Reproducibility of Magnetic Resonance Elastography for Quantification of Hepatic Stiffness

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Introduction: Magnetic Resonance Elastography (MRE) has been previously described for assessment of the mechanical properties of soft tissue, such as the liver[1]. The propagation of acoustic strain waves through the tissue is measured from motion encoded phase difference images using an inversion algorithm, and the elastic shear modulus of the tissue is calculated[2]. MRE has been shown to distinguish between cirrhosis and moderate to severe fibrosis[3], and has great potential as a quantitative biomarker that directly reflects the severity of hepatic fibrosis in patients with chronic liver disease[4]. An important gauge of quantitative biomarkers is reproducibility, and longitudinal studies must provide meaningful, reproducible results to accurately track stiffness changes from intervention or disease progression. Therefore, the purpose of this work was to determine the reproducibility of MRE hepatic stiffness measurements in healthy volunteers.

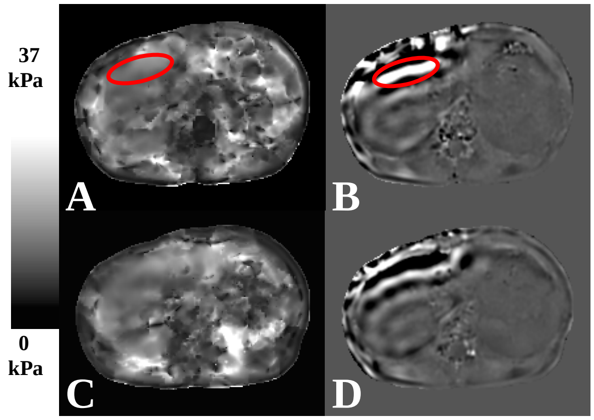

Figure 1: Stiffness (A) and wave image (B) of the first exam of a healthy volunteer. Corresponding stiffness (C) and wave images (D), respectively, of the same slice of the same volunteer acquired during the second exam. Exams were acquired sequentially, with the volunteer removed from the table between exams. The red circle indicates a region that was chosen as an ROI due to minimal wave interference.

Methods: Ten healthy volunteers (six men, four women) underwent two subsequent liver MR elastography exams. Mean age and weight were 30.9 years (range, 25-43) and 71.8 kg (range 45-98 kg). A passive pneumatic driver 19 cm in diameter was positioned on the rib cage and attached to an acoustic waveform generator.

The MRE exam consisted of the following parameters on a 1.5T Signa HDx (TwinSpeed, GE Healthcare, Waukesha, WI) using a 2D gradient echo sequence and an eight-channel cardiac coil: TE = 24.2 ms, TR = 100 ms, flip = 30, BW = ± 31.25 kHz, slice = 10 mm, 256 x 128 matrix, 75% asymmetric phase FOV, 4 slices, and FOV to fit each volunteer. A 60 Hz waveform with amplitude of 400 mV_{pp} was applied to the driver, and exam consisted of eight 22-second breath holds. Four axial slices were acquired; slices were chosen such that one slice was placed on the caudate lobe, two above the caudate lobe, and one below. Following the MRE scan, the volunteers were taken off the table, and the exam was repeated such that two exams were acquired sequentially on the same day.

Following imaging, two independent readers (CG and EB) took measurements of the stiffness images from both exams of volunteers. Regions of interest (ROI) from the anterior aspect of the liver (anterior, medial or lateral lobe) were copied from areas in the wave images with minimal wave interference to the stiffness images. An average and standard deviation of stiffness for each slice, exam, and volunteer was obtained by two readers.

ROI averages and standard deviations from both readers' exams analyzed with the following statistical tests: (1) means, standard deviations, and paired t-tests across exams and volunteers for each reader, (2) average correlations of each reader and exam, and (3) percent deviation between measurements across exams for each reader, and percent deviation between measurements across readers for each exam. Percent deviation is defined as the absolute difference in measurements between exams divided by their average.

Results: Figures 1A and B display representative stiffness (kPa) and wave images from the first scan from a healthy volunteer, respectively, and Figures 1C and D display stiffness and wave images from the repeat exam of this volunteer. Excellent subjective agreement is seen between the two exams, and Reader 1 reported stiffness values of 2.22 ± 0.28 kPa and 2.24 ± 0.44 kPa for Exam 1 and 2, respectively; Reader 2 reported 2.47 ± 0.31 kPa and 2.32 ± 0.32 kPa for the same volunteer.

The mean and standard deviation for Reader 1 and 2 for all volunteers was 2.56 ± 0.57 kPa and 2.65 ± 0.54 kPa, respectively. The mean and standard deviation across readers was 2.56 ± 0.28 kPa and 2.62 ± 0.33 kPa, respectively, for Exam 1and 2. Paired t-tests across exams found p = 0.94 for Reader 1 and 0.83 for Reader 2, showing that there were no statistically significant differences between readers and exams.

The correlation across exams for Reader 1 and 2 were found to be 0.78 and 0.80, respectively, for an average correlation of 0.78; correlations across readers for Exam 1 and 2 were 0.91 and 0.73, respectively, for an average correlation of 0.82. This demonstrates that there is greater correlation between repeated exams rather than between readers, which is an important feature for reproducibility.

The average percent deviation between measurements across exams was 8.4 ± 9.6% for Reader 1, and 10.3 ± 6.6% for Reader 2; average percent deviation between the readers was 9.5% (P = 0.59). Similarly, the average percent deviation across readers for Exam 1 was 7.5 ± 5% and 6.4 ± 6.1% for Exam 2; the average percent deviation between both exams was 6.9% (P = 0.69). These results imply a <10% variability between two different readers, but following stiffness measurements in both exams with one reader results in a <7% variability in the measurements.

Discussion: These results showed nearly identical means and standard deviations in stiffness values for each reader, with high correlation between exams for all volunteers. Additionally, two readers' results showed < 10% deviation between measurements on both exams. For only one reader and both exams, however, deviations between measurements dropped to < 7%, implying that changes greater than 7% are meaningful when one reader follows stiffness measurements longitudinally. Differences in stiffness values between exams and readers were not statistically significant. These results show a slightly closer correlation exists between the imaging findings than the readers; a greater error in imaging findings could lie in the readers, and not the imaging data. A limitation of this study is only healthy individuals were imaged and future work will examine the reproducibility of MRE in patients.

References: [1] Rouviere, et al. Radiology 2006; 240(2): 440-448. [2] Muthupillai, et al. Science 1995; 269(5232) : 1854-7. [3] Malik, et al. Clin Gastro Hepatol 2007 ; 5(10) :1144-6. [4] Yin, et al. Clin Gastro Hepatol 2007 ; 5(10) :1207-13.
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