Reproducibility of Renal Blood Volume Measurements in Mice

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Introduction: Susceptibility based relative blood volume (RBV) mapping methods are widely used to assess normal and pathological differences in tissue vascular density. Renal RBV measurements could provide a valuable tool to characterize abnormal renal perfusion in mouse models of kidney disease. In this study, we optimized MRI acquisition methods for RBV mapping in mouse kidneys and assessed the reproducibility of RBV measurements acquired on consecutive days.

Methods: Ten normal mice were studied on two different days to assess the repeatability of RBV measurements at 7T. Multi-slice T_2-weighted fast spin echo (SE) images (TR = 2000ms, TE = 48ms, RARE-factor = 8, 256^2 matrix, 25.6 mm^2 FOV, 0.5 mm slice thickness) of the kidneys were acquired before and after the injection of an intravascular iron oxide contrast agent (CA). To optimize CA dose, images were also acquired at multiple doses (between 2 - 12 mg / kg). To minimize motion artifacts navigator and respiratory gating was employed. Dynamic imaging was also employed to validate that the contrast agent remained within the vasculature.

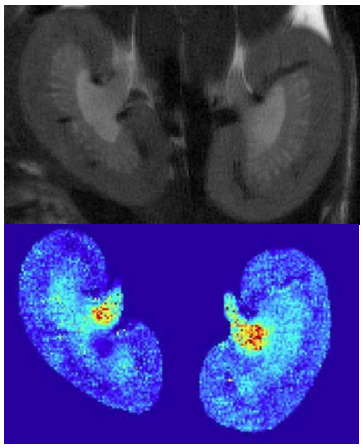

Figure 1: T_2 weighted image (top) and RBV map (bottom)

Results: **Figure 1** shows a T_2-weighted image and RBV map for a representative mouse. The contrast-to-noise ratio for multiple doses of CA in cortex (C), outer medulla (OM), inner medulla (IM) and papilla (P) regions of interest (ROI)s is illustrated in **Figure 2**. Based on this analysis the optimal CA dose for SE based RBV mapping in mouse kidneys at 7T is ~6 mg/kg. Dynamic SE imaging revealed that RBV values did not vary significantly in any kidney region over the course of an hour indicating that the CA is not filtered or excreted. **Figure 3** shows the mean RBV values in these ROIs across all mice. The mean kidney RBV measured on consecutive days was 19.97 ±1.50 and 19.86 ±1.62, yielding a concordance correlation coefficient of 0.94, indicating that this approach is highly reproducible.

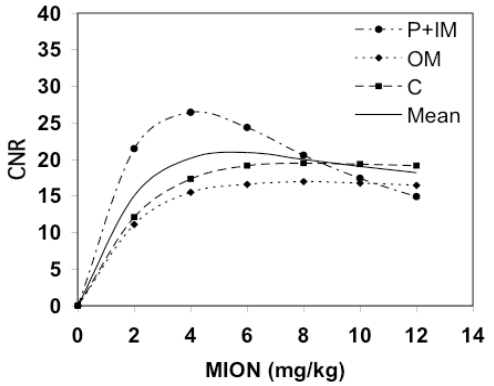

Figure 2: CNR versus CA dose in mouse kidney ROIs.

Discussion: The optimized RBV method used herein is ideally suited for evaluating mouse renal vasculature because it employs high-resolution, steady-state acquisition sequences, avoids the use of CA kinetic models and is highly reproducible across animals and days. The high blood volume in the papilla region is likely due to the major vessels traversing this region. Cortical perfusion is known to be higher than that in the medulla. The high inner medulla RBV values found in this study are likely due to the use of a spin-echo sequence preferentially weighted towards microvessels. Previous studies have found that microvascular density is higher in regions of the medulla as compared to that found in the cortex. We are currently validating the RBV maps by comparison to histological measures of vascular density and evaluating their use for the assessment of abnormal renal perfusion in multiple models of kidney disease. We are also comparing gradient- and spin-echo derived RBV maps given their differential sensitivity to vessel size. The RBV maps complement the physiological information obtained from conventional assays of kidney function and could facilitate an improved understanding of pathological mechanisms in kidney disease.

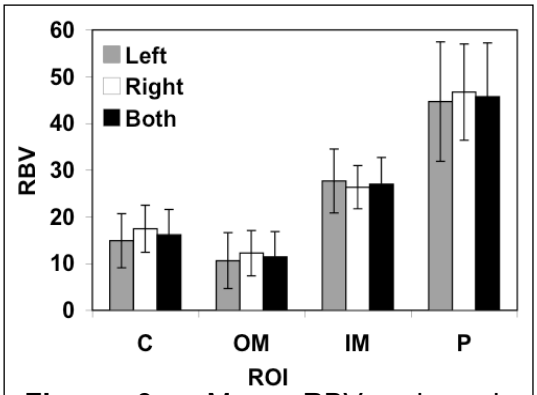

Figure 3: Mean RBV values in mouse kidney ROIs

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