Optimization of qBOLD Methods for the Assessment of Mouse Renal Oxygenation

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PURPOSE: Renal function is highly dependent upon adequate perfusion and oxygenation and their non-invasive assessment in mice could provide useful tools with which to interrogate disease models. Recently, an experimentally practical quantitative BOLD approach (qBOLD) was proposed that enables the quantification of local blood oxygen saturation (LSO_2) [1]. In this study, we evaluated the feasibility of this qBOLD protocol for application to mouse kidneys. Specifically, we optimized imaging sequences and protocols that enable mapping of T_2, T_2* (before and after the injection of a contrast agent), blood volume fraction (BV_f), LSO_2 and B_o.

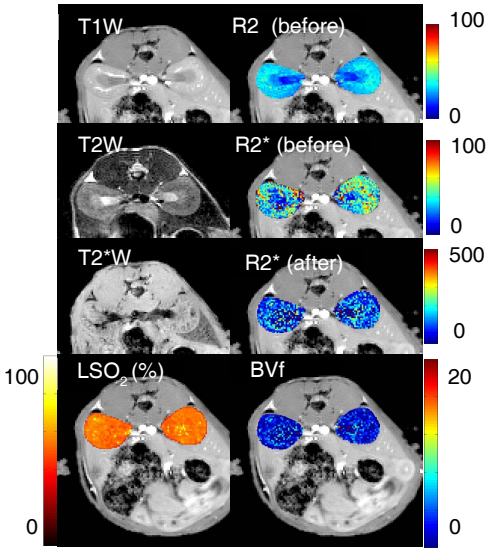

Figure 1. Parametric maps in mouse

METHODS: Mice were anesthetized (isoflurane 1.5-2%), and the body was stabilized in a MR compatible head/body frame. Respiration rate and body temperature were monitored and maintained throughout the imaging session. MRI protocols were optimized on Agilent 7T MRI system using a doty25 volume coil. Rapid acquisition MRI methods and respiration gating were applied to minimize motion artifacts. T_2 mapping was based on a 2D multi echo spin echo sequence (TR =3000 ms, TE=12 ms, number of echoes (NE)=18, echo spacing (ESP)=12ms, FOV=25.6×25.6 mm^2, matrix size=128×128, slice thickness=0.5 mm, 6 accumulations). T_2* mapping before contrast agent injection was based on a 2D multi echo gradient echo sequence (TR=200 ms, flip angle=30, TE=2.74 ms, NE=11, ESP=3.5ms, FOV=25.6×25.6 mm^2, matrix size=128×128, slice thickness=0.5 mm, 16 accumulations). T_2* maps were acquired before and ten minutes after the injection of the intravascular iron-oxide contrast agent, Molday-ION (MION, Biophysics Assay Labratory, MA, USA). The initial 8ms of the signal decay were not considered during the fitting, in order to comply with the characteristic time t_c given for extravascular compartments in the model [1]. The influence of MION dosage on the results was also evaluated using doses between 2-12 mg/kg. B_o maps were created using a high-resolution multi-echo gradient echo sequence. The LSO_2 maps were computed as previously described [1].

RESULTS: Example T_1-weighted, T_2-weighted and T_2*-weighted images and R_2, R_2* (before MION injection), R_2* (after 10 mg/kg MION injection), blood volume (BV), and LSO_2 maps are shown in **Figure 1.** In the BV_f map, outer strip of outer medulla showed slightly lower blood volume than cortex, while the papilla and inner medulla showed high blood volume (which is likely due to large-sized arteries and veins). The cortex exhibited slightly higher LSO_2 levels than that found in the outer medulla, but in general the LSO_2 maps were relatively homogeneous across the kidney. The mean LSO_2 in the kidney was 70%. These results are in good agreement with LSO_2 values measured with hyperspectral imaging oximetry [2]. At high doses of MION (**Figure 2**), the LSO_2 values in medulla (white arrows) are higher than those observed at lower MION dosages, potentially reflecting partial volume effects from large caliber arteries and veins.

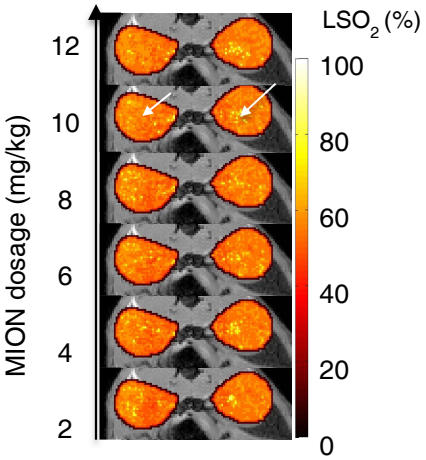

Figure 2. MION Dosage impact

DISCUSSION: These preliminary results indicate the feasibility of using qBOLD to map intrarenal blood volume and oxygenation. We are currently investigating ways to improve (and validate) the B_o correction schemes required for qBOLD analysis, particularly the use of high-resolution 3D multiple gradient echo sequences. We are also evaluating whether qBOLD can reliably detect changes in renal oxygenation following pharmacological manipulation of blood flow and hypoxic gas challenges. Once validated, qBOLD could shed new insights into abnormal renal oxygenation in mouse models of renal disease.

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References: 1.Christen T, et al. *NMR Biomed* 2011, **24**(4):393-403. 2.Scheeren TW, et al. *Transpl Int* 2011, **24**(7):687-696.