues. Previously, values of G^* determined by MRE have been compared to values from mechanical tests performed at lower frequencies. In this study, a novel dynamic shear test (DST) was used to measure G^* of a tissue-mimicking material at higher frequencies for direct comparison to MRE. A closed form solution, including inertial effects, was used to extract G^* values from DST data obtained between 20 and 200 Hz. MRE was performed using cylindrical “phantoms” of the same material in an overlapping frequency range of 100 to 400 Hz. Axial vibrations of a central rod caused radially propagating shear waves in the phantom. Displacement fields were fit to a viscoelastic form of Navier’s equation using a total least squares approach to obtain local estimates of G^* . DST estimates of the storage G' ($\text{Re}[G^*]$) and loss modulus, G'' ($\text{Im}[G^*]$) for the tissue-mimicking material increased with frequency from 0.86 to 0.97 kPa (20 – 200 Hz, $n = 16$), while MRE estimates of G' increased from 1.06 to 1.15 kPa (100–400 Hz, $n=6$). The loss factor ($\text{Im}[G^*]/\text{Re}[G^*]$) also increased with frequency for both test methods: 0.06 to 0.14 (20 – 200 Hz, DST) and 0.1 to 0.23 (100 – 400 Hz, MRE). Close agreement between MRE and DST results at overlapping frequencies indicates that G^* can be locally estimated with MRE over a wide frequency range. Low signal-to-noise ratio, long shear wavelengths and boundary effects were found to increase residual fitting error, reinforcing the use of an error metric to assess confidence in local parameter estimates obtained by MRE.

MeSH Keywords

Elasticity Imaging Techniques; Computer-Assisted Image Interpretation/methods; Imaging Phantoms; Viscoelastic Substances; Stress; Mechanical/instrumentation

1. Introduction

Magnetic resonance elastography (MRE) is a novel experimental technique for probing the dynamic shear modulus of soft biological tissue non-invasively in living subjects (Muthupillai *et al.* 1995). To perform MRE, shear waves are excited by external harmonic

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mechanical actuation, and a standard MRI scanner equipped with a specialized imaging sequence is used to capture spatiotemporal images of the propagating wave field. Regional estimates of tissue shear modulus are made by local analysis of the wave field using wavelength measurement, direct inversion of the wave equation, or inverse finite element methods. These modulus estimates can be used to assess baseline properties of healthy tissues or to identify local or regional changes in tissue properties associated with disease.

The majority of MRE studies have estimated the elastic shear modulus, often at a single frequency. The accuracy of the method has been assessed by comparing estimates of the elastic shear modulus in surrogate, non-tissue, samples to the results of mechanical tests of the same material or to estimates from ultrasound elastography (Oudry *et al.* 2009). The most common phantom materials include agar (Muthupillai *et al.* 1995; Hamhaber *et al.* 2003; Ringleb *et al.* 2005) and gelatin (Doyley *et al.* 2003; Chan *et al.* 2006; Doyley *et al.* 2007; Atay *et al.* 2008) or a blend of these materials (Oudry *et al.* 2009; Henni *et al.* 2010) with shear modulus values reported in the range of 0.5 to 60 kPa. A variety of mechanical test methods have been used: static compression (Muthupillai *et al.* 1995; Plewes *et al.* 2000; Hamhaber *et al.* 2003; Chan *et al.* 2006), oscillatory linear shear (Ringleb *et al.* 2005), oscillatory rotational shear (Atay *et al.* 2008), or oscillatory compression (Doyley *et al.* 2010; Perreard *et al.* 2010). These studies have shown reasonable agreement between the *elastic* shear moduli measured with MRE and those measured by mechanical tests, even though the frequency range of direct mechanical testing is usually lower than the frequency range used for MRE in the same studies. Similar trends in the elastic shear moduli measured by MRE and transient ultrasound elastography were found for frequencies from 60 to 220 Hz (Oudry *et al.* 2009).

More recently, MRE has been used to characterize the components of the *viscoelastic* shear modulus ($G^* = G' + iG''$, where G' is the storage modulus, and G'' the loss modulus) for brain, liver and skeletal muscle tissue (Sinkus *et al.* 2005; Klatt *et al.* 2007; Green *et al.* 2008; Sack *et al.* 2009; Klatt *et al.* 2010b; Streitberger *et al.* 2010; Wuerfel *et al.* 2010; Clayton *et al.* 2011; Riek *et al.* 2011). Substantial differences in viscoelastic shear modulus values of brain tissue have been observed in studies performed by different investigators. Differences in experiment setup, data collection, and data analysis may be confounding factors.

Oscillatory, or dynamic, shear testing (DST) has been frequently used to characterize soft biomaterials. Thin samples of the material are subject to oscillatory shear strains. These tests may be done on a commercial rheometer (Vappou *et al.* 2007; Bayly *et al.* 2008; Hrapko *et al.* 2008) or a custom-built system (Arbogast *et al.* 1997; Arbogast *et al.* 1998; Madsen *et al.* 2008). In these systems, shear force or shearing torque is measured and converted to shear stress, usually over a range of frequencies, and the data are analyzed to obtain the complex shear modulus. The data analysis method assumes that the shear displacement is linear and shear strain is constant through the thickness of the sample. In soft materials, very thin samples are typically used to avoid inertial effects (shear waves) at higher frequencies. As the thickness of the sample decreases, it is more difficult to cut samples of uniform thickness and to maintain structural integrity of the sample. Thus, in practice, shear modulus estimates of brain tissue and other soft materials using DST without inertial correction are limited to low frequencies (Madsen *et al.* 2008). Investigators who have used MRE to quantify the components of the viscoelastic shear modulus (i.e. the storage modulus, G' , and the loss modulus, G'') of porcine brain tissue (Vappou *et al.* 2007) and bovine liver tissue (Klatt *et al.* 2010a), have directly compared results to oscillatory rheometry. Both studies showed qualitative agreement of trends in the values of G' , and G'' with frequency, but rheological tests of porcine brain tissue were performed at a much lower frequency (0.1 to 10 Hz) than MRE (80 to 140 Hz), making quantitative interpretation of results difficult. Hrapko and co-workers (Hrapko *et al.* 2008) have emphasized the wide range of values of brain tissue shear

modulus obtained from mechanical tests, due to differences in temperature, hydration, sample size and boundary conditions.

The primary goal of this study is to assess the accuracy of MRE for determining the components of the *viscoelastic* shear modulus of a homogeneous, soft, tissue-mimicking material. Benchtop mechanical tests and MRE were performed in an overlapping frequency range to allow direct comparison of frequency-dependent viscoelastic behavior. Dynamic shear testing (DST) in this study was deliberately performed in a regime in which shear waves affect the force-displacement relationship. Shear wave effects in DST are explicitly taken into account as they provide valuable information for comparison to corresponding MRE measurements.

MRE studies were carried out using the same tissue-mimicking material in a cylindrical geometry. Axial displacement of a central rod created radially propagating shear waves. MRE displacement data is analyzed both by (1) direct (local) inversion of the shear wave equation and (2) using a closed-form solution of the specific boundary value problem. By using two different approaches for analysis of shear wave displacement fields, we are able to investigate the effect of algorithmic steps (numerical differentiation, discretization error and local fitting error) on estimates of both the storage and loss moduli.

