

## The Effect of Frequency on the Uniformity of Hepatic Shear Wave Illumination

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**Introduction:** MR elastography (MRE) has recently emerged as a tool for the noninvasive assessment of liver fibrosis and a number of studies have indicated its potential role as an alternative to biopsy [1-5]. MRE uses phase-contrast MR techniques to image the propagation of shear waves through tissue in order to determine the mechanical properties of the tissue. One of the advantages that MRE has over liver biopsy is that biopsies only sample a very small percentage of the liver volume and thus are subject to sampling errors. MRE, on the other hand, has the capability to measure tissue stiffness throughout the liver and is less susceptible to local sampling errors. The ability to differentiate healthy liver tissue from fibrotic tissue varies with fibrosis stage and is easier at the later stages. However, being able to identify the early stages of fibrosis is important for providing an early diagnosis and beginning early treatment of the underlying disease. Unfortunately, a challenge with performing MRE on patients with normal liver stiffness and those with mild fibrosis is that the liver is soft and can quickly attenuate the MRE acoustical vibrations. This characteristic can limit the volume of liver tissue which receives adequate shear wave illumination, thus increasing the likelihood of sampling errors in this segment of the patient population. One approach to trying to increase the wave penetration in these patients is to use a lower mechanical vibration frequency. The hypothesis of this study was that decreasing the frequency of the vibrations used for MRE would significantly increase the volume of hepatic tissue illuminated by shear wave motion.

**Methods:** This study was approved by our institutional review board and informed consent was obtained from all subjects prior to their enrollment in the study. All experiments were performed on a 3T system (MR750, GE Healthcare, Waukesha, WI). MRE was performed on 14 normal volunteers without any known liver disease. Subjects were imaged in the supine position using a pneumatic MRE driver system similar to the one described in [1]. The driver system consisted of an active component (consisting of a function generator, amplifier, and acoustic speaker) connected by an 8-m long, 3/4" diameter flexible PVC tube to a passive drum-like component placed over the abdominal wall of the subject. For this study, the passive driver was constructed from a minimally elastic, 1/8"-thick closed-cell vinyl foam sheet (with a built-in mesh to prevent it from stretching) wrapped around a 1" thick resilient, fibrous, and porous filling material to form a 20x40-cm pillow-like driver. The filling material prevents the driver from completely collapsing under load and allows the pressurized air to fill the driver. The flexible driver also had a 60-cm long, 1.75-cm diameter anti-kink supply tube which connects to the active driver system via the PVC tube. The flexible driver was wrapped around the right side of the subject, including the posterior, lateral, and anterior aspects of the body wall, and secured with an elastic strap wrapped around the subject. In separate acquisitions, continuous mechanical vibrations at 60, 50, 40, and 30 Hz were imaged with a 4-slice, axial, flow-compensated, single-shot, spin-echo EPI MRE acquisition with the following parameters: FOV=32-42 cm; acquisition matrix = 96x96; ASSET factor = 3; TR/TE = 1000-1067/58-61 ms; slice thickness/spacing = 7/3 mm; 1 pair of 4 G/cm, 15.4-16.7-ms long 1<sup>st</sup> gradient moment nulled motion-encoding gradients in the SI direction; and 4 phase offsets. The motion sensitivity of these acquisitions was 18.6, 22.8, 31.4, and 39.9  $\mu\text{m}/\pi$  radians for 60-, 50-, 40-, and 30-Hz motion, respectively. The active driver power level was decreased at 40 and 30 Hz to 60% and 40%, respectively, of the power used for the 60- and 50-Hz acquisitions because of the increased efficiency of the system for producing and transmitting motion at lower frequencies. Each acquisition was performed in 1 17-second breath hold performed at end expiration. For each acquisition, the phase/wave data were lowpass filtered to remove bulk motion effects and processed with a direct inversion algorithm to yield images of the shear stiffness of the liver (elastograms). The MR magnitude SNR (MSNR) was estimated using a 3x3(x4 offset) sliding window in which to calculate the mean and standard deviation of the magnitude signal. The inverse of the MSNR served as an estimate of the noise in the phase data, so that a phase-difference or wave SNR (PSNR) could also be calculated as the product of the wave amplitude in the processed phase data and the MSNR. To determine if there was a significant change in the degree of wave illumination of the liver at the various frequencies, first the liver was segmented to determine its total area in the 4 slices measured. Then the PSNR images were thresholded at 5 to define those locations which had satisfactory signal for processing. The ratio of the area of these regions to the total liver area was recorded and 2-sided, paired t-tests ( $\alpha=0.05$ ) were performed between each pair of frequencies to see if these areas changed at lower frequencies.

**Results:** Figure 1 shows an example set of the MRE data obtained at the various frequencies. The figure shows the MR magnitude data, phase/wave data, PSNR estimates, and elastograms obtained at each frequency. In the 60-Hz case, the shear waves did not penetrate all the way through the liver due to the soft, attenuating nature of the liver tissue. As the frequency of vibration was reduced, the degree of illumination increased with nearly the whole liver being covered at 30 Hz. The mean area of high PSNR increased with decreasing frequency: 39% at 60 Hz, 53% at 50 Hz, 56% at 40 Hz, and 71% at 30 Hz. Using the paired t-tests, only for the case comparing 40-Hz and 50-Hz wave motion could the null hypothesis of equal liver areas not be rejected, indicating significant improvement in wave penetration is typically seen by decreasing the frequency of vibration.

**Discussion:** The results of this study confirm that enhanced visualization of the liver can be achieved by decreasing the vibration frequency for MRE below the 60 Hz frequently used for clinical diagnosis. This means that the stiffness from a larger portion of the liver can be measured which may help in differentiating healthy from mildly fibrotic liver tissue by overcoming the significant attenuation frequently encountered in those patients.

### References:

[1] Yin M., et al., Clin Gastroenterol Hepatol 2007;5:1207-1213. [2] Klatt D., et al., Invest Radiol 2006;41:841-848. [3] Huwart L., et al., NMR Biomed 2006;19:173-179. [4] Asbach P., et al., Magn Reson Med 2008;60:373-379. [5] Huwart L., et al., Eur Radiol 2008;18:2535-2541.

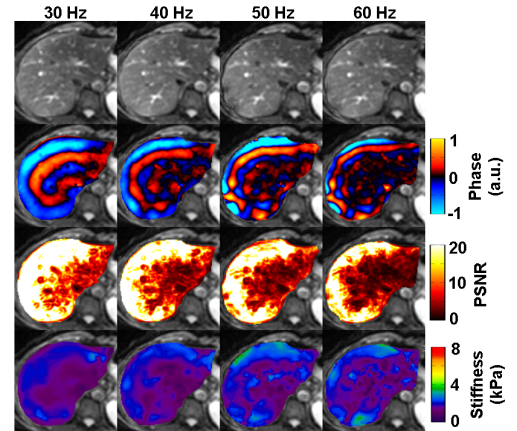


Fig.1: Example MRE data in 1 subject demonstrating the characteristics of the magnitude images (first row), phase/wave images (second row), PSNR estimates (third row), and the elastograms (last row) at each frequency. The illumination of the liver is improved at lower frequencies.