Non-invasively Quantitative Measurements of Intrarenal Oxygen Extraction Fraction (OEF) in Rabbits with Unilateral Renal Artery Stenosis Using MRI

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Introduction

Quantitative measurement of renal oxygenation is of central importance in understanding and treating renal diseases. In the context of Blood Oxygenation Level Dependent (BOLD) contrast, Gradient Echo (GRE) based sequences have been employed to estimate the normal human renal R2* non-invasively [1]. Moreover, according to the biophysical analytical model [2], R2′ is measured by using Asymmetric Spin Echo [3]. R2′ is linearly dependent on tissue oxygenation [2], however, R2′ contains the contributions from multiple factors including blood volume, oxygenation and renal tissue composition. Oxygen extraction fraction (OEF) is critically important to access the tissue oxygen metabolism under both normal and disease states [4], therefore, OEF able to provide a more specific and direct evaluation of renal oxygenation. In this study, a multi-echo gradient and spin echo (MEGSE) sequence [5] was implemented to estimate intra-renal OEF as a direct indication of the renal oxygenation level in rabbits. MEGSE sequence was used to assess the intra-renal OEF of normal health rabbits. Furthermore, we evaluated whether the MEGSE approach can reliably detect renal oxygenation changes under a pathological/physiological condition induced by the renal artery stenosis.

Materials and Methods

Three New Zealand rabbits weighting 2.8-3.5kg were study with an approved animal protocol by the Ethics Committee. Left Renal Artery Stenosis (RAS) was induced

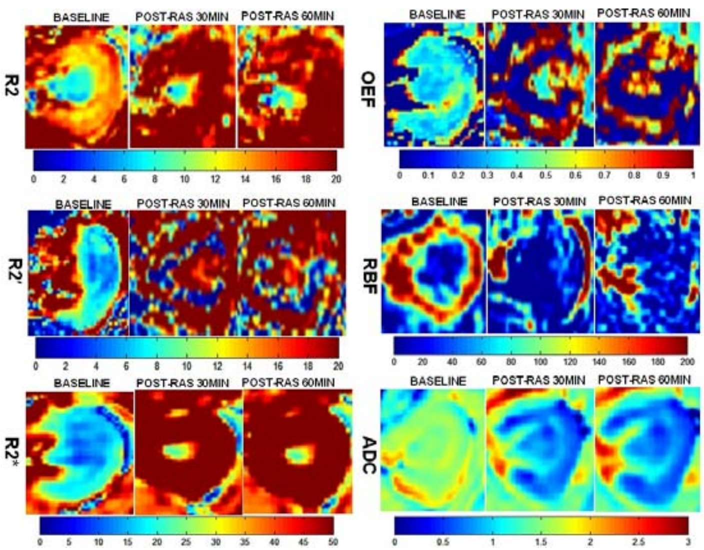

Figure. 1. Representative OEF, RBF, R2, R2′, R2* and ADC maps acquired pre-, post-RAS operation 30 and 60 minutes in the same rabbit. The unit of R2, R2′ and R2* are Hz, RBF is ml/(100g*min), ADC is 10^{-3}mm^2/s.

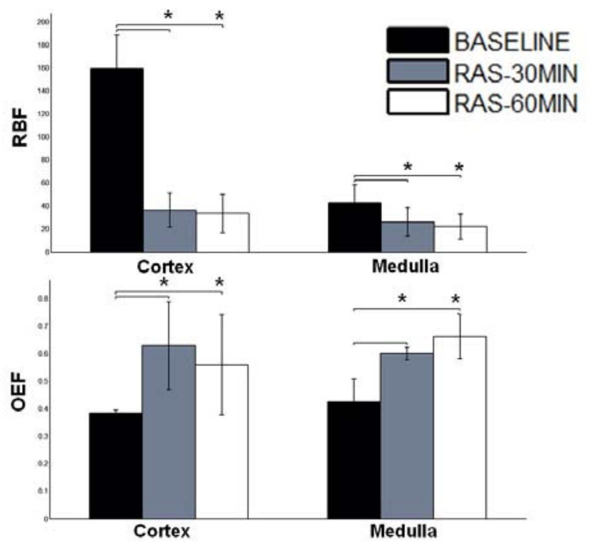

Figure. 2. Mean and intersubject deviation of intrarenal RBF and OEF in the cortex and medulla on baseline, post-RAS 30 and 60 minutes. Asterisk (*) indicates $p<0.05$ using paired Student's t-test.

surgically in all animals. MR images were acquired on a 3.0T whole-body MR scanner (Signa Excite™; GE Medical Sysgems, Milwaukee, Wisconsin, USA) with 8 Channel Phase Array KNEE coil in rabbits. Three sequential MR scans were acquired pre-, post-RAS operation 30 and 60 minutes for the baseline (tp1), RAS 30MIN (tp2) and RAS 60MIN (tp3) scans, respectively. Multi-echo gradient and spin echo (MEGSE), Arterial Spin Labeling (ASL), Blood Oxygen Level-Dependent (BOLD), and Diffusion weighted images (DWI, b = 800 s/mm^2), were acquired at all three time points (tps) in this sequential order. As in brain OEF applications[4], a 2D multi-echo gradient and spin echo (MEGSE) was used for the acquisition of the renal OEF signal. The MRI parameters for MEGSE images were: TR=1500ms; TE=56ms, # of echo = 32, echo spacing = 3.748ms, readout bandwidth = 62.5kHz, FOV=256*256mm^2, matrix size = 128*128, slice thickness = 5mm. Free hand ROIs were defined to encompass the renal cortex and medulla region of rabbits to obtain OEF, R2, R2′, R2*, RBF and ADC at all three time points. Paired student t test was employed to test whether measurements of renal OEF was significantly different pre- and post renal artery stenosis.

Results

Representative OEF, RBF, R2, R2′,R2* and ADC maps from one rabbit pre- and post-RAS are shown in Figure 1. At the Post RAS time points (tp2 and tp3), RBF and ADC decrease, meanwhile, OEF, R2, R2′ and R2* increase in the occluded cortex and medulla region. As shown in Figure 2, significant reductions of RBF and increments of OEF in the renal cortex and medulla were obtained (Cortex, RBF = 159.44±29.41 baseline vs. 35.25±15.01 post-RAS 30 min, 33.40±16.72 post-RAS 60 min, $P < 0.05$; OEF = 0.38±0.01 baseline vs. 0.63±0.16 post-RAS 30 min, 0.56±0.18 post-RAS 60 min, $P < 0.05$. Medulla, RBF = 43.00±15.30 baseline vs. 26.10±12.35 post-RAS 30 min, 22.15±10.88 post-RAS 60 min, $P < 0.05$; OEF = 0.42±0.08 baseline vs. 0.60±0.02 post-RAS 30 min, 0.66±0.08 post-RAS 60 min, $P < 0.05$), suggesting an increase of oxygen consumption in the cortex and medulla region after the renal artery stenosis.

Discussion and Conclusions

Renal artery stenosis decreases the supply blood flow to kidney tissue and may lead to a hypoxic state. It is expected that intra-renal OEF may increase due to insufficient blood flow under this pathological condition. In agreement of this concept, our results demonstrated that a consistent and significant increase of renal OEF in rabbits post renal artery stenosis, suggesting that MEGSE technique can be utilized to noninvasively detect pathophysiological changes in intra-renal OEF during an acute reduction of RBF, which may be potentially applicable in humans.

Reference

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