Title: Multifrequency Magnetic Resonance Elastography (MRE) of the Human Brain at 7T

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Introduction (50-250 words)

Magnetic resonance elastography (MRE) is a technique for determining the mechanical response of tissues using applied harmonic deformation and motion-sensitive MRI[1]. Studies using MRE to investigate the mechanical properties of the human brain are most commonly performed at conventional field strength (3 Tesla (T) or 1.5T), although there have been a few attempts at the ultra-high field strength, 7T[2–4]. Aiming for higher resolution scans of the human brain at 7T, MRE presents unique challenges of decreased signal-to-noise ratio (SNR) and lower shear wave motion sensitivity. Additionally, most biological tissues, including the human brain, exhibit a frequency-dependent mechanical response[5] which has yet to be explored at 7T. In this study, we investigate the frequency dependence of the mechanical properties of the human brain *in-vivo*. The purpose of this study is to perform Multifrequency MRE of the healthy human brain at the ultra-high field strength, 7T.

Materials and Methods (50-250 words)

Full brain coverage MRE was then performed on 10 healthy human subjects at 1.1mm isotropic resolution at 40, 50, and 60Hz, using a 32-channel head coil (Nova Medical) on a 7T Siemens Magnetom MRI Scanner. The MRE sequence was a modified single-shot multi-slice spin-echo 2D-EPI sequence with trapezoidal flow-compensated motion encoding gradients (MEGs), synchronized with the acoustic actuator by TTL triggering at the beginning of every TR. External vibration was applied to the surface of the phantom using a custom pneumatic actuator described in Triolo, *et al.*[6], with a 3000W power amplifier (Behringer) and high-pressure plastic tubing (3/4” ID). Phase images were reconstructed from raw data post-hoc using Gadgetron open-source image reconstruction, magnitude images were initially masked using SPM12[7], denoised using a MP-PCA algorithm[8] and unwrapped using a Segue Phase Unwrapping[9]. Curl filtering, Fourier decomposition, and a quartic smoothing kernel (scaled for resolution based on our previous investigation)[3] were used to acquire wavefield images, before Algebraic Inversion of the Helmholtz Equation was used to calculate the magnitude of the complex shear modulus ($|G^*|$)[10]. Octahedral Shear Strain Signal-to-Noise ratio (OSS-SNR)[11] was also calculated for each scan to ensure high enough quality for accurate viscoelastic inversion. Whole brain, white matter, and grey matter average $|G^*|$ for each subject at each frequency were calculated (Fig. 1).

Results, Conclusions, Discussions (50-350 words)

Using our custom 7T MRE sequence, pneumatic actuator, and advanced post-processing procedure, we successfully performed multifrequency MRE on 7 human subjects at 7T. Wavefield images and elastograms of a representative central slice for each frequency are shown in Fig 2. We found an increase in stiffness measurement with vibration frequency as consistent with previous literature at conventional field strengths (Fig. 1). Additionally, we determined that average $|G^*|$ white matter values are generally higher than that of grey matter, also consistent with literature (Fig. 1).

Of the initial 10 individuals scanned at each resolution, 3 were excluded due to low vibration amplitude in the 60Hz scan, resulting in an OSS-SNR value too low to be considered accurate for viscoelastic reconstruction (OSS-SNR < 3.0)[11]. This is due to hardware limitations of the MRE actuator, as vibration amplitude drop-off becomes more significant at higher frequencies. Multiple improvements to the MRE actuator to improve this, such as a thicker plate covering the subwoofer cone and smaller diameter, less compliant tubing, can be made and have been successfully implemented in other MRE setups. Additionally, geometric distortion becomes more apparent at higher frequencies, which should be addressed in future investigations.

In the future, this multifrequency MRE protocol can be used to determine region specific frequency-dependent mechanical properties as it has in the past at 3T[5], but at the ultra-high resolution possible at 7T. Additionally, with the suggested modifications to the custom MRE actuator, the frequency range of our multifrequency protocol can be extended to the 80-100Hz range to gather more frequency-specific mechanical properties of the human brain. By obtaining the multifrequency response of the human brain at the ultra-high resolution possible using 7T MRE, we can develop subfield specific material models. These material models can therefore be used to inform FE brain models and therefore simulate brain motion at the high frequency impacts accurately. Understanding brain movement and tissue deformation mechanisms during these impacts is a powerful strategy for predicting brain injury and developing preventative equipment.