2. Methods

2.1 Gelatin preparation

Food grade gelatin (Knox) was mixed with de-ionized water and glycerol to produce a mixture of 2.8% w/w gelatin. Glycerol stabilizes gelatin mixtures by increasing their melting temperature (Joly-Duhamel 2002) and shear modulus (Nixon *et al.* 1966; Baumberger *et al.* 2006) and was also found to reduce water loss during mechanical testing. First, 4.03 g of gelatin was sprinkled on 70 g of room temperature de-ionized water and allowed to stand for approximately 10 minutes. 70 g of glycerol was heated to 50 °C in a water bath and then added to the gelatin/water mixture. The gelatin/water/glycerol mixture was then heated to 60 °C in a water bath to fully dissolve the gelatin. The final mixture had a density of approximately 1.1 g/cm³.

2.2 MRE phantom preparation

Approximately 85 g of the warm gelatin mixture was poured into a 45 mm diameter cylindrical container (see figure 1a), filling the container with gelatin to a depth of 48–50 mm. The actuator fit into a custom cap placed on top of the container. A 3 mm diameter polypropylene actuation rod extended approximately 20 mm into the mixture. After the mixture set, the entire container was sealed and refrigerated overnight at 4 °C.

2.3 DST samples

A fixed mass (39.8 g) of the warm gelatin mixture was poured into 100 mm cell culture dishes for each experiment, resulting in samples that were approximately 5.8 mm thick. The dishes were thinly coated with vegetable oil so that punched samples could be easily removed. After the gelatin mixture had set, the dishes were sealed and refrigerated overnight at 4 °C. A circular punch (15 mm dia.) was used to punch cylindrical samples from the gel. Each cylindrical sample was weighed before and after testing.

2.4 MRE data acquisition

Elastography data were obtained for each phantom at 4.7 T using a Varian DirectDrive™ small-animal MR scanner. The scanner consists of an Oxford horizontal-bore magnet, Magnex self-shielded gradient coils, and high-performance, gradient power amplifiers

(Copley Controls Corp.) capable of providing 45 G/cm peak magnetic-field gradient amplitude within 0.20 msec. MRE data were collected with a commercial quadrature volume coil (Varian).

The gelatin-filled container was placed horizontally inside the volume coil (see figure 1b). Small foam spacers were used to center the container in the coil. Mechanical vibrations were generated by an amplified piezoceramic-actuator (APA100M-NM, Cedrat Technologies) and transmitted to the sample via a polypropylene rod that had been embedded in the gelatin mixture before it set. The actuator was powered by a low-current, high-voltage amplifier (EPA 105, Piezo Systems Inc). A sinusoidal voltage waveform was supplied to the amplifier by a transistor-transistor logic (TTL) equipped function generator (FG-7002C, Ez Digital Co., Ltd.).

A customized gradient-recalled echo NMR imaging pulse sequence, with a sinusoidal motion-encoding magnetic-field gradient event, was used to record spatiotemporal tissue motion as a shift in NMR signal phase. The imaging sequence was triggered by a TTL pulse, allowing the function generator to control image acquisition and scanner-actuator synchronization. The actuator was run uninterrupted for the duration of each experiment to ensure steady-state harmonic material response was measured.

A central section of each phantom was imaged with 11 contiguous trans-axial slices in an interleaved manner. The image acquisition parameters were: resolution: $250 \times 250 \times 500 \mu\text{m}^3$; TR/TE: 200/13.75 msec. Two excitations were acquired and averaged. A magnetic field gradient amplitude of 8 Gauss/cm was used throughout for motion encoding. The number of MR motion-encoding gradient cycles varied with the actuation frequency from 1 to 4 to accommodate constant TR/TE imaging parameters. Phase contrast was doubled by acquiring two sets of motion-encoded data, one each with positive and negative polarity motion-encoding gradients, which were subtracted from one another. Eight time points were acquired per actuation cycle.

MRE experiments were performed at actuation frequencies of 100, 150, 200, 250, 325, 350 and 400 Hz. With the exception of 100 and 400 Hz, the order of the actuation frequencies was randomized for each MRE experiment. The amplitude of the imposed displacement was independently measured with a special bench-top test rig and a capacitance probe. The z -displacement (u_z) amplitude of the gelatin-embedded polypropylene rod ranged from approximately 40 μm at 100 Hz to less than 10 μm at 400 Hz. During each experiment, all three displacement components [u_x , u_y , u_z], were acquired for a single frequency from 100 to 400 Hz. For all other frequencies in that experiment, only the through-image-plane component of motion, u_z , was recorded. Acquisition time was approximately 22 minutes per displacement component, and the total imaging time for each experiment was approximately 5 hours.

2.5 MRE data analysis

Phase wrapping artifacts, if present, were removed via commercial software (Phase Vision Ltd). The relationship between the phase and displacement is governed by the amplitude of the motion encoding gradient, G , and number of motion encoding cycles, N . The proportionality constant for converting phase ϕ (in radians) into displacement u , including the factor of two introduced by positive and negative polarity image subtraction, is given by the following:

$$\frac{u}{\phi} = \frac{\omega}{2N\pi G\gamma} \quad (1)$$

where ω is the driving frequency (rad/sec); G is the motion-encoding gradient amplitude (Gauss/cm); γ is the gyromagnetic ratio for ^1H nuclei ($\gamma = 26.537 \times 10^4$ rad/sec/ Gauss), and N is the number of motion encoding cycles. Equation (1) is valid for sinusoidal motion-encoding gradients with the frequency equal to the driving frequency.

For each voxel, displacement data from the eight acquisition phases $u_z(x,y,z,t)$ were Fourier transformed in the time domain, and the coefficient of the fundamental harmonic, $U_z(x,y,z,\omega)$, was extracted, resulting in three-dimensional (3-D) field of these complex frequency domain coefficients. A 3-D Gaussian filter was applied to the entire 11 image stack of complex displacement data using the smooth3 function in MATLAB (R2009a, The MathWorks) with a filter kernel of $13 \times 13 \times 7$ pixels ($3.0 \times 3.0 \times 3.0$ mm) in the x , y , and z directions and a filter standard deviation of 3 pixels (0.75 mm). To remove edge effects in the x - y plane, only voxels whose entire smoothing kernel lay within the masked region of the field of view were included in the smoothed displacement field.

2.6 Direct inversion of the wave equation

The correspondence principle was used to transform the linear, isotropic, locally homogeneous, *elastic* Navier equation into its *viscoelastic* analogue. The components of the complex modulus G^* were estimated by fitting the axial component of displacement to a reduced equation of motion in which the dilatational component of displacement was neglected (Clayton *et al.* 2011):

$$(G' + iG'')\nabla^2 U_z(x, y, z, \omega) = -\rho\omega^2 U_z(x, y, z, \omega) \quad (2)$$

where ρ is the material density (1100 kg/m^3). A simple central difference scheme was used to approximate the Laplacian of the displacement field. Inversion was performed by a local total least-squares (TLS) fit using a $13 \times 13 \times 7$ kernel. Details of the inversion method are given in Appendix A. The mean value and standard deviation of G' and G'' were reported using only voxels in which the NRE of the local fit, computed using (A.3), was less than 0.5. The mean values of G' and G'' from different experiments were grouped by frequency. For each frequency, the mean values of G' and G'' for all six experiments and the corresponding standard deviations were computed.

