

Effect of Water Diffusion on Intra-Renal Oxygenation Quantification

Xiang He¹, Serter Gumus¹, Ayaz Aghayev¹, and Kyong Tae Bae¹

¹Department of Radiology, University of Pittsburgh, Pittsburgh, PA, United States

Introduction: Renal tissue oxygenation is crucial in renal physiology and pathophysiology (1). While highly invasive apparatus such as microelectrodes (2) or optical oxygen probes (3) have been used in animal models to directly measure intrarenal oxygenation, they are not practically applicable to humans. Prasad *et al* (4) pioneered the development of MRI-based renal BOLD (blood oxygen level dependent) technique to non-invasively estimate intrarenal oxygenation. However, renal BOLD measurement ($R2^*$) contains the contributions from multiple factors including blood volume, oxygenation and renal tissue composition. In the previously proposed renal quantitative BOLD (qBOLD) technique (5), intra-renal oxygen saturation level was quantified by means of analytically separation of contribution from blood oxygenation level and the deoxygenated blood volume.

A 2D multi-echo gradient echo pulse sequence has been used for the acquisition of the renal qBOLD signal. As in brain qBOLD applications (6), a spin-echo based GESSE (gradient echo sampling of spin echo) sequence is preferred because it can capture the deviation from mono-exponential $T2^*$ decay occurring both before and after spin echo, leading to improved robustness and accuracy. In this study, we compared the gradient echo-based versus spin echo-based approaches to estimate intra-renal oxygenation. We also demonstrated that gradient-echo based technique, un-accounted for the effect from water diffusion, provided more accurate and robust estimation of intra-renal oxygenation than spin-echo based technique.

Methods: A total of four healthy volunteer subjects have been recruited for this study. All images were acquired on a Siemens 3T Trio MR scanner. To minimize kidney motion, all MRI images were acquired during an end-expiration breath hold. The MRI parameters for GESSE images were: FOV of 300x204 mm², sampling matrix of 128x87, voxel size of 2.34x2.34x6.0 mm³, flip angle of 120 degree (to increase SNR); TR of 250 ms, spin echo varying from 20 to 88 ms, gradient echo spacing of 2.4 ms, echo train length of 47, total acquisition time of ~23 s. The MRI parameter for gradient-echo based renal qBOLD images (GEPCI) were the same as GESSE except: sampling matrix of 208x156, voxel size of 1.44x1.44x6.0 mm³; TR of 125 ms, first echo at 3.12 ms with echo spacing of 2.81 ms and echo train length of 23, acquisition time of 20 s.

Result & Discussion: The figure shows a comparison between the spin-echo and gradient-echo based methods. In the first study (a), the estimated $R2^*$ and renal oxygen extraction fraction (OEF) clearly delineated the renal cortex and medulla. The gradient echo-derived (GEPCI) intra-renal oxygenation map demonstrated a much lower medullary oxygenation level than that of the SE-derived (GESSE) approach (spin echo at 40 ms), especially for the right kidney. A similar pattern was observed for the second subject (1b). When the spin echo time increased from 40 ms to 88 ms, the estimated medullary oxygenation level was further increased (OEF decreased). Meanwhile, the SNR of GESSE image was significantly lower [~130 (SE=40 ms) and ~85 (SE=88 ms)] than that of the GEPCI approach (~230, extrapolated to the same voxel size as in GESSE experiment). This is expected for the GESSE-based approach. To accommodate a spin-echo structure, TR used for the GESSE acquisition was significantly longer, which resulted in a reduction in spatial resolution to fit the entire image acquisition within a single breath-hold. Although the GESSE technique improves the detection of the deviation from mono-exponential $T2^*$ decay occurring both before and after spin echo for improved accuracy on qBOLD estimation, it is also associated with reduced SNR (due to $T2$ decay). This is evident from the much lower estimated coefficient of variance (COV) in GEPCI-based vs. GESSE-based intra-renal oxygenation (data not shown).

The reduced qBOLD effect observed in the spin-echo based GESSE approaches suggests that water diffusion plays an important role in renal qBOLD measurement that currently are not taken into account in our theoretical model. Our model is only valid under a static dephasing regime (SDR) framework, which assumes that the dephasing of the MR signal due to mesoscopic field inhomogeneities created by the blood vessel network is much faster than the phase averaging from rapid diffusive movement of water molecules. As demonstrated by Fujita *et al* (7) and Dickson *et al* (8) based on Monte Carlo simulations, the complexity of modeling water diffusion on venous blood oxygenation can be largely avoided using gradient-echo based approach. In the renal medulla, the existence of luminal flow within the extravascular compartment, i.e., renal tubules and collecting ducts, causes a much faster apparent decay of MR signal than diffusion alone (IVIM, intravoxel incoherent motion effect (9)). Because of this, spin-echo based approach may lead to a much lower estimated medullary oxygenation level compared to the gradient-echo derived value, even though the medullary venous vasculature (ascending vasa recta) has a mean diameter of ~ 20 μ m, which in a brain study is large enough to satisfy SDR.

Conclusion: In this study, we investigated the role of water diffusion on renal qBOLD-based assessment of intrarenal oxygenation. We demonstrated that due to IVIM effect, gradient-echo based strategy provides improved accuracy and robustness.

References: 1. Brezis M, *et al*, *NEJM* 1995;332:647. 2. Brezis M, *et al*, *AmJPhysiol* 1994;267:F1059-62; 3. Johannes T, *et al*, *JApplPhysiol* 2006;100:1301; 4. Li LP, *et al*, *JMRI* 2004;20:901; 5. He X, *et al*, *Proc. ISMRM* 2012; 6. He X, *et al*, *MRM* 2007;57:115; 7. Fujita N, *et al*, *Neuroimage* 2003;20:2071; 8. Dickson JD, *et al*, *JMR* 2011;212:17. 9. Le Bihan, *et al*, *MRM* 1989;10:324.

