EVALUATING MATERIAL MODELS FOR LOW-FREQUENCY MAGNETIC RESONANCE ELASTOGRAPHY OF AGAROSE GELS VIA FINITE ELEMENT SIMULATIONS

Julian A. Rey (1), Kulam N. Magdoom (1,2), Thomas T. Jones (3), Marcial Garmendia-Cedillos (3), Randall Pursley (3), Michal E. Komlosh (1,2), Thomas Pohida (3), Peter J. Basser (1)

(1) *Eunice Kennedy Shriver* National Institute of Child Health and Human Development, Bethesda, Maryland, USA
(2) The Henry M. Jackson Foundation for the Advancement of Military Medicine Inc., Bethesda, Maryland, USA
(3) National Institute of Biomedical Imaging and Bioengineering, Bethesda, Maryland, USA

INTRODUCTION

Magnetic resonance elastography (MRE) is an imaging technique used to estimate a tissue's mechanical properties remotely by measuring and analyzing the propagation of elastic body waves through the tissue. MRE of the liver provides a clinically approved assessment to support the staging of liver fibrosis [1]. In this setting, the mechanical waves are commonly produced at 20-200 Hz by an external actuator [1]. Preclinical MRE in animals is typically performed at a higher frequency range (200-1500 Hz) [1]. However, it is important to characterize the mechanical response of tissue at lower actuation frequencies because 1) mechanical properties tend to be frequency dependent, 2) new biomarkers owing to different mechanical phenomena may be available, and 3) body tissues undergo low-frequency displacements due to normal physiological processes which may be altered by disease.

In this study, various material models were employed to analyze and simulate the mechanical response of a cylindrical agarose gel sample to 10 Hz axial actuation. While pressure waves, as opposed to shear waves, are often ignored in MRE, a full viscoelastic inversion method was implemented to ascertain their potential contribution to the displacement field at low frequencies. Finite element method (FEM) models of the MRE experiment were developed to complement the inversion results by predicting the displacement field for a range of pressure and shear wave speeds.

METHODS

A cylindrical sample of 0.12% agarose gel measuring 60 mm in length and 19 mm in diameter contained in a glass vial was used as a tissue phantom for the MRE experiments. The free circular face of the gel was displaced axially by a piston 11 mm in diameter attached to a custom piezoelectric actuator operated at 10 Hz. A pulsed gradient spin echo (PGSE) sequence was used to acquire the 3D MRE data on a 7 T Bruker Biospin scanner. The displacement distribution data were acquired for 0.5 mm isotropic voxels in a 30 x 25 x 25 mm FOV using a Hadamard encoding scheme with b = 0, 250 s/mm^2, δ/Δ = 1.5/10 ms, and TR/TE = 200/16 ms.

Viscoelastic properties of the sample were estimated using the full algebraic inversion of the differential equation (AIDE) method described in Oliphant et al. [2]. In this method, the displacement field is substituted into the frequency domain formulation of the linear viscoelastic momentum equations assuming an isotropic, locally homogeneous material (Eq. 1)

$$\mu\nabla^2\boldsymbol{u} + (\lambda+\mu)\nabla(\nabla\cdot\boldsymbol{u}) = -\rho\omega^2\boldsymbol{u} \qquad (1)$$

Here λ and μ are Lame's first and second parameters, ρ is density, ω is the angular actuation frequency, and $\boldsymbol{u}$ is the complex-valued displacement at the actuation frequency. Complex-valued parameters λ and μ were estimated at each voxel by algebraic inversion and used to calculate the pressure and shear wave speeds by Eq. 2.

$$c_s = \sqrt{\frac{2|\mu|^2}{\rho(\mu'+|\mu|)}} \qquad (2)$$

Above, μ' is the real part of μ. The pressure wave speed c_p can be found by substituting the pressure wave modulus $\lambda+2\mu$ in place of μ. The full AIDE method was implemented in MATLAB R2022a.

FEM models were developed to predict the dynamic displacement field within the agarose gel phantom when subjected to the experimental loading conditions. The gel was modeled as either a compressible, isotropic linear elastic solid or a biphasic mixture. The biphasic mixture material consisted of a linear elastic solid matrix with pores through which an incompressible fluid phase may flow according to Darcy's law.

A half-cylinder geometry was subjected to sinusoidal axial displacement at 10 Hz on the piston-gel interface. No motion parallel or perpendicular to the tube walls was permitted. A symmetry boundary condition was prescribed on the remaining flat surface of the half-cylinder. The mesh consisted of 9,216 trilinear hexahedral elements with a maximum side length of 1.87 mm. The model was solved with the dynamic quasi-newton solver available in FEBio.

RESULTS

Axial actuation of the cylindrical agarose sample by a circular piston at 10 Hz produced a nearly axisymmetric displacement field consisting of alternately rotating toroids propagating axially (Fig. 1).

