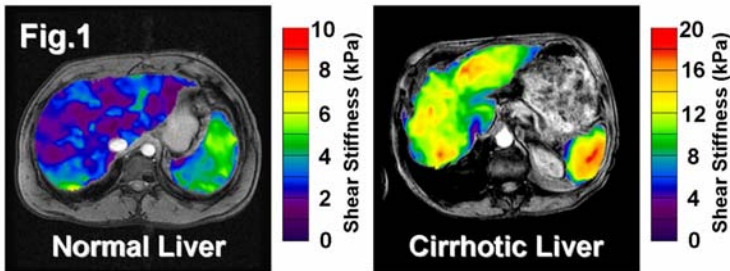


Increased Splenic Stiffness: A Potential Indicator of Portal Hypertension

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Introduction: Portal venous hypertension (PVH) is one of the most important consequences of chronic liver disease, leading to gastroesophageal varices and potential life-threatening hemorrhagic complications. Currently, portal venous pressure is assessed by hepatic vein catheterization and measurement of hepatic venous “wedge pressure”. Unfortunately, the invasive nature of this procedure severely limits the potential to use portal pressure data to guide clinical management. Conventional MRI and CT can only diagnose PVH by detecting late consequences such as varices, splenomegaly and ascites. Previous studies have demonstrated that MR Elastography, a technique for quantitatively assessing the mechanical properties of soft tissues, shows promise for diagnosing hepatic fibrosis in patients with chronic liver disease (1-4). The goal of this research was to explore the potential of Magnetic Resonance Elastography to measure changes in the stiffness of the spleen that may correlate with the presence of hepatic fibrosis and portal hypertension.



spleen were obtained by processing the wave images using an LFE inversion algorithm (5). At the time that this abstract was written, spleen and liver stiffness measurements had been obtained in 12 normal volunteers and 35 patients with biopsy-proven liver fibrosis.

Results: Figure 1 demonstrates elastograms of a normal volunteer and a patient with cirrhosis respectively. The mean shear stiffness values of the liver and spleen were 1.8 and 3.6 kPa respectively for the normal volunteer, while they were both markedly elevated to 12.0 and 14.0 kPa respectively, in the patient. Figure 2 summarizes the results obtained in all 47 subjects of this study. There was a strong correlation ($R^2 = 0.77$) between liver and spleen stiffness in the study cohort.

Discussion: Previous studies have established that there is a strong relationship between increasing liver stiffness, as measured by MRE, and the severity of hepatic fibrosis (2, 3). It is also known that portal venous pressures increase systematically with the severity of fibrosis. We speculate that the observed increase in splenic stiffness with hepatic stiffness is due to a parallel increase in portal venous pressure. The spleen can be modeled as a sponge, filled with blood at a portal pressure. As portal pressure rises, the stiffness of the spleen would be expected to increase.

As a preliminary model of the poroelastic behavior of the spleen we considered the equation of state for an ideal fluid expressed $P = -\beta \nabla \cdot \vec{s}$ where P is the pressure, β is the bulk modulus, and $\nabla \cdot \vec{s}$ is the divergence of the displacement. For a one-dimensional wave, we obtain $P = k\beta s$. Let us define the wavenumber, k , as ω/c , where ω is the radial frequency, c the velocity of longitudinal propagation $\sqrt{\beta/\rho}$, and ρ is the density of the medium. Therefore the previous equation may be reduced to the expression $P = \sqrt{\beta} \sqrt{\rho} \omega s$. For a particular calibration measurement, consider the expression $P_0/\sqrt{\beta_0} = \sqrt{\rho_0} \omega_0 s_0$, where the subscripts 0 imply a baseline measurement. If a second measurement is performed in which the pressure and bulk modulus vary, we may obtain the equality $P/\sqrt{\beta} = P_0/\sqrt{\beta_0}$. Rearranging yields $P(\beta) = P_0 \sqrt{\beta/\beta_0}$. Consider now the relationship between bulk modulus (β) and shear modulus (μ) which can be expressed as $\beta = \mu(2(1+\nu)/(1-2\nu))$, where ν is Poisson's ratio. Substitution of β into the previous expression, we obtain $P(\mu) = P_0 \sqrt{\mu/\mu_0}$.

This expression proposes a relationship between a baseline calibration measurement for pressure and shear modulus, current shear modulus, and the corresponding predicted pressure. Figure 3 shows the potential dependence of pressure on measured shear modulus, using a baseline calibration of 3 kPa for normal spleen at a normal pressure of 3 mmHg. Within the group of 35 patients in this study, hepatic wedge pressures were available in only one patient, with grade 3 fibrosis and a splenic shear modulus of 11 kPa. The portal pressure in this patient was measured to be 6 mmHg. This measurement, shown as + in figure 3, falls very close to the predicted curve.

Conclusion: MRE demonstrates changes in splenic stiffness in patients with hepatic fibrosis that may reflect the degree of portal venous hypertension. Our preliminary model relating splenic stiffness to portal pressure will be tested in ongoing research. Underlying splenic disease may also affect splenic stiffness, but in a clinical setting of known hepatic fibrosis, we speculate that measurement of splenic stiffness with MRE may be a useful method for estimating changes in portal venous pressure in response to therapy.

References: [1] R. Muthupillai, 1995, Science, 269: 1854-7. [2] O. Rouviere, 2006, Radiology 240(2): 440-8. [3] L. Huwart, 2006, NMR Biomed 19(2): 173-9. [4] M. Yin, ISMRM Workshop, July 2006, New York. [5] R. Grimm, 2007, ISMRM. [6] A. Manduca, 2001, Med Image Anal, 5(4): 237-254.

Materials and Methods: All experiments were implemented on a 1.5 T whole-body GE imager (Signa, GE Medical System, Milwaukee, WI, USA), using a body coil. Volunteers and patients were imaged in supine position, with a 19-cm cylindrical passive pneumatic driver placed against their anterior body wall. Continuous vibrations at 60 Hz were applied, producing shear waves throughout the abdomen. A gradient echo based MRE sequence with flow compensation was used to collect axial wave images with following parameters: FOV = 32~42 cm, Flip angle = 30°, Slice thickness = 10 mm, TR/TE = 50/32 ms, Matrix = 256x64, 1 pair of through-plane motion encoding gradients; 4 phase offsets. Several imaging planes containing much of the liver and spleen were selected. Images of shear stiffness (elastograms) of the liver and

