

# Evaluation of liver fibrosis and hepatic venous pressure gradient with magnetic resonance elastography in a novel swine model of cirrhosis.

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**Purpose:** Patients with cirrhosis suffer from complications of portal hypertension. Hepatic venous pressure gradient (HVPG) is an accurate method to stratify hemorrhagic risk associated with portal hypertension. Ultrasound-based transient elastography (UTE) is a non-invasive method to measure liver fibrosis by assessing liver stiffness (LS) [1]. Prior reports have shown a correlation between LS and HVPG [2]. UTE, however, is limited by ascites, obesity, hepatic steatosis, and narrow intercostal spaces. Magnetic resonance elastography (MRE) is a newer, non-invasive technique to measure LS without the limitations posed by UTE. Excellent correlations have been shown between MRE-measured LS and liver fibrosis [3], though studies confirming the correlation between MRE-measured LS and HVPG are lacking. We recently developed a large animal model of liver cirrhosis in swine [4]. The development of a large animal model of cirrhosis is attractive because of the anatomic and physiologic similarities between the porcine and human liver. We hypothesize that MRE-measured LS will correlate with liver fibrosis and HVPG in a swine model of cirrhosis.

**Methods: Pulse sequence design** -- A 10 cm diameter acoustic driver was placed against the body wall over the liver with the animal in supine position, and held in place with an abdominal binder. 60 Hz sinusoidal acoustic waves were applied during imaging with an MRE phase contrast gradient echo sequence. The sequence parameters were repetition time (TR) 150 ms; echo time (TE) 23 ms; flip angle 30; field of view 34-38 cm; matrix size 128 x 64; slice thickness 8 mm; interslice gap 4 mm; number of wave phases 4. Three axial slices were acquired, each with a 30 second breathhold. The wave phase images were then processed to generate elastograms, which were analyzed by measuring shear stiffness in a manually depicted region conforming to the liver margins, but excluding major blood vessels.

**Experiments** -- Institutional animal care and use committee approval was obtained for all experiments. Three adult swine were used as controls while liver fibrosis was induced in eight adult swine by transarterial embolization with iodized oil and ethanol. Liver stiffness (MRE/GRE), HVPG, and biopsy specimens were obtained at baseline and 4 weeks (pre-necropsy) following induction of liver fibrosis. Necropsy was performed on explanted livers.

**Results:** Four weeks following the induction of liver cirrhosis, the experimental animals developed an increase in HVPG of 8.0 +/- 6.4 mm Hg compared with 0.3 +/- 1.2 mm Hg for the controls (P=0.08). Over the same timeframe, mean LS, as measured on MRE, increased 0.82 +/- 0.39 kPa for the experimental animals and 0.1 +/- 0.05 kPa for the controls (P=0.01). Representative MRI/MRE images from a swine at baseline and 4 weeks following transarterial embolization are shown in figures 1 and 2, respectively. A positive correlation was observed between increases in LS and HVPG ( $\rho=0.6816$ ; P=0.02), figure 3. Liver fibrosis was measured on the explanted livers at 4 weeks and yielded mean fibrosis scores of 2.8 for the experimental animals and 0 for the controls (P=0.0016). A positive correlation was observed between higher liver stiffness and liver fibrosis ( $\rho=0.9000$ ; P=0.0002), figure 4.

**Conclusions:** MRE is a reliable noninvasive technique to measure LS in a swine model of cirrhosis. Significant correlations were observed between LS and HVPG as well as LS and fibrosis. Our results corroborate the reproducibility of producing a porcine model of cirrhosis and portal hypertension.

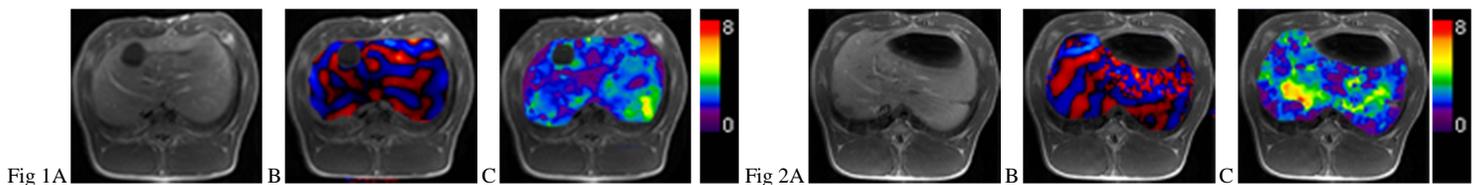


Figure 1 & 2. MRI and MRE of swine liver before (fig 1A-C) and 4 weeks after (fig 2A-C) transarterial embolization. Anatomic images (fig 1A & 2A) demonstrate mild tissue heterogeneity following embolization (fig 2A). Figures 1B & 2B show wave image data in the liver, superimposed on the corresponding anatomic images. The resulting elastograms in figures 1C & 2C show that mean shear stiffness of fibrotic liver was higher than that of normal liver (2.96 kPa versus 2.04 kPa, respectively).

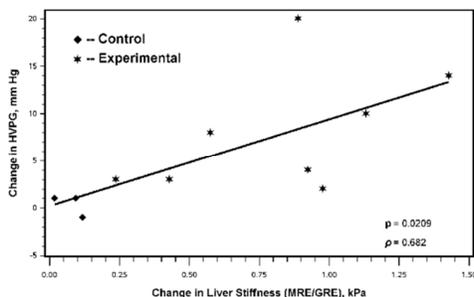


Figure 3. HVPG increases with mean liver stiffness for cirrhotic swine livers

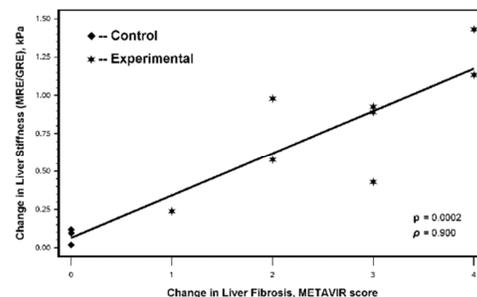


Figure 4. Mean liver stiffness increases with fibrotic stage for cirrhotic swine livers

**References:** [1] Castera L. et al. J Hepatol. 2008;48(5):835-47. [2] Vizzutti, F. et al. Hepatology. 2007;45(5):1290-7. [3] Rustogi, R. et al. J Magn Reson Imaging. 2012;35(6):1356-64. [4] Avritscher, R. et al. J Vasc Interv Radiol. 2011;22(9):1329-34.