Measuring the characteristic topography of brain stiffness with magnetic resonance elastography

Matthew C Murphy[1], John Huston[1], Clifford R Jack[1], Kevin J Glaser[1], Matthew L Senjem[1], Jun Chen[1], Armando Manduca[2], Joel P Felmlee[1], and Richard L Ehman[1]
[1]*Department of Radiology, Mayo Clinic, Rochester, MN, United States,* [2]*Department of Physiology and Biomedical Engineering, Mayo Clinic, Rochester, MN, United States*

Introduction: Magnetic resonance elastography (MRE) is an MRI-based technique to noninvasively measure tissue stiffness [1]. MRE is a three step process beginning with the introduction of shear waves into the tissue of interest. The shear wave motion is imaged with a phase-contrast MRI pulse sequence, and finally the shear wave images are mathematically inverted to calculate a stiffness map (or elastogram). Several groups have investigated MRE-based measurements of global brain stiffness as a novel biomarker of neurological diseases [2-4]. Since diseases of the brain have characteristic topographies, MRE will be most useful if it is capable of measuring brain stiffness on a regional basis. The purpose of this work was to develop a method for measuring regional brain stiffness free of edge- related biases that demonstrates high test-retest reliability.

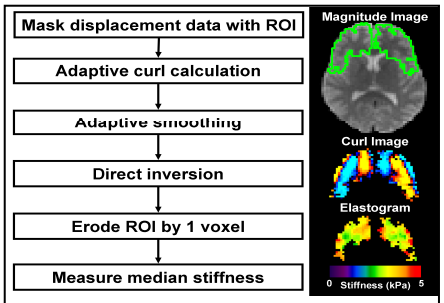
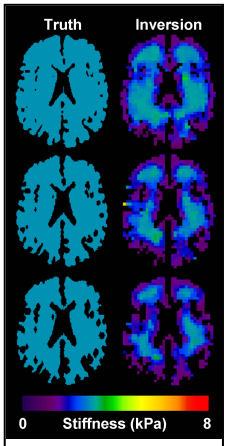


Figure 1. MRE postprocessing pipeline for regional brain stiffness measurement.

Methods: This study was approved by our IRB. After obtaining informed written consent, 10 volunteers were scanned 3 times each to assess test-retest reliability. MRE data were collected with a modified SE-EPI pulse sequence with the following parameters: 60 Hz vibration; TR/TE=3600/62 ms; FOV=24 cm; 72x72 image matrix reconstructed to 80x80; 48 contiguous 3 mm thick axial slices one 18.2 ms motion encoding gradient on each side of the refocusing RF pulse; x, y and z motion encoding directions; and 8 phase offsets spaced evenly over one period of 60 Hz motion. The resulting images had 3 mm isotropic sampling and were acquired in just under 7 minutes. Our approach to MRE postprocessing can be summarized by 3 steps: 1) calculate the curl of the displacement images; 2) smooth the data with a quartic smoothing kernel [5]; and 3) calculate stiffness using a direct inversion of the Helmholtz wave equation [6]. These steps are implemented by convolution with a particular kernel, and introduce edge artifacts when the kernel extends beyond the edge of the brain. To reduce the edge artifact, we used adaptive methods for the first two of these steps by creating unique convolution kernels for the edge voxels that did not extend outside the region of interest (ROI). We investigated 7 ROIs including global, frontal lobes, occipital lobes, parietal lobes, temporal lobes, deep gray matter/white matter (insula, deep gray nuclei and white matter tracts), and the cerebellum. The ROIs for each subject were calculated by warping an atlas in standard space to the subject's T1-weighted image, which were then registered and resliced to the T2-weighted MRE magnitude image. The pipeline for MRE-based regional brain stiffness measurement is summarized in the left panel of Figure 1. Example images from the frontal lobe ROI are shown in the right panel beginning with the MRE magnitude image with the ROI outlined in green, followed by the ROI-specific curl image and the ROI-specific elastogram. Test-retest reliability was measured by coefficient of variation (CV). Differences in regional brain stiffness across both regions and individuals were tested using ANOVA for repeated measures.



Figre 2. Effects of simulated atrophy in FEM simulations.

Results: The effects of atrophy are demonstrated in a series of finite element model (FEM) simulations that are shown in Figure 2. In the left column are the true stiffness maps given to the FEM, and in the right column are the corresponding elastograms after downsampling the wave images, calculating the curl, smoothing and calculating the stiffness by direct inversion as done in a brain MRE exam. Note the underestimated stiffness values near the edge of the elastograms, and also that the proportion of these edge voxels to the total number of voxels increases with increasing simulated atrophy (from the top to the bottom row). When using traditional postprocessing techniques, simulation experiments indicate that the ROI must be eroded by 3 voxels from every edge to measure a stiffness that is not biased by edge artifacts (top panel of Figure 3). On the other hand, this bias is removed by 1 erosion using adaptive methods (bottom panel of Figure 3).

Within the 10 volunteers, the median and maximum CVs for global brain stiffness were 0.72% and 1.15%, respectively. Stiffness can also be reliably measured within the smaller regions with a median CV no greater than 1.96% and a maximum CV no greater than 4.53% in all of the remaining ROIs. Furthermore, ANOVA indicates significant differences both between individuals ($p<0.01$) and between regions ($p<0.001$). The significant region-wise differences are indicative of a characteristic topographical distribution of brain stiffness. Considering the 4 lobes of the brain, stiffness is greatest in the occipital lobes (3.11 ± 0.16 kPa, median ± standard deviation), followed by the frontal lobes (3.05 ± 0.13 kPa), the temporal lobes (3.02 ± 0.18 kPa) and finally the parietal lobes (2.77 ± 0.15 kPa). Stiffness is lower in the cerebellum (2.31 ± 0.04 kPa), consistent with the findings of Zhang et al. [7].

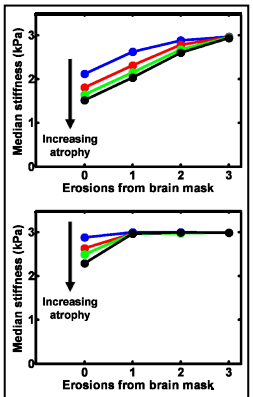


Figure 3. Stiffness as a function of ROI size using traditional (top) or adaptive (bottom) methods.

Discussion: In this work, novel methods were presented for measuring regional brain stiffness that are free of edge-related bias and provide high test-retest reliability. By masking the displacement images first and then calculating ROI-specific elastograms, this pipeline ensures that the regional stiffness measurements are independent of one another. This pipeline would not be possible in subjects with significant atrophy using traditional postprocessing techniques given the typical resolution of brain MRE exams, as 3 erosions would leave no voxels in some ROIs. Our results indicate that stiffness follows a characteristic topography within the brain. This technique provides a tool for improving the sensitivity of brain stiffness as a biomarker of neurological diseases (by optimizing the ROI), and also for evaluating its specificity (by demonstrating that changes in brain stiffness follow the known topography of disease).

References: [1] Muthupillai et al. Science 1995. 29(5232): 1854. [2] Streitberger et al. PLoS One 2012. 7: e29888. [3] Murphy et al. JMRI 2011. 34(3): 494 [4] Xu et al. Acta Rad 2007. 48: 327. [5] Romano et al. IEEE Trans UFFC 2000. 47: 1575. [6] Manduca et al. Med Image Anal 2000. 5: 237. [7] Zhang et al. J Biomech 2011. 44: 1909.