2.7 Mathematical model of MRE experiment and closed-form solution

The MRE phantom geometry and the axial displacement due to the harmonic vibration of the displacement rod can be described accurately by a straightforward mathematical model. The appropriate boundary value problem is posed, using the wave equation in cylindrical coordinates and the viscoelastic correspondence principle. This model was used to independently estimate the values of G' and G'' from shear wave displacement data. Since the system is approximately axisymmetric, the displacement field is assumed to depend only on the radius, r , neglecting any variations in the angular coordinate, θ . Under these conditions, the reduced equation of motion in cylindrical coordinates becomes:

$$(kr)^2 \frac{d^2 U_z}{d(kr)^2} + kr \frac{dU_z}{d(kr)} + (kr)^2 U_z = 0 \quad \text{where } k = \sqrt{\frac{\rho\omega^2}{G^*}} \quad (3)$$

For a viscoelastic material, the wave number k and the displacement $U_z(kr)$ are complex quantities. The solution to the boundary value problem is the sum of Bessel functions of the first kind (J_0) and second kind (Y_0), both of order zero:

$$U_z(kr, \omega) = AJ_0(kr) + BY_0(kr) \quad (4)$$

We found analytical solutions to (4), specifying boundary conditions at the outer radius of the actuating rod ($r = r_i$) and at the outer radius of the gel (r_o) that matched the measured displacements at those locations for each frequency and experiment. The values of the constants A and B were determined from the boundary conditions. For an outwardly propagating wave, the displacement at the outer radius, $U_z(r_o)$, is zero and, if the amplitude of the displacement at the actuating rod is u_{ri} , then:

$$A = \frac{u_{ri}Y_0(kr_o)}{J_0(kr_i)Y_0(kr_o) - J_0(kr_o)Y_0(kr_i)}; B = -A \frac{J_0(kr_o)}{Y_0(kr_o)} \quad (5)$$

At frequencies of 250 Hz and above, we also observed an inwardly propagating wave (i.e. the displacement at r_o was not zero due to vibration of the gel container). With the same approach, we found the values of constants describing the inwardly propagating wave in terms of the displacement measured at the outer radius, u_{ro} :

$$A' = \frac{u_{ro}Y_0(kr_i)}{J_0(kr_o)Y_0(kr_i) - J_0(kr_i)Y_0(kr_o)}; B' = -A' \frac{J_0(kr_i)}{Y_0(kr_i)} \quad (6)$$

The four constants A , B , A' , B' were calculated determined from U_z values at r_o and r_i for $\theta = 0^\circ$ and $\theta = 180^\circ$ at each frequency using a single imaging plane (slice 6 of 11). Then the values of the complex modulus that best fit the unfiltered z -displacement data at that frequency were determined using a non-linear fitting function. This produced a global estimate of G' and G'' based on a complete 2-D displacement field. These values were compared to the mean values of G' and G'' found via local estimation as described in section 2.6.

2.8 Dynamic Shear Testing

In order to overcome the frequency limits of conventional DST for our soft gel material, we extended the frequency regime of DST by deliberately introducing shear waves in the sample, which created corresponding peaks in the measured shear force. The frequency and magnitude of this peak allowed us to determine the complex shear modulus of the material up to 200 Hz using a custom built DST system (figure 2b). The mass, m , and the approximate thickness of each punched circular DST sample were measured prior to testing. A punched circular DST sample (figure 2a) was placed on the flexure, which was displaced horizontally by the voice coil, causing the lower surface of the sample to undergo small amplitude (~ 0.03 mm) horizontal oscillations. We used a circular sample because it was easier to punch circular samples than to trim rectangular samples of consistent size. The voice coil was excited with sinusoidal oscillations at a constant frequency or with a “chirp”, which sweeps through frequencies from 0 to 200 Hz in 15 seconds using a SigLab data acquisition system (Spectral Dynamics, Inc). The horizontal displacement of the flexure, u_x , was measured with a capacitance probe. The difference between the signals of two piezoelectric force transducers (Model PCB209C, PCB Electronics) was used to calculate the net shear force when the sample is in contact with the upper plate. The 200 Hz frequency limit was chosen to avoid mechanical resonances of the upper assembly which occurred at frequencies above 280 Hz, as measured by an accelerometer attached to the upper assembly.

With the flexure operating at a low frequency, the vertical position of an upper assembly was adjusted with a digital micrometer until the upper circular plate touched the sample, as

indicated by the presence of a shear force signal and a slight change in normal force. Because the shear force transducers are stationary, inertial effects in the shear force measurement are limited to the sample. Once contact was established, the thickness of the sample was computed. The sample was compressed by 5% of this measured thickness, h , to provide consistent contact on the upper and lower surfaces (Chen *et al.* 2005) and a chirp signal was applied to the voice coil. Time domain signals from the force and displacement transducers were transformed into the frequency domain and a complex transfer function (net shear force/flexure displacement) was obtained.

Data analysis was performed using custom scripts in MATLAB. As shown in figure 3, the shear force, F_s , is divided by the sample cross-sectional area, A , to obtain an average shear stress. The amplitude of the harmonic shear strain is initially assumed uniform through the sample thickness and estimated as the amplitude of vibration (u_o) divided by the thickness of the sample, h . The “apparent” complex shear modulus is then calculated from the force/displacement transfer function multiplied by the ratio h/A :

$$G_{app}^*(i\omega) = \frac{\tau(i\omega)}{\gamma(i\omega)} = \frac{F_s(i\omega)/A}{u_o(i\omega)/h} \quad (7)$$

As other investigators (Arbogast *et al.* 1997; Madsen *et al.* 2008) have commented, sample inertia can cause shear waves to propagate within the DST sample. This invalidates the assumption of uniform shear strain and leads to deviations between the “apparent” shear modulus and the shear modulus of the material being tested. These deviations are usually avoided by using thin samples or testing at low frequencies. Because we wanted to directly obtain estimates of shear modulus of soft materials at frequencies above 100 Hz, we could not avoid measurements that included inertial effects in the sample. For thick samples of the gelatin/glycerol mixture, we found that two peaks in the shear force measurements were observed in the tested frequency range of 0 to 200 Hz.

Using an analytical model described by Berry (Berry 1958), we derived a relationship between the measured force/displacement relationship and the complex shear modulus of the material. This equation is valid when the shear force is measured on the stationary surface of the gel, as in our test setup. Shuck and Advani (Shuck *et al.* 1972) derived a similar relationship for thick circular samples of brain tissue undergoing torsional shear testing – in those experiments, the shear force transducer was located on the oscillating surface, similar to the setup in most oscillatory rheometers.

