MR Elastography in the Liver at 3T using a 2nd Harmonic Approach

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Introduction: Liver fibrosis is an intermediate stage in the progression to cirrhosis and occurs as a result of many different chronic liver injuries. Percutaneous liver biopsy is considered the gold standard for the diagnosis and monitoring of liver fibrosis. However, this technique has many shortcomings, particularly relevant for chronic patients, including sampling variability and adverse events [1]. MRE has been shown to provide a noninvasive measure of liver fibrosis resulting from diseases such as hepatitis C [2-5]. Though shown before at 1.5T [2,3], *in vivo* liver MRE at 3T has not been demonstrated. With the promise of increased available signal and the flexibility it affords, we develop and demonstrate an MRE imaging protocol for acquisitions at 3T, along with the necessary modifications for a viable measurement, including the use of "2nd harmonic" imaging. Data obtained are compared to those in literature.

Methods: All imaging took place on a 3.0T Achieva (Philips Medical Systems, Best, The Netherlands) using a commercial elastography package (Philips Research Laboratories, Hamburg, Germany) described in previous work [2]. *Sequence:* In summary, MRE used a spin echo sequence with additional sinusoidal motion sensitizing gradients (MSGs) between the π/2 and π RF pulses, followed by a 3-echo EPI readout. The MSGs oscillated at 120 Hz, twice the driving frequency of the mechanical transducer, and were phase locked to the continuous mechanical vibration. A variable time delay changed the phase of the acquisition relative to the mechanical wave as it traversed the tissue, permitting the voxel-wise reconstruction of the wave. *Optimization:* The application of MSGs extended TE to an unacceptable value (>40ms) yielding artifacts induced both by motion and signal decay. Therefore, TE was shortened by imaging using a "2nd harmonic" acquisition in which the MSG frequency is twice the mechanical vibration frequency. Thereby, it was possible to shorten the time required for MSGs (16.7 vs 8.3 ms) at the expense of motion sensitivity, which was recovered by taking advantage of the higher gradient strengths possible with our system (maximum grad. amp. of 60mT/m vs 40mT/m typical). Also, a shorter π pulse was used (sinc, no side lobes). Note that using a half period sinusoid for the MSGs would also have permitted shorter TEs at the expense of severe image artifacts due to bulk motion. *Experiments:* Seven normal volunteers (NV) (4 male) were imaged as approved by our institutional review board. The MRE scans were respiratory navigator-gated, lasting ~2:10 min for each of three directions, before taking into account navigator efficiency. The NVs lay supine on the transducer, which was placed against the lower portion of the ribcage (as in [2]). Typical imaging parameters were: TR = 233-333ms, TE = 33 ms, 6 2D sagittal slices, 4.0mm^3 resolution, 0.4mm slice gap, NSA=1, and 8 phase delays. In one volunteer, scans with NSA=2 were acquired for comparison. No differences were observed so all data was pooled. *Analysis:* The included software, based on methods in [2], was used to determine shear stiffness modulus (Eiso) and mean shear viscosity (Visc), reported as mean ± RMS error. To determine the capability of MRE to assess global disease, one measurement was taken by drawing the largest possible rectangular ROI encompassing the liver. A second localized measurement was applied to test accuracy and used an ROI manually drawn to avoid vasculature.

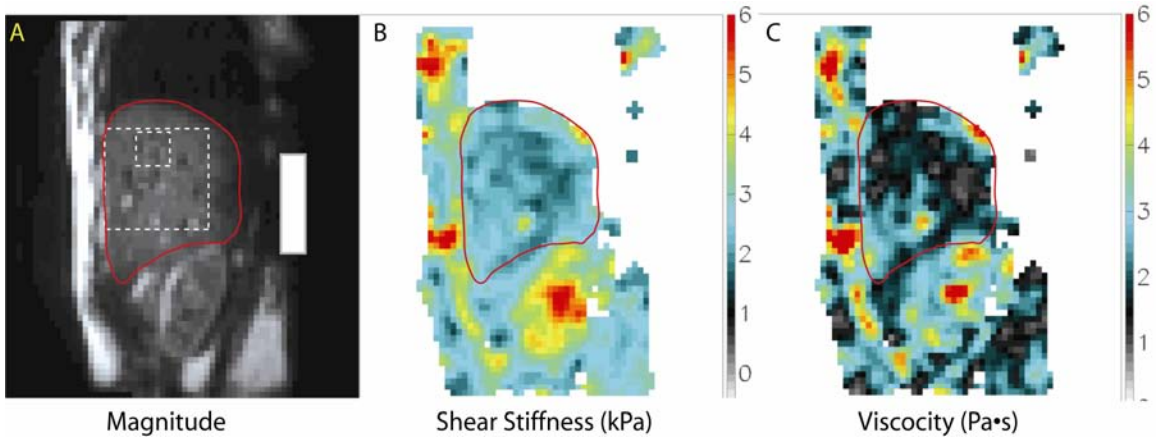

Figure 1: (A) Magnitude image and the corresponding (B) sheer modulus map (Eiso kPa), and (C) viscosity map (Pa·s) of a normal liver (red line). Location of mechanical transducer is denoted by white rectangle. Sample global (large) and local (small) ROIs are depicted on the magnitude image.

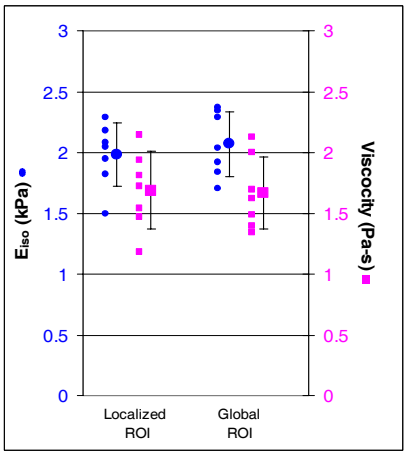

Figure 2: Results from localized (left) and global (right) ROI measurements display reasonable values for both Eiso and Visc.

Results: Fig 1 displays sample magnitude, elasticity (Eiso), and viscosity images. Fig 2 displays the results of the ROI measurements: $Eiso_{gloval}$ = 2.07±0.27 kPa, $Eiso_{local}$= 1.98±0.26 kPa; $Visc_{global}$ = 1.67±0.30 Pa·s, $Visc_{local}$ = 1.69±0.32 Pa·s. No significant difference was found between local and global ROI-based values (P>>0.05).

Discussion: The shear stiffness modulus and viscosity for NVs were very comparable to those reported in the literature (2.0±0.3 kPa in [3] and 0.2-5.1kPa compiled by [3], 2.06±0.26 kPa and 1.72 ±0.15 Pa·s in [2]). Furthermore, the stiffness values reported in patients with liver fibrosis were significantly higher, making the ~10% variability in the measurement observed here acceptable. For example, Ziol et al [4] report liver stiffness measures of ~5.5, 6.6,10.3,30.8 kPa for patients with histology-correlated fibrosis in stages F0-F1,F2,F3 and F4, respectively, on the scale proposed by [6].

Conclusion: We present a liver elastography experiment based on 2nd harmonic imaging which provides viable measurement of liver stiffness and viscosity. Imaging at 3T yielded improvements in signal, permitting shorter acquisitions (i.e. NSA=1 vs NSA=2 [2]). To counteract the extra difficulties associated with higher field imaging and to minimize artifacts from longer TEs, we used higher amplitude MSGs, shorter refocusing pulses and imaged using the second harmonic. The values obtained in these examinations of NVs compare faborably with values previously published [2,3] and are quite distinct from those expected at the different stages of fibrosis [2,4].

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