Hardware and Software Design for Serial and Longitudinal Rat MR Elastography Studies

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Introduction: Magnetic resonance elastography (MRE) has become an important tool for hepatic imaging [1]. MRE provides a noninvasive assessment of tissue mechanical properties (e.g., stiffness) which can indicate changes due to fibrosis, inflammation, perfusion, and cancer. Animal studies are invaluable for investigating disease characteristics and treatments and frequently involve large numbers of animals and longitudinal monitoring of individual animals. To make this practical, it is beneficial to design such studies for rapid imaging of the animals with minimal down time for switching animals. The purpose of this work is to present a study design for the longitudinal assessment of hepatic stiffness in rats. Results are shown from a study of hepatic changes over 4 weeks due to a bile duct ligation (BDL) procedure.

Methods: ***Animal Preparation*:** 32 Sprague-Dawley rats were used in this study approved by our Institutional Animal Care and Use Committee. Each rat either had a bile duct ligation (BDL) surgery (N=14) or a sham procedure (N=18) and was anesthetized before the MR examination. No intubation, respiratory/cardiac monitoring, or artificial heating source was used to minimize the amount of extra equipment that would have to be attached to and removed from each rat. The imaging protocol was designed to have negligible respiratory and cardiac artifacts and to be short enough so the body temperature of the rats would remain stable.

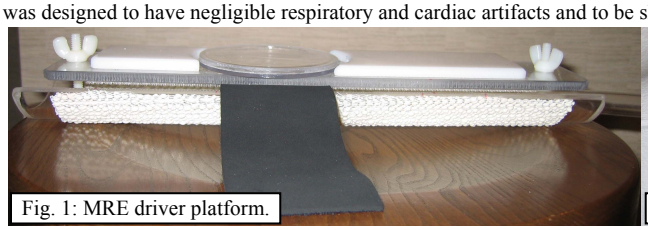

Fig. 1: MRE driver platform.

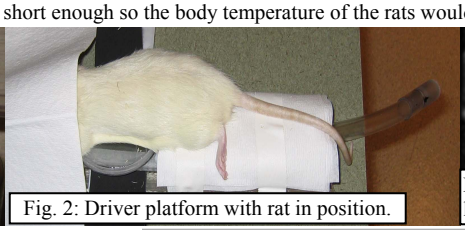

Fig. 2: Driver platform with rat in position.

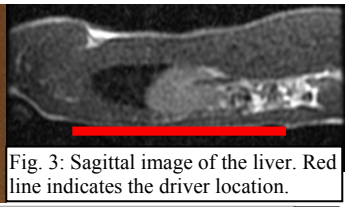

Fig. 3: Sagittal image of the liver. Red line indicates the driver location.

***Driver*:** The MRE driver was designed to operate efficiently at 200 Hz for liver imaging and to allow for an easy transition from one animal to the next. It was built into a plastic tray (Figs. 1 & 2) designed to be inserted into a 10-cm diameter, 20-cm long, 4-channel receive-only RF coil. In the middle of the tray was an 8-cm diameter, 3-mm thick passive driver used to deliver vibrations pneumatically from an active acoustic driver into the liver analogous to human liver MRE studies (e.g., [2]). The rat could be positioned quickly on the large driver by positioning the xyphoid process on the front half of the driver (Fig. 3). The rat was secured to the driver using an elastic strap and then the tray was centered in the imaging coil. The passive driver was supplied by a 30-cm long, 13-mm diameter elastic tube connected to a 7.3-m long, 19-mm diameter elastic tube attached to the active driver.

***Acquisition*:** SE-EPI MRE was performed with the following parameters: axial FOV = 12.8 cm, 80x80 acquisition matrix, ASSET factor of 2, 32 2-mm slices acquired in 2 passes, TR/TE = 1360/38.6 ms, RL frequency-encoding direction, 2 shots, 1 NEX, 1 5-ms 4-G/cm motion-encoding gradient (MEG) on each side of the 180° pulse, and 4 time offsets. Motion encoding in 3 orthogonal directions was performed and the MEG were not gradient moment nulled, but the rest of the imaging sequence was. The MRE acquisition time was 2.5 minutes with the rat breathing freely. A coregistered anatomical acquisition was also performed using a gradient-moment-nulled SE acquisition with the following parameters: axial FOV = 12.8 cm, 128x128 acquisition matrix, 0.5 FOV in the phase-encoding direction, TR/TE = 450/20 ms, RL frequency-encoding direction, 32 2-mm slices acquired in 2 passes, and 32-kHz bandwidth (1.25 minutes acquisition time with the rat breathing freely). The total experiment time for each animal (including set-up, imaging, and switching animals) was about 12 minutes.