The displacement, $u_x(y,t)$, is assumed to be the separable product $U_x(y) e^{i\omega t}$ (i.e., the product of a function of y , multiplied by a harmonic time function $e^{i\omega t}$). From a force balance in the x -direction, the function $U_x(y)$ must satisfy the one-dimensional wave equation:

$$G^* \frac{d^2 U_x}{dy^2} + \rho \omega^2 U_x = 0 \quad (8)$$

where G^* is the complex shear modulus and ρ is the density of the material being tested. The homogeneous solution for $U_x(y)$ is:

$$U_x(y) = A_1 \cos(ky) + A_2 \sin(ky); k^2 = \frac{\rho \omega^2}{G^*} \quad (9)$$

Applying the boundary conditions $U_x(0) = u_0$ and $U_x(h) = 0$, the solution for the displacement is:

$$u(y, t) = [u_0(\cos(ky) - \cot(kh) \sin(ky))] e^{i\omega t} \quad (10)$$

The shear stress at the stationary surface ($y = h$) is :

$$\tau_{yx} = G^* \frac{\partial u}{\partial y} \Big|_{y=h} = -G^* k [u_0(\sin(kh) + \cot(kh) \cos(kh))] \exp(i\omega t) = -\frac{G^* k u_0}{\sin(kh)} \exp(i\omega t) \quad (11)$$

If the material is elastic, then G^* is a real quantity and τ_{yx} is singular when kh is equal to multiples of π , or when:

$$h = \frac{n\pi}{k} = \frac{n\pi}{\omega} \sqrt{\frac{G}{\rho}} \quad n=1, 2, \dots \quad (12)$$

For a viscoelastic material, $\sin(kh)$ is complex and the maximum magnitude of τ_{yx} is finite. For a given h , the value of ω at which τ_{yx} reaches a maximum will depend upon the specific functional form of G^* and the values of the function's parameters. In general, the ratio of the maximum magnitude of τ_{yx} to u_0 will be smaller for more viscous materials. For the model, the relationship between the shear stress and the nominal shear strain (u_0/h), i.e. the apparent modulus, is given by:

$$G_{app}^*(i\omega) = \frac{\tau(i\omega)}{(u_0/h)} = -\frac{G^* kh}{\sin(kh)} \quad (13)$$

We fit the experimental DST data to three viscoelastic material models: a “spring-pot” (Koeller 1984), a standard linear solid (or “Zener”) model and a fractional Zener model (Kohandel *et al.* 2005). These models have been used for interpreting MRE data obtained at multiple frequencies (Klatt *et al.* 2007; Sinkus *et al.* 2007). The best-fit values of material model parameters were obtained for each sample by minimizing the difference between the apparent modulus given by (7) and determined from experimental data and the predicted “apparent” modulus obtained from the closed-form solution given by (13). These fits were performed in MATLAB using standard functions and customized scripts.

3. Results

3.1 MR displacement fields and estimates of viscoelastic moduli by direct inversion of the wave equation

MRE experiments were performed on six gelatin phantoms on six different days. In one experiment, we also acquired a set of images with the imaging plane parallel to the z -axis at 250 Hz. These images were used to verify that the displacements were uniform in the region where the transverse images were obtained (figure 4). In addition, the magnitudes of U_x and U_y in transverse images were compared to the magnitude of U_z over the range of 100 to 400 Hz. The RMS magnitude of U_x and U_y was less than 25% of U_z at all frequencies, indicating that the dominant direction of displacement was along the z -axis.

The real and imaginary parts of the fundamental time harmonic of the displacement field, U_z (x, y, z, ω), are shown (figure 5, rows 1 and 2) for one experiment at frequencies of 100 to 400 Hz. The data shown is not spatially filtered.

The corresponding shear modulus estimates, computed from the spatially filtered displacement field using a fitting kernel of $13 \times 13 \times 7$, are shown in figure 5, rows 3 and 4. The modulus values at each pixel were spatially averaged to obtain mean values of G' and G'' for each frequency (figure 7a). The standard deviations of G' within the displacement field were less than 7% of the mean values; the standard deviations of G'' within the displacement field were less than 30% of the mean values.

3.2 MRE estimates of viscoelastic moduli by global fit of the closed-form solution

To verify the estimates of G' and G'' obtained by direct inversion, a single row of displacement data, passing through the center of the actuation rod (see figure 6a and 6c), was fitted to the closed-form solution of the boundary value problem in cylindrical coordinates. At frequencies below 250 Hz, shear waves propagated outward from the actuation rod and the shear wave amplitude decayed toward the outer radius of the cylinder (see figure 6b). At 250 Hz and above, there was also a noticeable inwardly propagating shear wave. This may have been caused by rigid body vibration of the gel cylinder container. In some cases this caused destructive interference of the inwardly and outwardly propagating wave in portions of the cylinder. However, it was possible to fit both wave fields simultaneously using a single estimate of G' and G'' (see figure 6d) by using the measured MRE displacements at both the inner and outer radii to determine the constants in (5) and (6). In addition, using the best-fit coefficients for the closed-form solution, the maximum shear strain (dU_z/dr) at each frequency was also computed and averaged for frequencies between 100 and 400 Hz. The maximum shear strains were all less than 3% and generally occurred near the actuation rod. Estimates of G' and G'' for all six experiments using both direct inversion and the closed-form solution were averaged at each frequency (see figure 7b and 7c).

As noted in the methods section, we observed that the estimates of G' and G'' at a particular frequency were strongly influenced by the order in which frequencies were tested in each experiment. The test order was randomized for frequencies between 150 and 350 Hz, but was not randomized for 400 Hz (always the first frequency tested) and 100 Hz (usually the last frequency tested). We examined the effect of test order by performing two additional MRE experiments, each at a single frequency (150 Hz or 400 Hz), with repeated data acquisition over a six-hour period. The estimates of G' and G'' decreased monotonically in those experiments, reaching an equilibrium value after about four hours.

As described in Appendix B, we found that this time-related decrease was likely caused by increasing temperature in the phantom over the course of each experiment and we developed a method to estimate the equilibrium values of G' and G'' for each experiment.

A comparison of the measured values of G' and G'' and the estimated equilibrium values is shown in figure 8. The equilibrium values of G' increased slowly from 1.06 ± 0.07 kPa (100 Hz) to 1.15 ± 0.16 kPa (400 Hz). G'' increased from 0.11 ± 0.01 kPa (100 Hz) to 0.27 ± 0.04 kPa (400 Hz). The loss factor increased from 0.11 to 0.23 over the same frequency range.

3.3 Dynamic shear testing (DST) results

For each MRE experiment, three samples from the same batch were tested by DST. During one experiment, two of the samples were damaged; hence data from a total of 16 samples were analyzed (table 1). The presence of two shear wave peaks within the tested frequency range was consistent among all the samples.

Using (9) and (13), we fit individual sets of experimental data to the three material models, as illustrated in figure 9a and 9b. In this figure, the apparent shear modulus amplitude and phase are plotted because they clearly illustrate the amplitude peaks at the frequencies where $|k| \approx \pi/h$ or $2\pi/h$. In general, we found that all three models could closely fit the data from DST tests. The primary difference in the model fits was the predicted magnitude of the first and second amplitude peaks. If the loss factor (G''/G') increases with frequency, the height of the second peak will be relatively smaller than the first.

