

Mapping of Intra-Renal Oxygenation by Quantitative BOLD

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Introduction: Renal medullary hypoxia is a hallmark of the pathogenesis in both acute and chronic renal diseases, including renal artery stenosis, diabetic nephropathy, hypertension and transplantation related renal dysfunction (1-3). Renal BOLD imaging is a useful semi-quantitative method for monitoring the *relative* tissue oxygenation changes under physiological or pharmacological maneuvers (4). It is known that changes in renal BOLD signal may not directly relate to the intra-renal oxygenation, and multiple factors other than blood oxygenation may influence tissue R2*, such as blood volume, perfusion, oxygen consumption, and changes in tissue composition.

A previously proposed MRI-based quantitative BOLD (qBOLD) technique allows for the separation of contributions to the BOLD signal from blood oxygenation level and the deoxygenated blood volume, thereby providing regional *in vivo* measurement of blood oxygen saturation in the brain (5-7). In this study, we have developed a framework for MR qBOLD-based quantification of regional and absolute intra-renal blood oxygenation in the baseline and under an acute water-loading challenge.

Methods: Seven healthy volunteers have been recruited for this IRB approved study. All images were acquired on a Siemens 3T Trio scanner using spinal and body matrix coils as receivers. A multi gradient-echo 2D GEPCI (Gradient Echo Plural Contrast Imaging) sequence (8) was employed. The MRI parameters were: sampling matrix of 208x208, voxel size of 1.4x1.4x6.0 mm³; TR of 95 ms, first echo at 3.16 ms with echo spacing of 2.88 ms, echo train length of 23, total acquisition time of 20 s within a single breath-hold. Six repetitions were acquired for each slice position. Field map was acquired by a 3D double-echo sequence with voxel size of 2.5x2.5x1.5 mm³. Regular 3D renal BOLD images were acquired with echoes at 2, 5.28, 8.56, 11.84, 15.12, 18.4 and 21.68 ms. Three subjects were instructed to conduct an acute water-loading challenge after a 12 hour overnight fast without food or water. After baseline acquisition, the subjects were asked to drink 1200 ml of sodium-free water within 15 min to induce water diuresis.

Results & Discussions: The observed T2* MR signal evolution profile for a given renal voxel was fitted to a renal MR signal qBOLD model, which combines contributions from water signal in intravascular blood and extravascular parenchyma, similar to the brain study (6). Fig. 1 shows representative signal profiles from two voxels selected within renal cortex (red triangles) and inner medulla (blue circles). The estimated signal contributions from parenchyma water and intravascular blood were also presented. The estimated venous blood oxygen saturation level was 86.2% (PO₂ of ~51 mmHg) for the cortical voxel, and 45.0% (PO₂ of ~24 mmHg) for the inner medullary voxel. Fig1 also illustrates a map of the mean intra-renal blood oxygen saturation level, and the estimated R2* map from 3D renal BOLD. In renal cortex, the estimated blood oxygenation was very high (~85%). Significantly lower blood oxygenation was detected in the renal medulla close to the cortex/medullary boundary (~60-80%), and in the inner-medulla (~20-40%). Our observations correlated well with findings from renal tissue PO₂ and microvascular pPO₂ using invasive techniques in animal models (9,10). We also noted heterogeneities of venous blood oxygenation across different medulla pyramids, and heterogeneities within the same medulla pyramid. Combining the data from neighboring slices, for most of the medullary pyramids, areas further away from the cortex/medulla boundary tended to have a lower blood oxygenation level, supporting the existence of renal arterial-to-venous (A-V) oxygen shunting (11).

Fig. 2 shows changes in intra-renal blood oxygenation and R2* induced by acute water loading in one of the three subjects. Improved medulla blood oxygenation and reduced R2* were evident in both the inner medullary and cortical/medullary boundary, whereas the cortical blood oxygenation and R2* were not significantly affected.

Conclusion: The proposed renal qBOLD approach, for the first time, provides an in-vivo non-invasive regional quantification of the intra-renal blood oxygenation level. When fully validated, this technique could be used as a simple but sensitive tool for the diagnosis and clinical management of patients with a wide range of renal diseases prone to ischemic injury, including acute tubular necrosis, diabetic nephropathy, and drug or contrast-induced nephropathy.

References: (1) Prasad, AmJPRP 2006; 290:F958. (2) Sadowski, et al., MRI 2010; 28:56. (3) Sadowski, et al., Radiology 2005; 236:911. (4) Haque, et al., JMRI 2011; 33:898. (5) He & Yablonskiy, MRM 2007;57:115; (6) He, et al., MRM 2008;60:882. (7) Yablonskiy & Haacke, MRM 1994;32:749. (8) Luo, et al, Proc. ISMRM 2010; p2089. (9) Auland, ActaPhysiolScand 1962; 56:315. (10) Johannes, et al, JAppPhysiol 2006; 100:1301. (11) Evans, et al., AmJPRP 2008;295:F1259.

