EVALUATION OF SPIN-ECHO BASED SEQUENCES FOR MR ELASTOGRAPHY OF LIVER WITH IRON OVERLOAD

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Introduction. Magnetic Resonance Elastography (MRE[1]) is a noninvasive elasticity imaging technique that can measure the shear stiffness of soft tissues and is being clinically used for the assessment of hepatic fibrosis[2] . While the gradient-echo (GRE) MRE sequence most commonly used for hepatic MRE has a high technical success rate, in diseases such as hemochromatosis where the MR signal of the liver exhibits significant T_2 /T_2^*-dependent signal reduction, the technique can fail due to low SNR. It was reported in a large study of 1377 patients[3] that while technical failures occurred in only about 5.6% of cases, nearly 75% of those failures were likely due to high iron deposition. This is an important clinical problem since iron deposition is known to be a coexistent condition in various chronic liver diseases. To address this issue, spin-echo MRE (SE MRE) and spin-echo echo planar imaging MRE (SE-EPI MRE) pulse sequences with short echo times were developed and were shown to be able to successfully measure the stiffness of livers with iron overload[4]. Since the tissue mechanics and wave propagation physics underpinning MRE is expected to be unaffected by the presence of iron in liver tissue at the concentrations encountered clinically, it was hypothesized that the new sequences would provide stiffness measurements equivalent to the current clinical standard, which would allow for the continued use of the same critical stiffness values for clinical analysis (e.g., fibrosis grading) that are used with the standard GRE MRE technique. The goal of this work was to test this hypothesis in healthy volunteers and to assess the use of the modified pulse sequences in a cohort of patients with liver iron overload.

Methods. All experiments were conducted in accordance with institutional review board guidelines and were performed on a 1.5-T whole-body MR scanner (Signa EXCITE, GEHC, Waukesha, WI). The two modified pulse sequences (SE MRE and SE-EPI MRE) were included in the routine clinical imaging protocol for patients undergoing diagnostic liver MR examinations and data were acquired in all patients who underwent clinically indicated MR Elastography. MRE data from 130 subjects imaged between March and June 2013 who authorized that their data could be used for research purposes (excluding patients with iron overload, segmentation and breath hold artifacts) were analyzed and the stiffness values calculated using the automatic liver segmentation[5]. A paired equivalence t-test was performed between stiffness values calculated from SE and GRE MRE, and between SE-EPI and GRE using the commercially available software JMP (JMP9.0, Cary, NC) with the significance (α) of 0.05 and an equivalence margin of 5% of the measured stiffness. In addition, MRE data and other relevant laboratory data such as serum ferritin (where available) were retrospectively obtained and analyzed from patients where the conventional GRE MRE sequence failed (total 17 patients). Common imaging parameters included motion frequency = 60 Hz; axial imaging plane; and SI motion-sensitizing direction.

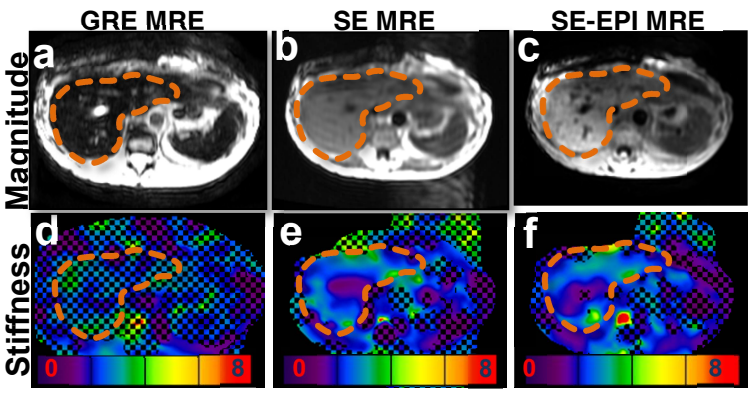

Figure 1: **Advantage of the Spin Echo sequences**. MRE data obtained from a patient with liver iron overload using the GRE MRE, SE MRE sequence and the SE-EPI MRE sequences. The checker board pattern indicates the regions with low confidence. While the GRE MRE failed to measure the liver stiffness (d), the SE and the SE-EPI sequences (e,f) had improved SNR and successfully provided shear stiffness values for this patient.

Results and Discussion. Liver iron overload was confirmed in those patients with failed GRE MRE exams using a combination of serum ferritin, total iron binding capacity, serum iron levels and assessment of signal intensities in the in- and opposed-phase gradient echo images routinely obtained in the liver MRI study. An example of the images obtained with the three sequences on a patient with liver iron overload is shown in Figure 1. The low signal within the liver in the magnitude image from the GRE MRE sequence can be noted which resulted in noise-dominated phase images and hence no valid shear stiffness estimation. In comparison, the spin-echo sequences provided sufficient signal to produce reliable liver stiffness measurements. Figure 2 shows the results obtained from the equivalence study of patients without iron overload. Figures 2a and 2b demonstrate that the stiffnesses obtained from the three sequences were similar. Statistical analysis of the data confirmed the equivalence of the SE MRE and SE-EPI MRE sequences to the GRE MRE sequence with p-values of 0.0212 and 0.0001, respectively. The confidence intervals for the percent differences of SE MRE and SE-EPI MRE with GRE MRE were -4.35% to -1.14% and - 2.52% to 0.65%, and were fully within the equivalence range. This suggests that these sequences could be used clinically for the assessment of hepatic fibrosis with the current diagnostic stiffness thresholds. MRE data obtained for the 17 patients with liver iron overload are shown in Figure 2c. The GRE MRE acquisition failed to provide valid stiffness maps in all patients except one. Based on the stiffness values obtained from the spin-echo sequences, 10 patients had stiffness values in the abnormal range.

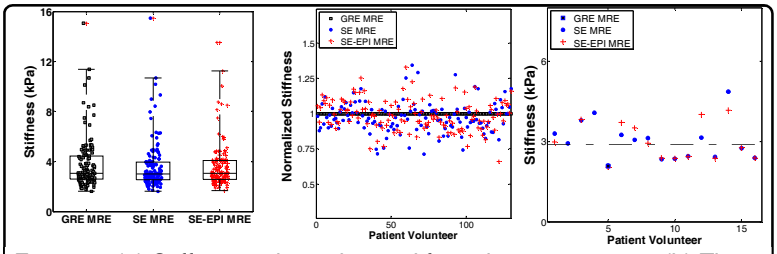

Figure 2: (a) Stiffness values obtained from the 130 patients. (b) The stiffnesses normalized to the GRE MRE stiffness, the similarity between the values can be noted. (c) Shear stiffness values obtained from all 17 patients with iron overload. Based on the SE MRE data, 8 patients had fibrosis.

Conclusions. Our results suggest that the modified SE and SE-EPI liver MRE sequences can be used to quantify hepatic fibrosis in patients with liver iron overload by providing stiffness values that are in good agreement with the standard MRE technique. Therefore, the current clinically used critical stiffness values can continue to be used for the assessment of liver fibrosis in patients with iron overload when using these sequences as well. Future studies will include a prospective study of patients with liver iron deposition to correlate the iron content, fibrosis and inflammation level, and the tissue stiffness.

Acknowledgements. This work was supported by NIH EB07593, NIH EB001981

References. (1) Muthupillai et al., *Science* 269: 1854-1857, 1995. (2) Huwart et al., Radiology 245 :458-466, 2007. (3) Yin et al., ISMRM 19th Annual meeting, 2010. (4) Mariappan et al., ISMRM 21st Annual meeting, 2012. (5) Dzyubak et al., JMRI 38: 371-379, 2013.