The fractional Zener model was initially fit with the fractional exponent β fixed at values between 0.25 and 0.9. The value $\beta = 0.5$ allowed the model to best fit the height of both peaks simultaneously, as shown in figure 9a. Because the values of τ and β tend to vary inversely if both parameters are fitted, we fixed $\beta = 0.5$ and computed the best fit values of the remaining three parameters for each sample. In figure 9c, the predicted values of G' and G'' from the three models are plotted as a function of frequency from 0 to 400 Hz for one sample. All models predict an increase in G' and G'' with frequency.

The models differ primarily in their predictions of G' and G'' when extrapolated beyond the measurement range of 20 Hz to 200 Hz. The mean values of the parameters for each model (± 1 standard deviation) are shown in table 2, along with the mean predicted values of G' and G'' at 20 and 400 Hz. We used the fractional Zener model to compare DST predicted storage and loss moduli with the estimates from MRE experiments because that model most closely approximated the height of both shear wave peaks for the DST samples.

3.4 Comparison of MRE and DST predicted complex shear modulus

The values of G' and G'' predicted by the individual fractional Zener model parameters were averaged for all DST tests and compared to the average MRE-predicted equilibrium values of G' and G'' , obtained by scaling the experimental values according to the method described in Appendix B. As shown in figure 10, both MRE and DST estimates of the storage and loss moduli show a similar slow increase in G' and G'' with frequency. At frequencies above 200 Hz, the DST predicted loss modulus is lower than the MRE estimate. As shown in figure 9c and table 2, the predicted values of G'' are more sensitive to the choice of model than G' . For the fractional Zener model, increasing the parameter β will increase the predicted values of G'' at high frequencies so there is a greater variability in the predicted values of G'' in the Zener model, equivalent to the fractional Zener model with $\beta = 1$.

4. Discussion

We have estimated the complex shear modulus of a soft viscoelastic material over a broad range of frequencies. Previous validation studies have used MRE frequencies below 100 Hz (Muthupillai *et al.* 1995; Doyley *et al.* 2003; Ringleb *et al.* 2005; Doyley *et al.* 2007; Doyley *et al.* 2010; Pattison *et al.* 2010; Perreard *et al.* 2010), similar to frequencies used in MRE of human tissues. Other validation studies have performed MRE over a higher frequency ranges, e.g. Hamhaber *et al.* (2003): 125 to 400 Hz; Chan *et al.* (2006): 50 to 200 Hz; Atay *et al.* (2008): 200 to 800 Hz; but in these studies, only the elastic shear modulus was computed with MRE and mechanical tests were performed at frequencies below those used for MRE.

Our results are the first in which estimates of the viscoelastic shear modulus from direct mechanical tests and from multi-frequency MRE are directly compared in a tissue-mimicking material in an overlapping frequency range above 100 Hz. MRE data were analyzed by direct, local inversion of the equation of motion and by globally fitting the displacement field to the closed-form solution of the axisymmetric boundary value problem. We showed that both analyses gave similar estimates of G' and G'' over the entire frequency

range studied. We used DST to directly measure the storage and loss moduli and extended its frequency range into the shear wave regime by accounting for sample inertia in our data analysis.

In order to validate our extension of DST prior to conducting our study, we checked that the modulus values obtained from DST in the shear wave regime were consistent with conventional DST. The frequency of the shear wave peak and the sample thickness were used to estimate the storage modulus using (12). Since reference values were not available for the viscoelastic shear modulus of the gelatin-glycerol blend we used, we prepared and tested samples of similar thickness while varying the gelatin concentration from 75% to 200% of the baseline value. We observed a linear increase in the frequency of the shear wave peak, consistent with a quadratic increase in modulus of gelatin-glycerol blends with gelatin concentration (Nixon *et al.* 1966). We also tested different sample thicknesses at the baseline gelatin concentration. The frequency of the shear wave peak increased linearly with decreasing thickness, in agreement with (12). As an additional consistency check during our study, we compared the apparent storage and loss moduli measured at 10 Hz in each sample with the model predicted values. At this low frequency, inertial effects are small. Model-predicted values using the fractional Zener model with $\beta = 0.5$ ($G' = 853 \pm 54$ Hz and $G'' = 34 \pm 2$ Pa) agreed closely with the measured values ($G' = 846 \pm 63$ Pa, $G'' = 39 \pm 34$ Pa).

When making quantitative estimates of the complex shear modulus using MRE, obtaining the displacement data is only the first in a series of data analysis steps. These steps include extraction of the fundamental time harmonic to separate the spatial and temporal variations in displacement, spatial filtering of displacement data, and calculation of G' and G'' on a point-wise basis or using a local fit to the wave equation. The end result of the data analysis is usually an "elastogram" (e.g. figure 5, rows 3 and 4), where the computed values of the storage and loss moduli are displayed. Spatial averages may be calculated within an anatomical region of interest (Sinkus *et al.* 2007), in a region where the displacement amplitude is deemed sufficiently large (Riek *et al.* 2011), or where a goodness-of-fit parameter has been estimated (Atay *et al.* 2008; Clayton *et al.* 2011). Since biological tissues may be heterogeneous, it is not always clear whether spatial variations in elastograms of G' and G'' are due to real differences in tissue properties or caused by limitations in the data collection or data analysis. In this study, we used a homogeneous material, so we do not expect G' and G'' to vary with location. The normalized residual error (NRE) of the local fit of G' and G'' provides useful information about the reliability of the fitted values of G' and G'' at a particular location. In regions of the sample where displacement amplitude is small, NRE tends to be larger, reflecting the lower signal-to-noise values in those regions. Longer wavelengths relative to the field of view reduce the magnitude of the Laplacian and increase its sensitivity to noise in the displacement values. In our study, the 3-D Gaussian filtering of a single displacement component across a stack of images slightly reduced the NRE compared to using a single slice, because signal noise was smoothed across adjacent imaging planes. However, the in-plane filter parameters were the most important factor for decreasing NRE in regions of low signal amplitude. Increasing the Gaussian filter kernel size usually decreased NRE, but the Gaussian filter kernel should not span more than a wavelength. Furthermore, in possibly heterogeneous tissue samples, a large spatial filter kernel can span boundaries between different regions. Selection of a NRE threshold is specific to the experiment being performed and high NRE thresholds may be unavoidable. *In general, using a larger NRE threshold implies a larger uncertainty in the estimated values of G' and G'' .*

The good agreement between the MRE and DST results provides confirmation that local, direct inversion of the equation of motion can estimate both the storage modulus and loss modulus of a viscoelastic material. The Kramers-Kronig (K-K) causality relation provides a

way to check the consistency of the frequency dependence of the MRE estimates of the storage and loss moduli. The exact K-K relation requires measurement of both G' and G'' as continuous functions of frequency over an infinite domain. This is not feasible with MRE, where discrete frequencies are tested over a finite frequency domain. We used a low-order, local approximation of the K-K relation to predict the value of the storage modulus based on measured values of the loss modulus (Tschoegl 1989; Madsen *et al.* 2008). First, G'' was fit to a first-order polynomial and substituted into the low-order approximate relation between the storage and loss moduli obtained from the K-K relation, i.e.:

$$\frac{dG'(\omega)}{d \ln \omega} \approx \frac{2}{\pi} G''(\omega) \quad \text{where } G''(\omega) = a_1 \ln \omega + a_o \quad (14)$$

This approximate relation was then integrated to estimate the storage modulus. This method gives a solution up to an arbitrary integration constant, which is chosen to match the measured value of G' at one experimental frequency, denoted ω_o :

$$G'(\omega) - G'(\omega_o) = \frac{2}{\pi} \int_{\ln \omega_o}^{\ln \omega} (a_1 \ln \omega + a_o) d(\ln \omega) = \left(\frac{a_1}{2} (\ln \omega)^2 + a_o (\ln \omega) \right) \Big|_{\ln \omega_o}^{\ln \omega} \quad (15)$$

Using this approximation, the trends in the mean equilibrium values of the storage and loss moduli appear consistent with the K-K causality relations (figure 11).

