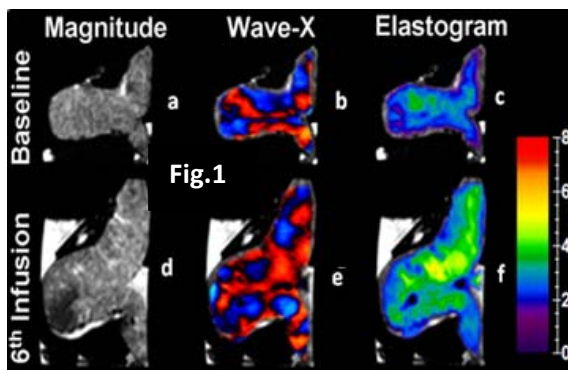# Toward non-invasive estimation of portal pressure via MR Elastography

S. Aristizabal[1], M. Yin[1], K. J. Glaser[1], A. Kolipaka[1], A. Manduca[1], and R. L. Ehman[1]
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Introduction: Portal Hypertension is the hemodynamic abnormality frequently associated with cirrhosis of the liver, and less commonly with various hepatic and extra hepatic diseases. Potential complications of liver cirrhosis directly related to the presence of portal hypertension include hemorrhage from gastroesophageal varices, hepatic encephalopathy, ascites and functional renal failure [1]. Thus, a noninvasive technique capable of measuring portal venous pressure (PVP) would aid clinicians in diagnosis of such diseases and would be beneficial in clinical settings. Currently, portal venous pressure is commonly assessed by hepatic vein catheterization and measurement of hepatic venous(wedge) pressure. The highly invasive nature of this procedure limits the potential use of portal venous presssure to guide clinical management. Increase in the stiffness of the spleen has been directly associated with presence of esophageal varices [2,4], and magnetic resonance elastography (MRE) measurements of spleen stiffness have led to potentially important correlation between spleen and liver mechanism [3,2]. Preliminary studies with healthy and chronic liver disease volunteers suggest that the bulk stiffness of the spleen is strongly related to the portal venous pressure through a poroelastic effect[4]. The purpose of this research is to provide a starting point for the development of a noninvasive technique for estimation of the portal venous pressure from the MRE measurements of splenic stiffness.

Materials and Methods: All the experiments were performed in a 1.5T whole-body MRI scanner (Sigma, GE Healthcare, Milwaukee, WI, USA) on 7 *ex-vivo* porcine spleens immediately after extraction. During the extraction process, a qualified surgeon removed the spleen from the pig, taking special care in the cleavage site of the vein; the portal vein branch was cut approximately 4 cm from the spleen in order to maintain some natural conditions. Following the extraction, a catheter was inserted in the portal vein and the rest of the vasculature was occluded. The specimen was preserved in a 0.9% sodium chloride solution and then it was placed inside a

Fig.1

cylindrical container (10-cm diameter, 18.5-cm height) and the catheter was connected to a saline bag via an infusion tube. The saline bag was placed on an IV pole of adjustable height which was used to vary the hydrostatic pressure inside the portal vein and the spleen. The portal vein pressure was varied by adjusting the IV pole to different heights, which were determined prior to data collection. *DP25B-S Strain Gage Panel Meter* (Omega Engineering, Inc., Stamford, CT) was attached to the infusion set up to obtain real-time digital pressure measurements. The bottom of the cylindrical container was the vibrating membrane of a passive driver, which is driven by varying acoustic pressure guided from active driver at 100 Hz continuously. A spin echo EPI MRE sequence was used to collect 3-D/3-axis axial wave images (x/y/z/t/axis: 80×80×36×4×3, FOV = 16 cm, slice thickness = 2.5 mm) with a birdcage head coil. Elastograms were obtained with a 3-D local frequency estimation (LFE) inversion incorporating all three components of motion [5]. ROI's were determined for the central 20 slices, excluding any non-splenic tissues and areas with poor shear displacement (phase-to-noise ratio (PNR) < 3). The volume changes of the spleen tissue were obtained with a multi-slice spoiled gradient echo sequence as well. Previous investigation suggests that the increase in splenic stiffness with hepatic stiffness is due to the accompanied increase in portal venous pressure, and that the spleen can be modeled as a sponge-like material filled with blood at the portal pressure. A model of the poroelastic behavior of the spleen relating the baseline pressure and shear modulus (μ_0) with the shear modulus (μ) at higher pressures can be modeled in a parabolic relationship $P(\mu) = \sqrt{\mu / \mu_0}$ [6]. Based on this study, a parabolic function was fit to the data of shear stiffness versus hydrostatic pressure for each spleen.

Results: Among all the experimental spleens, the mean spleen stiffness values increased systematically with a progressive increase in the portal vein pressure. Fig. 1(a)-(c) and (d)-(f) show the magnitude, wave image in one orthogonal directions and the shear stiffness map (elastogram) of one of the samples at the baseline and the 6th infusion respectively. Fig.2 shows parabolic curve fittings to the elasticity increment versus pressure change is in good agreement with the experimental data model, suggesting the hydroelastic behavior of the spleen. As summarized in Table 1, the parabolic relationships between the spleen stiffness and the portal pressure values showed an average R^2 value of 0.9288. Further analysis shows that the spleen stiffness changes with the volume as well as with the pressure. It demonstrated that some spleen samples underwent isovolumetric change, some underwent isobaric change and others were in a mixed phase.

Table 1

		R^2
1		R^2 = 0.9918
2		R^2 = 0.8902
3		R^2 = 0.9006
4		R^2 = 0.9840
5		R^2 = 0.8826
6		R^2 = 0.9923
7		R^2 = 0.8598

Discussion: Our *in vitro* studies provide the starting point of investigation of feasibility of using MR Elastography to estimate portal venous pressure, and the results provide motivation for moving forward to *in vivo* animal experiments. With increasing hydrostatic pressure, most spleen tissues (6 out of 7) underwent slight stiffness changes with substantial volume changes, which can simulate situations of splenomegaly in early phases of portal hypertension. Only one spleen tissue has dramatically increased stiffness without significant volumetric change (orange dot), which may simulate later phases of portal hypertension.

Conclusion: Our results provide strong evidence that MRE-assessed spleen stiffness is correlated with pulp pressure an ex-vivo animal organ model. The use of MRE to assess changes in tissue associated with the hydrostatic pressure could provide new insights into the pathophysiology of portal hypertension and could have other novel applications as well.

References: [1] Groszmann, R. J, 2005, *J Clin Gastroenterology,* 39(2):S125-S130. [2] Yin, M, 2009, *Topic in Magnetic Resonance Imaging*, 20(2):79-87. [3] Muthupillai, R, 1995, Science, 269: 1854-1857. [4] Talwalkar, J. A, 2009, *AJR Am J Roentgenol*, 193:122-127. [5] Manduca, A, 2001, *Med Image Anal*, 5(4): 237-254. [6] Yin, M, 2007, ISMRM.