Influence of Perfusion on Tissue Stiffness Assessed with MR Elastography


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Introduction:
MR Elastography (MRE) is an MRI-based technique for quantitatively assessing the mechanical properties of soft tissues by studying the propagation of shear waves. Multiple studies have reported on developments of MRE to quantitatively assess the viscoelastic properties of organs including the brain (1), breast (2), heart (3), lung (4), muscle (5), liver (6), spleen (7), kidneys (8) and pancreas (9). Recent studies have suggested that MRE-assessed tissue stiffness may have several components: a static component reflecting intrinsic structural properties, a dynamic component reflecting loading and contractile function and a dynamic component reflecting extrinsic perfusion changes. In one such study, postprandial liver MRE (10), food intake was used to increase mesenteric blood flow, which led to a postprandial increase in hepatic stiffness that is different in patients with hepatic fibrosis than in normal volunteers. In another study, renal arterial stenosis (RAS) MRE (11,12), renal occlusions were used to threaten the viability of the kidney by diminishing blood flow leading to irreversible tissue fibrosis, while the decrease of blood flow and perfusion had a competing influence on the tissue stiffness. The purpose of this study was to investigate the influence of perfusion on the shear stiffness of abdominal organs in two controlled in vivo animal models in which tissue perfusion could be controlled without additional factors related to disease processes. (a) Liver Model with Varying Systemic Blood Flow: A pig model with an intravenous infusion of Dextron-40, which causes an increase in both blood volume and blood pressure in a short time, was used to investigate hepatic stiffness changes related to blood flow (hypothesis: blood flow↑, perfusion↓, hepatic stiffness↓). (b) Kidney Model with Varying Renal Blood Flow: An acute pig model was developed with varying degrees of occlusion of the renal artery to investigate changes in renal tissue stiffness with changes in renal perfusion (hypothesis: blood flow↓, perfusion↑, renal stiffness↓).

Methods and Materials:
Liver Model: Two normal pigs were imaged in the supine position with an acoustic pressure-activated driver placed against the body wall adjacent to the liver. Continuous vibrations at 60 Hz were used deliver shear waves throughout the abdomen. A 2-D spin echo EPI MRE sequence was used to collect 3-D/3-axis wave images (xyz/3-axis; 96×64×4×3). Elastograms were obtained with a 3-D local frequency estimation (LFE) inversion algorithm. After baseline scanning, the pig underwent an intravenous infusion of Dextron-40 (10% of blood volume). The infusions were repeated 8 times approximately 10 minutes apart. Immediately after each infusion, hepatic MRE data were acquired while a left ventricle (LV) catheter was used to measure the blood pressure simultaneously. Kidney Model: Four normal pigs had their renal arteries isolated to insert a vascular occluder and an embedded Doppler flow probe. The renal blood flow (RBF) was gradually reduced from the baseline level to total occlusion of 100% in 20% increments with MRE acquisitions performed at each step. The renal MRE protocol (11,12) included both 2-D/3-axis gradient echo and 3-D/3-axis spin echo EPI MRE acquisitions using 90 Hz mechanical vibrations.

Results:
Liver Model: Fig. 1 shows the MRE wave data and elastograms for one slice (pig #1) after the first three infusions. For both pigs, the hepatic stiffness increased after each Dextron-40 infusion (#1: from 2.82±0.20 to 7.39±0.89 kPa; #2: from 2.03±0.17 to 6.64±0.67 kPa). The concurrently measured LV end-diastolic blood pressure had a sustained increase as well (#1: from 13.4 to 45.6 mmHg; #2: from 10.3 to 60.3 mmHg), as demonstrated in Fig. 2 (pig #1). Kidney Model: The shear stiffness of the cortex and medulla of the kidneys at baseline were not significantly different. The cortex and medulla of the acutely stenotic kidneys decreased in stiffness as the degree of stenosis was increased to 60% and above (p<0.05), as shown in Fig. 3-4 (one of the pigs). Conversely, the cortex and medulla of the contralateral kidney slightly increased in stiffness during the same period. The systemic blood pressure also rose during the acute decrements in RBF (from 75±3 to 96±3 mmHg).

Discussions:
The liver model results suggest that hepatic stiffness includes a dynamic component that reflects perfusion linked to blood pressure, which causes increased tissue tension. Alternatively, the observed dynamic component of liver stiffness may represent a transient change in the mechanical state of cells with contractile characteristics, such as vascular smooth muscle cells and activated stellate cells in the perisinusoidal spaces. The perfusion-induced liver stiffness change could be a predictor of intrahepatic pressure or portal pressure changes. In graded acute reductions in RBF, we observed that the shear stiffness was higher in the contralateral kidney compared to the stenotic kidney. Together with the decreased shear stiffness accompanying the decreases in renal perfusion of the stenotic kidney, these results demonstrate a functional component of stiffness that is related to perfusion pressure. The compensatory increase in contralateral RBF, supported by increases in blood pressure, may cause increased tissue turgor. Since renal vascular occlusive diseases lower the RBF and perfusion pressure of the affected kidney, these results may help explain the lowered and elevated shear stiffness of the stenotic and contralateral kidneys, respectively, reported previously in a chronic RAS model (11,12).

Conclusions:
These results provide strong evidence that MRE-assessed hepatic and renal stiffness have a dynamic component that can increase or decrease following a fluctuation in perfusion. The use of MRE to assess changes in tissue mechanics associated with the dynamic perfusion of tissue could provide new insights into the pathophysiology of hepatic and renal diseases and could have novel applications that should be explored. Diagnostic and longitudinal MRE studies should take into account dynamic perfusion effects on tissue stiffness as a potential cause of variability.

References:
9. Yin M, ISMRM 2008; Toronto, Canada. p 2627
10. Yin M, ISMRM 2009; Honolulu, Hawaii, USA. p 110
12. Yin M, ISMRM. 2009; Honolulu, Hawaii, USA. p 2042