We found that our MRE phantoms reached temperature equilibrium three to four hours after the MRE experiments began. The initial rise in the gel's temperature appears to coincide with decreases in G' and G'' over the same time frame. One explanation for the time-dependent change in modulus is the sensitivity of the gelatin-glycerol blend to temperature. Our DST tests were conducted at room temperature, which was 22 – 24 °C. DST samples are much smaller than the MRE phantom and will reach equilibrium with the surroundings more quickly. Since the DST samples experience significant mechanical work, including a brief pass through a type of mechanical resonance with the apparatus during the test, it is likely that the sample temperature increased above room temperature. When our MRE predicted storage and loss moduli are adjusted to equilibrium values (i.e., the values we would expect if the gel phantom had been in the scanner for 4–5 hours prior to MRE data collection), the values of G' and G'' in the overlapping frequency range show reasonable agreement and similar increase with frequency.

All of our measurements were made between 24 and 32 hours after mixing the gel ingredients. Frequency test order was randomized and modulus estimates were consistent with frequency after correcting for temperature change during the test, suggesting that sample mechanical behavior remains stable during the test period. Compared to gels made with gelatin and water only, gelatin-glycerol gels lose much less mass due to evaporation during storage, and can be stored for weeks without apparent degradation. We did not investigate whether mechanical properties were affected by extended storage.

The loss factor (G''/G') is used as a measure of a material's dissipative (viscous) behavior. Shear waves in a material with a large loss factor will attenuate over fewer wavelengths, making penetration of shear waves into a material more difficult. The loss factor for the gelatin-glycerol mixture was 0.12 to 0.20 over the range of 100 to 400 Hz, which is larger than values found for agar or agar-gelatin mixtures in rheologic measurements, but comparable to values reported for 15% gelatin-20% glycerol mixtures (Perreard *et al.* 2010) at frequencies of 75 to 125 Hz or agar-gelatin blends at frequencies of 60 to 220 Hz (Oudry *et al.* 2009). Sack and co-workers (Papazoglou *et al.* 2008; Riek *et al.* 2011) have used an

agar-glycerol-water mixture as a soft, viscoelastic tissue-mimicking phantom, but its properties have not been characterized with independent mechanical tests. Previous *in vivo* MRE studies suggest that the loss factor of brain tissue is in the range of 0.4 to 0.6 at 50 Hz (Klatt *et al.* 2007; Sack *et al.* 2009). Thus, while the gelatin-glycerol mixture we used is viscoelastic, its behavior is still markedly more elastic than brain tissue.

The sensitivity of the viscoelastic properties of the gelatin-glycerol blend to temperature changes during testing is a limitation that should be considered when choosing a phantom material. Hall and co-workers (Hall *et al.* 1997) measured the elastic properties of agar and of gelatin crosslinked with formaldehyde to improve stability for ultrasound elastography. The cross-linking process takes several weeks to months to complete in the gelatin and the increase in melting temperature is accompanied by a large increase in elastic modulus, making fabrication of soft phantoms difficult. The authors also reported that agar gels exhibited non-linear elastic behavior. Ease of fabrication, cost and tunability are also important factors in choosing a phantom material, and in these areas the gelatin-glycerol blend has advantages. In future studies, the sensitivity to temperature changes can be mitigated by allowing the MRE phantoms to equilibrate for several hours before use – this should reduce time-dependent changes in the shear moduli that we observed and characterized.

Conclusions

The viscoelastic properties of a tissue-mimicking material were measured using a novel mechanical test technique (DST in the shear wave regime) and compared to properties obtained from MR elastography experiments. Storage and loss moduli were estimated from MRE displacement fields using (1) direct inversion and (2) by fitting a closed-form solution appropriate for our phantom geometry. The two methods gave similar values for both components of the shear moduli over the range of frequencies studied. We found that the trends in MRE storage and loss moduli were similar to those obtained from DST, though the mean values were about 10% higher in the overlapping frequency range. These results confirm that both storage and loss moduli of a moderately viscoelastic material can be reliably estimated using MRE. Confidence in these parameter estimates should be assessed by a “quality of fit” measure such as normalized residual error. These findings can also provide a basis for assessing the quantitative accuracy of shear moduli obtained from MRE of soft tissues *in vivo*.

Acknowledgments

This work was supported by NIH R01 NS055951 (Bayly) and NIH R21 EB005834 (Bayly). Special thanks to Kate Wilson, who assisted with mechanical testing, and the Biomedical Magnetic Resonance Laboratory at Washington University, whose scanner was used for MRE studies.

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Appendix A. Local approximation of the complex shear modulus by direct inversion

According to (2a) and (2b), the components of the complex shear modulus can be determined from the displacement field and the corresponding Laplacian field, computed from finite difference approximations of the second spatial derivatives of the displacement field. In practice, noise in the displacement and Laplacian fields leads to errors in local estimates of the complex shear modulus. In ordinary least squares (OLS), it is assumed that there is no error in the measurement of the independent variable, i.e. the variance of the independent variable measurement error, ε_{η} , is zero. The variance in the error of

measurements of the dependent variable, ε_β , is inferred from a goodness-of-fit metric. If there are measurement errors (noise) in both the independent and dependent variables, then the total least squares (TLS) method may provide a closer approximation to the values of G' and G'' than OLS. We implemented TLS in MATLAB, using singular value decomposition (Golub *et al.* 1980). The variables were centered and scaled prior to fitting:

$$\hat{x} = \frac{(x - \bar{x})}{\sigma_x}; \hat{y} = \frac{(y - \bar{y})}{\sigma_y} \quad (\text{A.1})$$

where $\bar{x}$ and $\bar{y}$ are the mean values, σ_x and σ_y are the variances, and $\hat{x}$ and $\hat{y}$ are the centered and scaled values of the independent and dependent variables, x and y . The correlation coefficient r (Mendenhall 1983) can be computed directly from $\hat{x}$ and $\hat{y}$:

$$r = \frac{\text{cov}(\hat{x}, \hat{y})}{\sqrt{\hat{\sigma}_x \hat{\sigma}_y}} \quad \text{or } r^2 = \text{cov}(\hat{x}, \hat{y})^2 \quad (\text{A.2})$$