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Figures:

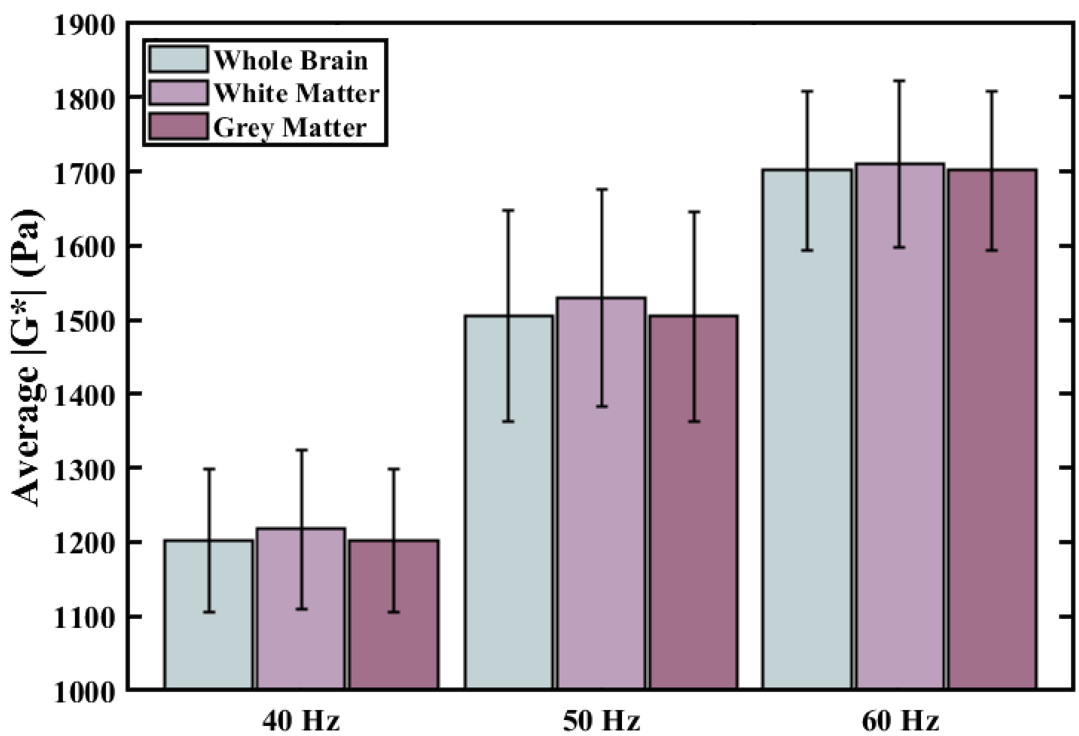

Figure 1: Average Whole Brain. White Matter, and Grey Matter |G*| Values at 40, 50, and 60 Hz Vibration Frequency Over Seven Healthy Human Subjects where Error Bars Indicate Standard Deviation

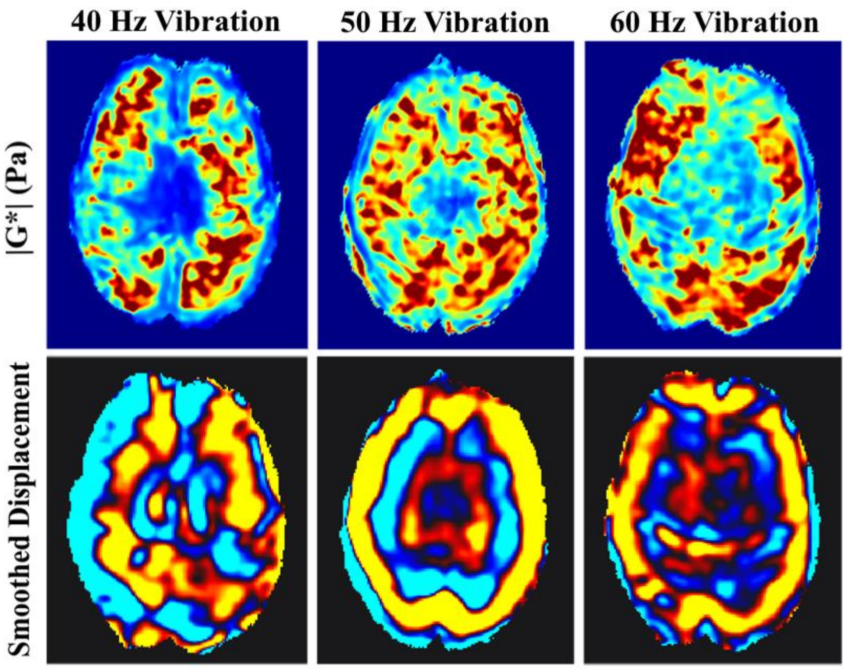

Figure 2: |G*| (top) and Smoothed Displacement (bottom) for the Central Slice of One Healthy Human Subject at 40, 50, and 60 Hz Vibration Frequency

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