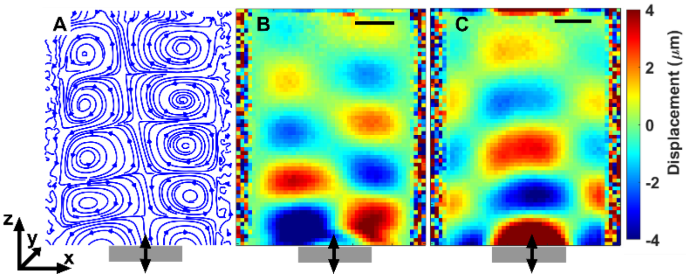

Figure 1: Measured displacement field in a sagittal cross-section. A) Displacement streamlines. B) X-direction displacement. C) Z-direction displacement. Scale bar = 5 mm. The piston is represented by the gray bar at the bottom of each panel moving along the sample axis.

While the X-direction displacement is orthogonal to the propagation direction, indicative of a transverse shear wave, the Z-direction displacement is parallel to the propagation direction, suggesting a longitudinal wave is present. An axially alternating pattern of positive and negative dilatation is apparent near the centerline of the sample (Fig. 2).

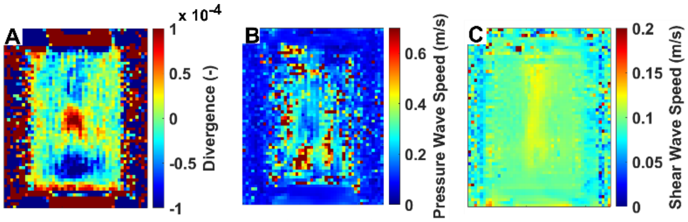

Figure 2: Viscoelastic wave properties derived from the displacement field. A) Divergence of the displacement field. B) Pressure wave speed. C) Shear wave speed.

Algebraic inversion of the viscoelastic momentum equation resulted in a shear wave speed estimate of ~0.1 m/s and a pressure wave speed approximately 3 to 6 times greater for many voxels in the sample, although the latter estimate is considerably noisier.

A linear elastic solid FEM model of the MRE experiment showed that in a material with lower compressibility (pressure wave speed = 2.4 m/s) the axial wavelength of the displacement waves is longer than in the experiment. A more compressible material (pressure wave speed = 0.6 m/s) resulted in a displacement field with a shorter axial wavelength, which is more like that observed in the experiment (Fig. 3).

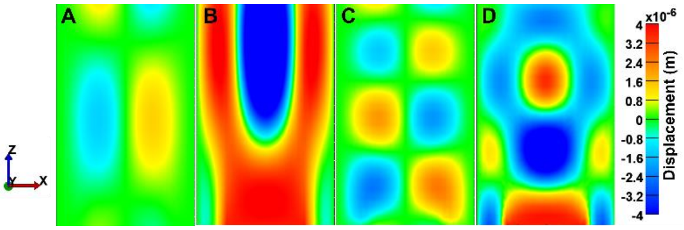

Figure 3: Varying pressure wave speed in solid FEM models. A) X-direction displacement and (B) Z-direction displacement for c_p = 2.4 m/s and c_s = 0.1 m/s. C) X-direction displacement and (D) Z-direction displacement for c_p = 0.6 m/s and c_s = 0.1 m/s.

An FEM model of a biphasic material consisting of a solid matrix with fluid-filled pores produced better agreement with the experiment than the linear elastic solid model (Figure 4). The solid and fluid velocities are nearly the same for this material, meaning they tend to move in-phase at this actuation frequency. However, dynamic changes in volume fraction of each phase appear to enable the development of axially shorter displacement waves.

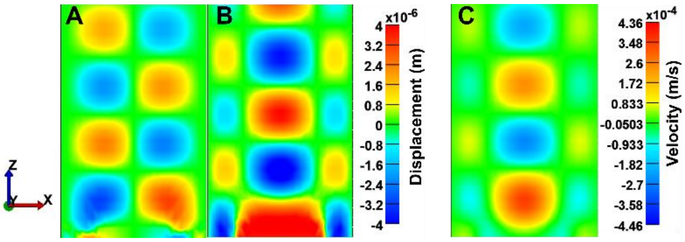

Figure 4: Modeled displacement and velocity fields for a biphasic material. A) X-direction displacement. B) Z-direction displacement. C) Solid and fluid phase velocity (same appearance).

DISCUSSION

This study demonstrates that low-frequency actuation of agarose gel can produce complex displacement fields exhibiting both transverse and longitudinal waves. While the longitudinal wave evident along the centerline of the sample in Fig. 1C may be an example of a "longitudinal shear wave" [3], our viscoelastic inversion (Fig. 2B) and FEM analyses (Fig. 3) suggest that slower pressure wave speeds (0.3 - 0.6 m/s) than typically assumed for tissue (~1540 m/s) [1] are present in the sample. The corresponding "compressibility" of the gel is not likely an intrinsic property of the gel constituents since the gel is mostly water but may instead be a consequence of changes in the local volume fraction of fluid. Such poroelastic effects may be relevant at lower actuation frequencies [1], and our biphasic model (Fig. 4) matches the measured displacement field better than the solid model (Fig. 3). The unexpected behavior of the gel at 10 Hz suggests the need to characterize mechanical properties of tissues at low frequencies to better understand their mechanical response to normal physiological loading.

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REFERENCES

[1] Manduca, A et al., *Mag Res Med*, 85:2377-2390, 2021.
[2] Oliphant, T et al., *Mag Res Med*, 45:299-310, 2001.
[3] Zhu, J et al. *Appl Phys Lett*, 110, 201101, 2017