The normalized residual error (NRE) is defined as:

$$\text{NRE} = \sqrt{1 - r^2} \quad (\text{A.3})$$

The variances $\hat{\sigma}_x$ and $\hat{\sigma}_y$ of the centered and scaled variables are equal to one by definition. The TLS procedure then calculates the maximum likelihood slope, $\hat{a}_1$, by minimizing the perpendicular distances from the centered and scaled data points to line with intercept $\hat{a}_0 = 0$. The actual slope, a_1 and intercept, a_0 , are found by transforming the scaled variables back to x and y . The variances in the un-scaled and scaled measurement errors are given by:

$$\begin{aligned} \varepsilon_\beta &= \sum_{i=1}^N \frac{(x_i^* - x_i)^2}{N} = \sigma_\beta^2; & \varepsilon_\eta &= \sum_{i=1}^N \frac{(y_i^* - y_i)^2}{N} = \sigma_\eta^2; \\ \hat{\varepsilon}_\beta &= \frac{\sigma_\beta^2}{\sigma_x^2} = \sum_{i=1}^N \frac{(\hat{x}_i - \bar{\hat{x}})^2}{N}; & \hat{\varepsilon}_\eta &= \frac{\sigma_\eta^2}{\sigma_y^2} = \sum_{i=1}^N \frac{(\hat{y}_i - \bar{\hat{y}})^2}{N} \end{aligned} \quad (\text{A.4})$$

The TLS procedure minimizes the distances from $\hat{x}$ and $\hat{y}$ to the line $\hat{y}^* = \hat{a}_1 \hat{x}^*$ by satisfying the following equation:

$$\frac{-1}{\hat{a}_1} = \frac{(\hat{y}_i^* - \hat{y}_i)}{(\hat{x}_i^* - \hat{x}_i)} \quad (\text{A.5})$$

Rearranging, then squaring and summing both sides shows the relationship between $\hat{\varepsilon}_\beta$ and $\hat{\varepsilon}_\eta$ and the slope that is implicit in this TLS procedure:

$$\sum_{i=1}^N \frac{(\hat{x}_i^* - \bar{\hat{x}})^2}{(\hat{a}_1)^2} = \sum_{i=1}^N (\hat{y}_i^* - \hat{y}_i)^2 \quad \text{or} \quad \frac{N \hat{\varepsilon}_\beta}{(\hat{a}_1)^2} = N \hat{\varepsilon}_\eta \quad \text{so} \quad \frac{\hat{\varepsilon}_\beta}{\hat{\varepsilon}_\eta} = (\hat{a}_1)^2 \quad (\text{A.6})$$

Because both variables are centered and scaled, the magnitude of $\hat{a}_1$ will be unity, implying that $\hat{\varepsilon}_\beta \hat{\varepsilon}_\eta = 1$. This constraint can be removed by specifying an additional parameter λ .

(Golub *et al.* 1980). If, after centering and scaling the data, $\hat{y}$ is multiplied by λ , then (A.4) and (A.5) become:

$$\frac{-1}{\hat{a}_1} = \frac{\lambda(y_i^* - \hat{y}_i)}{(x_i^* - \hat{x})} \quad \text{and} \quad \frac{\hat{\varepsilon}_\beta}{\hat{\varepsilon}_\eta} = \lambda(\hat{a}_1)^2 = \lambda \quad (\text{A.7})$$

Since the Laplacian (the independent variable in our fitting procedure) is derived from the smoothed displacement field by numeric second order differentiation (the `del2` function in MATLAB), it tends to be relatively noisier than the displacement field, i.e. we expect $\lambda > 1$. To verify this, we simulated outwardly propagating shear waves in a circular cylinder using our closed form solution (5). We sampled the solution at intervals equivalent to the in-plane pixel resolution of 0.25 mm and duplicated this solution over 11 slices to create a simulated image stack of $192 \times 192 \times 11$ voxels. We added Gaussian noise to each voxel in masked image stack. This process was repeated using different amplitudes of Gaussian noise, and λ was computed using all voxels in the masked stack. We found that the magnitude of λ depended on both the simulated noise level and the size of the Gaussian smoothing kernel. For noise amplitude ranging from 0.05 to 0.25 times the prescribed displacement (u_{ri} in the closed form solution) and smoothing kernel size from $5 \times 5 \times 3$ to $13 \times 13 \times 7$, the range of λ extended from 1.0 (low noise, large smoothing kernel) to 70 (higher noise, small smoothing kernel). Based on these simulations, we set $\lambda = 10$ when fitting experimental MRE data.

Appendix B. Correction of shear moduli to equilibrium values

When analyzing the values of G' and G'' obtained from our MRE studies, we observed that the modulus values were larger when a given frequency was tested early in a particular experiment. In addition, the measured moduli at 400 Hz were consistently higher than those at other frequencies. Since we had always tested the 400 Hz frequency first, this led us to suspect that the properties of the gelatin phantoms were changing during the experiment. Such changes were likely due to warming of the sample, partly due to heat transfer from the environment, and partly to “RF heating” from the MR pulse sequence. To verify our observations, we ran two additional MRE experiments where we held the actuation frequency constant at 400 Hz or 150 Hz and repeatedly acquired MRE data for up to six hours. The data was analyzed using the 3-D direct inversion and 2-D closed form methods using the same filter and fitting kernels as for the previous experiments. The values of G' and G'' decreased rapidly, then approached an equilibrium value after four to five hours. We fit the relative decrease in G' and G'' with time to decaying exponential functions:

$$\frac{G' - G'_{eq}}{G'_{eq}} = a_0 \exp(-t/\tau_0) \quad (\text{B1.a})$$

$$\frac{G'' - G''_{eq}}{G''_{eq}} = a_1 \exp(-t/\tau_1) \quad (\text{B1.b})$$

Data were combined for both frequencies and fit to the exponential relation, obtaining constants of $a_0 = 1.00$ and $\tau_0 = 89$ minutes. G'' approached an equilibrium value faster than G' and decreased proportionately less ($a_1 = 0.71$ and $\tau_1 = 67$ minutes).

In another experiment, a small temperature probe was inserted into the gelatin-glycerol mixture when cast and left in place during overnight refrigeration at 4 °C. The phantom was

then subjected to typical MRE imaging pulse sequences, but image data was not acquired because of image noise caused by probe. The ambient temperature in the scanner room was $T_{\text{amb}} = 19\text{ }^{\circ}\text{C}$. The gel temperature, T_{gel} , reached T_{amb} in two hours and reached an equilibrium temperature of $21\text{ }^{\circ}\text{C}$ after 4 hours. We also prepared another gel phantom under the same conditions, and measured T_{gel} as the phantom sat on lab bench ($T_{\text{amb}} = 22\text{ }^{\circ}\text{C}$). In this case T_{gel} reached equilibrium at T_{amb} in approximately 2 hours. From this data, we concluded that the increase in T_{gel} could explain the decrease in the shear moduli, and that the primary cause of the temperature increase was the ambient temperature with a smaller, secondary effect due to RF heating. While the addition of glycerol to gelatin increases its melting temperature, there is a gradual decrease in G' and G'' below the melting temperature (Joly-Duhamel 2002) which is consistent with our observations.

