

Tabletop magnetic resonance elastography for the measurement of viscoelastic properties in soft tissue micro samples

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Target audience: physicists and physicians interested in the viscoelastic properties of biological tissue.

Background: MR elastography (MRE) [1] is a unique imaging technique for mapping viscoelastic tissue parameters in vivo. Previous MRE studies have shown the high sensitivity of MRE to various diseases [2]. Studies in mouse models and tissue samples were conducted to reveal the relationship between viscoelastic constants and micro structural changes in the underlying viscoelastic network based on histopathological analyses [3-7]. However, directly linking histopathology with MRE requires: 1) small samples volumes of the same specimen used in MRE and histopathology and 2) fresh tissue samples, which imposes the need of fast MRE examinations which ideally take place near the histopathologist's lab.

Purpose: To develop and demonstrate a tabletop MRE system for measuring viscoelastic parameters of tissue micro samples.

Methods: The MRE system was developed based on a benchtop MRI scanner (Pure Devices GmbH, Würzburg, Germany) equipped with a 0.5T permanent magnet and research console drive. A spin echo sequence was implemented under Matlab (Mathworks, Natick, MA, USA) with trapezoidal motion-encoding gradients synchronized to the vibration frequency (MEG, 250 mT/m @ 2000 T/ms, through-plane direction, and toggled polarity for phase difference imaging). A loudspeaker was used for inducing vibrations of 0.5 to 1 kHz into small tissue samples (~1 cm³) placed in a glass tube (Ø 10 mm) as sketched in Fig.1. Further wave image acquisition parameters: 64x64 matrix, 15 mm FoV, 3 mm slice thickness, 40 ms TE, eight dynamic scans over a vibration period, MEG cycle number: 16, 18, 22, 26, 28, 32 (for 0.5, 0.6 to 1 kHz, respectively), total scan time approximately 15 min per frequency. The complex shear modulus G^* with real part G' (storage modulus) and imaginary part G'' (loss modulus) was calculated by direct Helmholtz inversion. The feasibility of MRE in this tabletop MRI system was demonstrated on a Sonogel sample and porcine liver tissue.

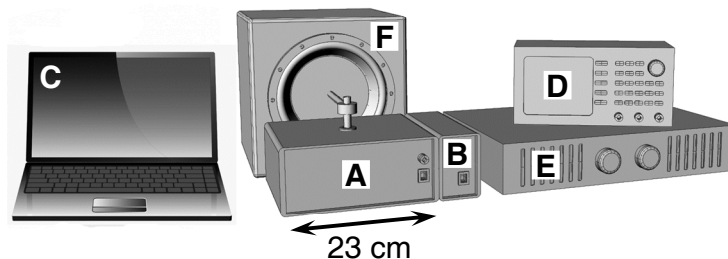


Fig. 1: Setup of the tabletop MRE system. (A) 0.5 T permanent magnet, (B) console drive, (C) control computer, (D) waveform generator, (E) amplifier, (F) transducer.

Results: Fig.2 shows representative magnitude MRE images and wave images for the gel and liver. The depicted regions of interest (ROI) were used for parameter averaging (the central part of the liver was omitted due to high wave damping). G' values of both samples are shown in Fig.3 as functions of drive frequency indicating the strong viscoelastic dispersion in both samples.

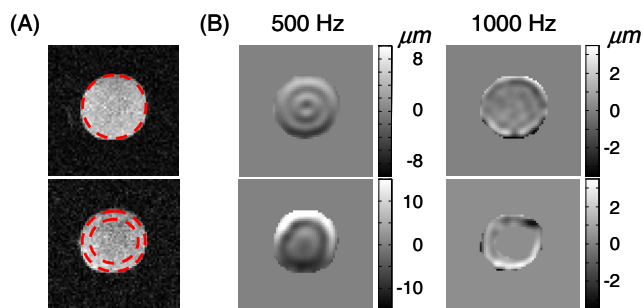


Fig. 2: Results for gel (upper row) and porcine liver (lower row): (A) magnitude images with ROIs used for further analysis, (B) wave images for 500 Hz / 1000 Hz vibration.

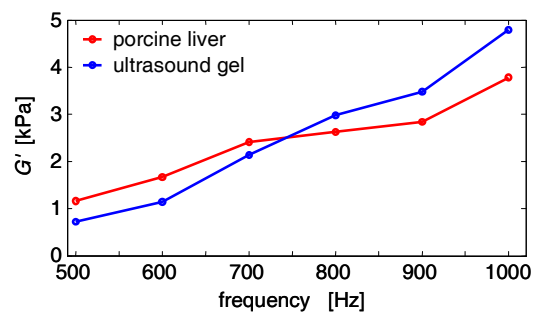


Fig. 3: Frequency dispersion of G' for the gel and porcine liver sample.

Discussion: The tabletop MRE system allowed us the measurement of viscoelastic parameters in soft tissue samples in a frequency range of 500-1000 Hz. The observed frequency dispersion in porcine liver is in good agreement with previously published data with lower absolute values (e.g. @ 800 Hz: $G' = 3.1$ kPa vs. $G' = 4.9$ kPa) than reported in [8]. We attribute this difference to degradation of the tissue in our current liver sample as well as to possible differences between porcine and bovine tissue in addition to age and temperature effects [6]. The strong dispersion seen in our gel sample is due to the very high viscosity of Sonogel which exhibits almost fluid material properties. Although encouraging first results were obtained, our new modality has still some technical limitations concerning acquisition time, motion sensitivity and automation. These issues can be resolved by (i) advanced 3D MRE implemented in Matlab including automated acquisition of full wave fields at multiple drive frequencies and (ii) the use of an external gradient amplifier providing gradients of 2 T/m. This eightfold increase in motion sensitivity should even enable vibration frequencies above 1 kHz and the analyses of stiffer tissue samples like cartilage.

Conclusion: The presented tabletop MRE system allows the fast measurement of viscoelastic parameters of small tissue samples at low costs with little requirements for space and maintenance. Therefore, it might support developments towards mechanics based histopathology that links MRE with etiology and pathogenesis of diseases.

References: [1] Muthupillai R, et al. Magnetic resonance elastography by direct visualization of propagating acoustic strain waves. *Science*. 1995; 269:1854-7. [2] Glaser KJ, et al. Review of MR elastography applications and recent developments. *J Magn Reson Imaging*. 2012; doi: 10.1002/jmri.23555. [3] Sack I, et al. Structure-sensitive elastography: on the viscoelastic powerlaw behavior of in vivo human tissue in health and disease. *Soft Matter*. 2013; 9: 5672-80. [4] Guo J, et al. Fractal network dimension and viscoelastic powerlaw behavior: II. An experimental study of structure-mimicking phantoms by magnetic resonance elastography. *Phys Med Biol*. 2012; 57: 4041-53. [5] Posnansky O, et al. Fractal network dimension and viscoelastic powerlaw behavior: I. A modeling approach based on a coarse-graining procedure combined with shear oscillatory rheometry. *Phys Med Biol*. 2012; 57: 4023-40. [6] Klatt D, et al. Viscoelastic properties of liver measured by oscillatory rheometry and multifrequency magnetic resonance elastography. *Biorheology*. 2010; 47: 133-41. [7] Schregel K, et al. Demyelination reduces brain parenchymal stiffness quantified in vivo by magnetic resonance elastography. *Proc Natl Acad Sci USA*. 2012; 109: 6650-5. [8] Klatt, et al. Wide-range dynamic magnetic resonance elastography. *J Biomech*. 2011; 44: 1380-6.