Kidney Stiffness Measured in an Animal Model of Unilateral Renal Arterial Stenosis Using 2D MR Elastography

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Introduction: Renal arterial stenosis (RAS) is a narrowing of the renal artery, usually due to arthrosclerosis, which often diminishes the blood supply to the kidneys and leads to irreversible tissue fibrosis. We have previously shown in a swine model that by six weeks of RAS the stenotic kidney exhibits moderate but significant interstitial fibrosis [5]. Fibrosis threatens the viability of the kidney, and may ultimately lead to kidney failure [1]. In addition, the kidney is normally richly perfused, and its distension (and in turn stiffness) may be determined by renal perfusion pressure, blood flow, and filtrate volume, which together sustain around 25% of renal volume. Both fibrosis and turgor may affect the mechanical properties of tissues, which have been investigated by several newly emerging imaging techniques [2-3], such as MR Elastography (MRE) [4]. However, renal tissue elasticity in RAS remains uncharacterized. The goal of this study was to quantitatively determine *in vivo* the effect of RAS on the mechanical properties the swine kidney.

Materials and Methods: Five swine were implanted in one renal artery with a local irritant coil that induces a variable degree of arterial obstruction. One additional swine served as control. At ten weeks of RAS, fluoroscopic angiography was used to determine the degree of stenosis, and multi-slice 2-D MRE was then used to assess tissue stiffness in regions of interest (ROI) corresponding to cortex and medulla. MRE is a modified phase-contrast MRI technique for quantitatively assessing the mechanical properties of soft tissues by visualization of propagating shear waves [4]. It acquires 2D displacement data with motion sensitizing in the x, y and z directions and allows the calculation of tissue shear modulus and the generation of images that map tissue elasticity/stiffness. MRE exams were implemented on a 3.0 T whole-body GE imager (Signa, GE Medical System, Milwaukee, WI, USA), using the 8-channel torso coil. Animals were imaged in a supine position, with a 19-cm cylindrical passive pneumatic driver placed against their posterior body wall. Continuous vibrations at 90 Hz generated shear waves throughout the tissues of the abdomen. A gradient echo based MRE sequence with flow compensation was used to collect 2-D axial wave images with following parameters: TR/TE = 33.3/18.9 ms, Matrix = 256×96, 1 pair of trapezoidal motion encoding gradient along x, y and z directions. Stiffness maps were generated with MRE / Wave (MRI Research Lab, Mayo Clinic). Cortical and medullary ROI were selected based on anatomical correlations with exponential axial magnitude images.

Results: Fig. 1 demonstrates the smaller stenotic right kidney and larger contralateral kidney in one of the experimental animals. Dashed lines indicate representative slices used in the 2-D GRE MRE acquisition. Shear stiffness was calculated from 2-D GRE MRE acquisitions, as shown in Fig. 2. The red stars indicate the stenotic kidney with RAS. The mean shear stiffness for the normal and RAS kidneys is shown in Fig.3. The shear stiffness was similar in normal kidneys between the cortex and medulla. The stenotic cortex and medulla of pigs with hemodynamically significant RAS (≥ 75%) showed lower shear stiffness levels vs those in the contralateral kidney (4.9±0.6 and 5.3±0.4 kPa) compared to (6.0±0.7 and 6.5±0.6 kPa, p<0.05).

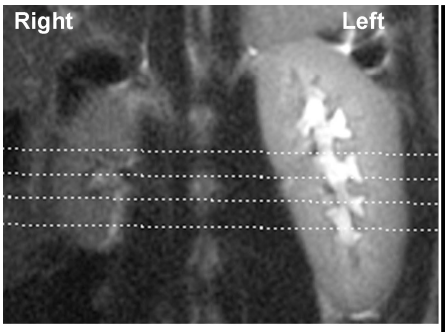

Figure 1. Right (stenotic) and left (contralateral) kidney in experimental RAS.

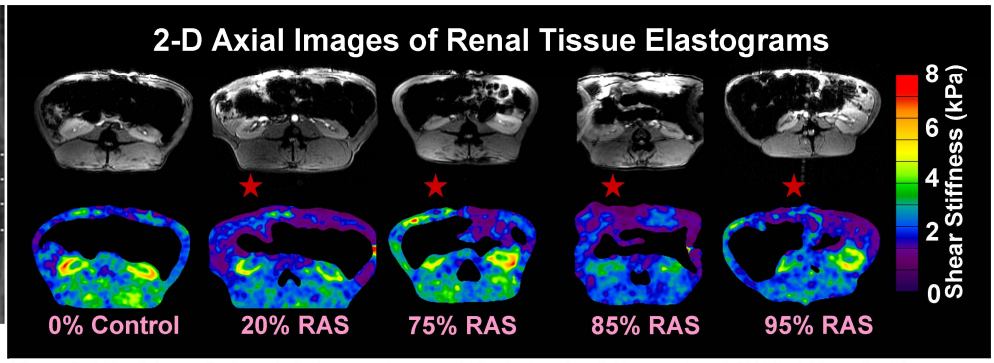

Figure 2. 2-D axial magnitude and elastograms for normal (Control) and variable experimental RAS at 10 weeks. The elastogram shear stiffness color legend is on the far right. Red stars indicate stenotic kidneys. The images were oriented to show the stenotic kidney on the left.

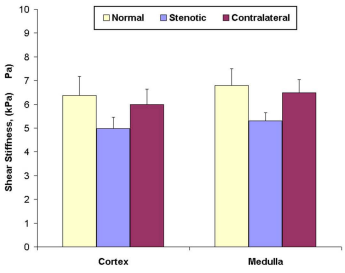

Figure 3. Mean shear stiffness in the control kidneys and the stenotic and contralateral kidney of the RAS group.

Discussion: The kidney is a richly perfused organ, receiving 25% of cardiac output. RAS diminishes renal blood flow and perfusion pressure, and threaten the viability of the kidney by leading to irreversible tissue fibrosis and ultimately kidney failure. Using an experimental model of renovascular hypertension and a 2-D MRE technique to quantitatively assess the mechanical properties of renal tissue *in vivo*, we observed that the shear stiffness was higher in the contralateral compared to the stenotic kidney. This is despite histological evidence that indicates the presence of renal fibrosis in RAS [5]. However, in addition to induction of fibrosis, vascular occlusive diseases lower renal blood flow and perfusion pressure to the affected kidney. This may be sufficient to counterbalance the stiffness due to fibrosis.

Conclusion: Our preliminary evidence suggests that after 10 weeks of experimental RAS, tissue stiffness is reduced in stenotic kidneys. This may suggest that the effect of decreased blood flow and pressure in the stenotic kidney to diminish renal stiffness at least initially overrides the development of fibrosis, and overall reduces renal turgor and increases its elasticity. Future studies will need to monitor renal elasticity in kidneys with greater levels of fibrosis, such as those after more prolonged RAS or in the presence of co-existing renal disease. Our preliminary results encourage further evaluation of renal hemodynamics, the presence of fibrosis, and techniques that may be employed to assess tissue stiffness in RAS.

References:

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