Figure 1. Experimental setup for MRE. (a) MR phantom (b) orientation of phantom in MR scanner. Vertical dashed lines show approximate bounds of the transverse imaging planes used for MRE.

Figure 2.

a) Sample of gelatin-glycerol mixture used for dynamic shear testing (DST) b) Setup for DST. Samples were placed on the tester and subject to small amplitude vibrations of 0 to 200 Hz. For details, refer to the text.

Figure 3. Dynamic shear testing sample, illustrating nomenclature used in equations (7) to (13).

Figure 4.

The real component of the fundamental harmonic of the axial displacement, U_z , of a long axis (coronal) slice at an excitation frequency of 250 Hz, after spatial filtering with a 3-D Gaussian kernel of $9 \times 9 \times 5$ pixels. Dashed lines shows boundary of container and actuation rod; the green box outlines the approximate boundary of the stack of contiguous transverse slices.

Figure 5.

Example displacement fields and estimates of viscoelastic shear modulus parameters for each excitation frequency for one MRE sample. Rows 1 and 2: External mechanical motion induces propagating waves within gel cylinder. The real and imaginary parts of the fundamental harmonic coefficient, U_z , of the through-plane displacement are shown for the sixth of eleven contiguous slices used for inversion. Rows 3 and 4: Elastograms (images of the storage modulus, G' , and loss modulus, G''), calculated from the displacement fields of rows 1 and 2 after spatial filtering with a 3-D Gaussian kernel of $13 \times 13 \times 7$ pixels ($3.0 \times 3.0 \times 3.0$ mm). In this experiment, the data was acquired in the following order: 400 Hz, 250 Hz, 350 Hz, 325 Hz, 200 Hz, 150 Hz, 100 Hz. Scale bar at lower left equals 20 mm. Outer white circles indicate outer radius of gel cylinder, inner white circles indicate location of actuation rod.

Figure 6. (a) and (c): Real and imaginary parts of complex displacement field, $U_z(x,y)$, obtained by MRE at 150 Hz and 350 Hz respectively. Dashed yellow lines show the orientation of data used in closed-form solution. (b) and (d): Comparison of real and imaginary parts of unfiltered MRE displacement data (black solid line) and best fit parameters using closed-form solution (red dashed line).

Figure 7.

(a) Spatially averaged values of G' and G'' for a single experiment. Error bars show +1 SD.
 (b) and (c) Components of the viscoelastic shear moduli estimated from MRE displacement data using direct inversion (solid line, mean, error bar: + 1 SD) and the axisymmetric closed-form solution (dashed line, mean; error bar: - 1 SD). (b) G' or storage modulus (c) G'' or loss modulus

Figure 8. Viscoelastic shear moduli estimated from MRE displacement data using direct inversion (solid line, mean, error bar: + 1 SD) and the corrected equilibrium values (dotted line, mean; error bar: - 1 SD). (a) G' or storage modulus. (b) G'' or loss modulus.

Figure 9.

Typical results of DST test. (a) Magnitude of apparent shear modulus (see equations 9 and 13) (b) phase angle, ϕ , of apparent shear modulus. The phase angle changes rapidly at each shear wave peak. Experimental data (solid line) and best fits to standard linear solid (blue dashed line), fractional Zener (thick red dotted line), and springpot (green dashed line) models are shown. (c) Predicted G' and G'' from 0 to 400 Hz based on best-fit model parameters from test shown. The legend for each model is the same as for (a) and (b).

Figure 10.

Comparison of the viscoelastic shear moduli estimated from DST and MRE. Solid line shows DST model fit to fractional Zener model ($n = 16$; error bar: 1 SD). Dotted lines show extrapolation of DST model fit beyond the measured frequency range. Dashed lines show equilibrium values of G' and G'' using direct inversion of MRE data ($n = 6$; error bar: 1 std deviation). Modulus values for MRE have been corrected to equilibrium values as described in Appendix B. (a) G' or storage modulus. (b) G'' or loss modulus.

Figure 11.

Estimate of the frequency dependence of the viscoelastic storage modulus from MRE measurements of the loss modulus using a low-order approximation to the Kramer-Kronig (K-K) causality relation. Modulus values for MRE have been corrected to equilibrium values as described in Appendix B. (a) Equilibrium values of G'' from MRE (solid line, open circles) and predicted values based on K-K (dashed line, squares). Note that the vertical scale is magnified compared to previous figures. (b) Equilibrium values of G'' from MRE (solid line) and linear fit of mean values of G'' (dashed line) used to obtain estimates of G' . The integration constant was chosen to match the value of G' at 150 Hz.

Figure B.1.

(a) Normalized components of the viscoelastic shear moduli estimated from MRE displacement data at 150 Hz and 400 Hz taken over a period of 7 hours. Measurements of G'/G_{eq} (circles) and G''/G_{eq} (squares) are shown with open symbols (150 Hz) or filled symbols (400 Hz). Solid and dashed lines show decaying exponential function for G'/G_{eq} and G''/G_{eq} respectively, with parameters given in text. (b) Temperature measured using probe at center of another gel phantom. The gel reached an equilibrium temperature of 21 °C after 4 hours. Dashed line shows exponential fit to temperature with time constant of 1.3 hours.

Table 1 Properties of DST samples ($n=16$)

Property	Mean $\pm$ 1 SD	Units
In-plane area, A	177 ± 6	mm^2
Thickness, h	5.5 ± 0.2	mm
Density, ρ	1.1	g/cm^3
1 st peak frequency	83 ± 4	Hz
2 nd peak frequency	167 ± 9	Hz

Table 2

Best fit parameters for three DST models

Model	Model Equation	Parameters (Mean $\pm$ 1 SD, $n = 16$)	Mean storage and loss moduli (Pa)	
			20 Hz	400 Hz
Springpot	$G(\omega) = \kappa (i\omega)^\alpha$	$\kappa = 557 \pm 46 \text{ Pa}\cdot\text{s}^{-\alpha}$ $\alpha = 0.08 \pm 0.14$	$G' = 814 \pm 53$ $G'' = 103 \pm 6$	$G' = 1034 \pm 60$ $G'' = 131 \pm 9$
Zener	$G(\omega) = G_o \frac{1 + d(i\omega\tau_1)}{1 + (i\omega\tau_1)}$	$G_o = 918 \pm 68 \text{ Pa}$ $d = 1.79 \pm 0.21$ $\tau_1 = 0.24 \pm 0.14 \text{ ms}$	$G' = 919 \pm 68$ $G'' = 19 \pm 1$	$G' = 1128 \pm 54$ $G'' = 314 \pm 77$
Fractional Zener	$G(\omega) = G_o \frac{1 + d(i\omega\tau)^\beta}{1 + (i\omega\tau)^\beta}$	$G_o = 820 \pm 57 \text{ Pa}$ $d = 6.75 \pm 1.64$ $\beta = 0.5 \text{ (fixed)}$ $\tau^\beta = (1.48 \pm 0.70) \times 10^{-6} \text{ s}^{0.5}$	$G' = 868 \pm 57$ $G'' = 47 \pm 2$	$G' = 1036 \pm 57$ $G'' = 196 \pm 13$