Evaluation of Intra-Renal Oxygenation in Mice by BOLD MRI at 3.0T Human Whole Body Scanner

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INTRODUCTION

Renal medullary hypoxia plays a role in the pathophysiology of ischemic nephropathy, hypertension and diabetic nephropathy [1, 2]. We have previously shown that BOLD (blood oxygenation level dependent) MRI can non-invasively evaluate intra-renal oxygenation levels under normal conditions and during physiological and pharmacological maneuvers at both 1.5T and 3.0T field strengths both in human subjects and in rats [3-5]. Deoxyhemoglobin is paramagnetic, which affects the R2* (=1/T2*) relaxation rate of the neighboring water molecules, and in turn influences the MRI signal on T2*-weighted images. The content of deoxyhemoglobin in blood is related to pO_2 in the tissue and reflected in BOLD MRI parameter R2*.

Mouse models are commonly used as surrogates of humans in the laboratory [6-8]. Transgenic and gene-deleted mice provide researchers with unique opportunities to study the impact of specific genes in the pathophysiology [8, 9]]. Mouse MRI is usually performed using dedicated small animal scanners at high field strength (typically 4.7 T and above) [10, 11] because of the low signal related to the small size of the animal. However, imaging of rodents on a whole body human scanner may have some practical advantages. These include: relatively more widespread availability especially in major academic medical centers, easy access to the animals during scanning for monitoring purposes, and ability to extend the findings to larger animal models and humans in a more straightforward fashion. In addition, for BOLD MRI studies higher field strengths potentially introduce more bulk susceptibility related artifacts. In this study, a specially designed coil was used to receive signals from mouse kidneys. Furosemide which improves renal medullary oxygenation was administered *via i.v.* in order to modulate medullary oxygenation.

MATERIAL AND METHODS

The study protocol was approved by the Institutional Animal Care and Use Committee. Eight inbred male mice (Jackson Lab, Bar Harbor, ME, US, weight 24.63±0.96 g) were anesthetized using ketamine (50mg/kg, ip) and xylazine (10mg/kg, ip). Imaging was performed on a 3.0T scanner (CV/i, GE, Milwaukee, WI, USA) using a multiple gradient recalled echo sequence (TR/TE/flip angle/bandwidth/FOV/slice thickness/NEX =101.5ms/6.3-31.2 /30 /31.25kHz/4cm/0.5mm) to acquire 6 T2* weighted images. The in plane spatial resolution is 0.156mm. The mouse kidney was positioned in the middle of the custom designed 2 cm receive only loop coil. One transverse slice was selected in the middle of the kidney. Furosemide (10 mg/kg) was administered *i.v.* after obtaining 3 sets of baseline T2*-weighted images. Further sets of T2*-weighted images were obtained every 3 minutes for about 30 minutes post furosemide. The signal intensity *vs.* echo time data were fit to a single decaying exponential function to generate R2* map. ROIs of at least 4 pixels were chosen on the maps to obtain values for the mean and standard deviation of R2* in the renal medulla and cortex. The statistical significance of the differences between pre- and post-furosemide R2* was evaluate by two-tailed paired Student's t-test.

RESULTS

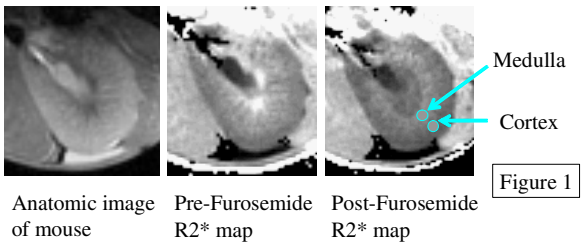

Figure 1. Representative pre- and post-furosmide R2* maps from one mouse. The relatively darker medulla in the post-furosemide R2* map as compared to pre-furosemide map, signifying an increase in medullary oxygenation. The window and level settings for both the maps are exactly the same.

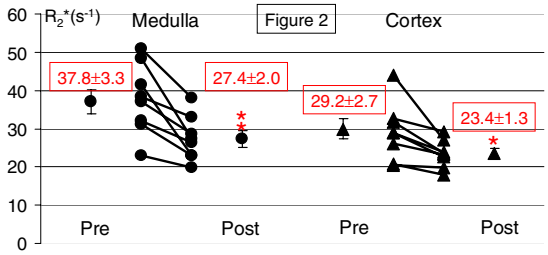

Figure 2. Summary of individual changes in medullary and cortical R2* post furosemide in 8 mice at 3.0T. A statistically significant decrease in medullary R2* post-furosemide was observed. p=0.0026 in medulla and p=0.014 in cortex.

CONCLUSION AND DISCUSSION

In conclusion, preliminary results presented here demonstrate that 3.0T human whole body scanner combined with custom coils can be used to image mouse kidneys *in vivo*. The results with furosemide from this study are consistent with our previous experience with both human and rat kidneys.

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