***Processing*:** The MRE processing used the following procedure. The vector curl of the measured displacement data was calculated using 3x3x3 derivative kernels on the wrapped phase data [3]. The curl data were directionally filtered using 20 3D directional filters oriented isotropically with a radial 4th-order Butterworth bandpass filter with cut-off frequencies of 0.001 and 40 cycles/FOV [4]. A direct inversion of the Helmholtz wave equation was performed in 3x3x3 windows on each filtered dataset [5]. The liver was manually segmented and the mean stiffness was recorded.

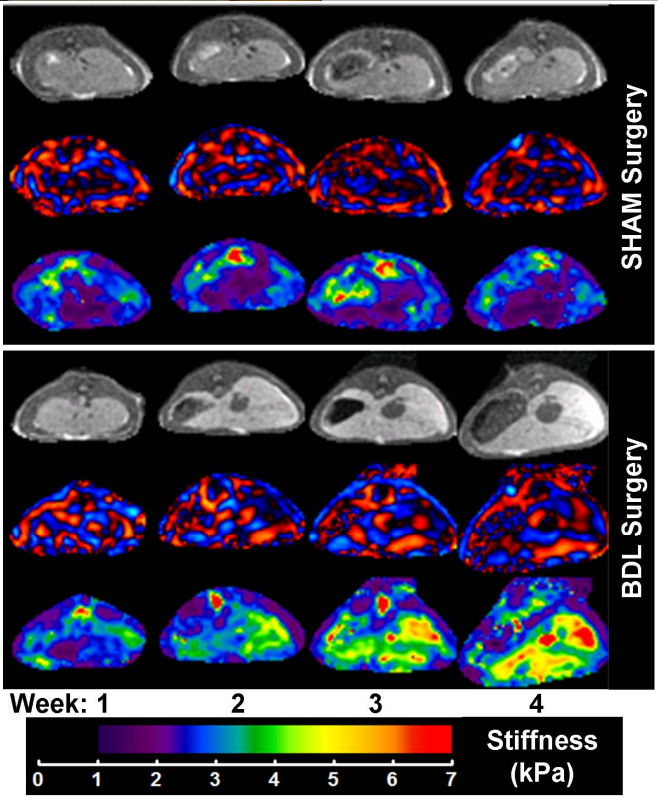

Fig. 4: MRE images of a sham and BDL rat for 4 weeks after surgery.

Results: Fig. 4 shows an example of a sham and BDL rat imaged at various time points after surgery. In each case, SE magnitude images, MRE wave images, and elastograms are shown in the top, middle, and bottom rows, respectively. The liver stiffness increases over time in the BDL rat while the stiffness in the sham rat remains constant. A large cyst can also be seen growing in the BDL rat (the hypointense circle within the liver) due to the accumulation of bile. Fig. 5 shows the mean stiffness and standard deviation of the 32 rats for each group and also shows that the BDL rats have progressively elevated stiffness compared to the sham rats.

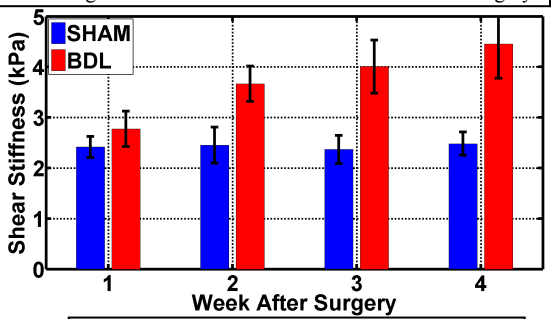

Fig. 5: Summary of MRE results.

Conclusions: These results demonstrate a practical and efficient approach for the serial and longitudinal assessment of hepatic stiffness in rats. This approach may make it practical to study a number of models investigating drug efficacy or disease progression. Future improvements to this design could include equipment for physiologic monitoring, anesthesia delivery, or simultaneous animal imaging (e.g., [6]).

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Bibliography: [1] Talwalkar, J.A., Hepatology 2008, 47(1):332-42. [2] Yin, M., Clin Gastroenterol Hepatol. 2007, 5(10):1207-1213.e2 [3] Glaser, K.J., ISMRM 2009, 4669. [4] Manduca, A., Med Image Anal 2003, 7(4):465-73. [5] Manduca, A., Med Image Anal 2001, 5(4):237-54. [6] Bock, N.A., MRM 2005, 54:1311-16.