

Regional BOLD parameters are correlated with renal filtration and perfusion in healthy human kidneys

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INTRODUCTION

Adequate oxygen is critical for maintaining normal function of a kidney. In a healthy kidney, ~20% of plasma is filtered into tubules, and about 1/4 of it is reabsorbed along medullary thick ascending limb (mTAL). Water and sodium reabsorption at mTAL consume a large amount of oxygen. With low medullary perfusion, even in healthy kidneys the renal medulla is in a continuous state of hypoxia. Since further reduction of pO₂, e.g. due to lower perfusion, is a common cause of both acute and chronic kidney disease (1), development of a technique for measuring and monitoring renal pO₂ would have a significant clinical impact. In the last decade, blood oxygen level dependent (BOLD) MRI has shown to be promising in estimating tissue pO₂ noninvasively. Spin-spin relaxation rate (R2*) was shown to be sensitive to stimuli that change medullary pO₂ level (2). However, as microprobe technique is not applicable for human kidneys, direct correlation between R2* and tissue pO₂ has never been studied in human subjects. In order to validate BOLD as a marker of renal oxygenation we have measured the correlation between BOLD signal and renal functional parameters such as glomerular filtration rate (GFR) and tissue perfusion (F) in normal human kidneys. To our knowledge, this study has never been done in literature.

MATERIALS AND METHODS

Five healthy subjects (3 females and 2 males, age 45±13 yrs) consented to participate in this study. All scans were performed in a 1.5T MRI unit (Avanto, Siemens Medical Systems, Erlangen, Germany). BOLD and T₂-weighted imaging were performed with the following parameters: BOLD: 2D gradient-echo, 25 echoes with monopolar gradient echo readout and echo time (TE) from 1.78 to 58.42 ms with equal interval of 2.36 ms; voxel size 1.64 mm×1.64mm; matrix 256×208; repetition time (TR) 80 ms; flip angle 25; bandwidth 700 Hz/pixel; 1 average. T₂-weighted imaging: 2D turbo-spin-echo (TSE) sequence, eight echoes with TE from 18 to 142 ms with equal intervals of 18 ms; turbo factor 4; voxel size 0.88×0.88; matrix 480×400; TR 800 ms; bandwidth 495 Hz/pixel; number of averages 1. Imaging of a single coronal slice 7 mm thick was completed in one breath hold. For gadolinium enhanced MR renography, coronal 3D FLASH was performed with parameters: TR/TE/flip angle=2.84ms/1.05ms/12°, FOV 425×425 mm², voxel 1.7×1.7×2.5 mm³, acquisition time 3s). A 4 ml bolus of Gd-DTPA was injected, followed by 20 ml saline flush both at 2 ml/s. Eight seconds following the start of Gd-DTPA injection, 10 acquisitions were repeated continuously for 30 s, during which the subject suspended respiration. 12 additional volumes were acquired during separate breath-holds over 5 min.

Exponential decay model was fitted to the multi-echo BOLD images to obtain R2* map. Regions of interest (ROI) for cortex and medulla were drawn by an expert observer and copied to R2* maps to get averaged R2* values, R2*_{Cx} and R2*_{Med}. The same method was applied to T2-weighted data, yielding R2 values, R2_{Cx} and R2_{Med}. After subtracting R2 from R2*, we obtained R2'. MR renography data was analyzed using published techniques to yield GFR and a perfusion map. Correlation coefficient was calculated between the BOLD/T2 parameters (R2*, R2') and the parameters derived from MR renography (GFR, F, GFR/F).

Table 1: Correlation coefficients (CC) between BOLD parameters and MR renography parameters. CCs larger than 0.60 are shaded and the corresponding P values are in parentheses.

	R2* _{Cx}	R2* _{Med}	R2' _{Cx}	R2' _{Med}
GFR	-0.01	0.01	0.20	0.24
F _{Cx}	-0.48	-0.30	-0.51	-0.27
F _{Med}	-0.45	-0.42	-0.16	-0.27
GFR/F _{Cx}	0.44	0.31	0.65 (0.043)	0.49
GFR/F _{Med}	0.37	0.68 (0.030)	0.17	0.62 (0.058)

RESULTS AND DISCUSSION

Table 1 shows the correlation coefficients (CC) between BOLD and the filtration and perfusion parameters. The strongest associations (CC > 0.60) were found for GFR/F_{Med} vs R2*_{Med} (0.68), GFR/F_{Cx} vs R2'_{Cx} (0.65), and GFR/F_{Med} vs R2'_{Med} (0.62). Since perfusion determines the amount of oxygen delivered to the tissue and GFR might relate to the oxygen consumption (the higher GFR, the more water need to be reabsorbed), we presumed that the ratio of GFR and F (especially medulla perfusion) may correlate with tissue pO₂ and thus BOLD measurements. This might be the reason for the high correlation between GFR/F and R2* or R2'. Note that subtracting R2_{Med} from R2*_{Med} did not increase the correlation coefficient further, which is contradicted with our expectation. This is probably due to the additional noise introduced by R2 values.

The highest correlation coefficients (2 have P value<0.05) are larger than 0.6, which is remarkably strong, in view of measurement noise. The noise includes (1) low SNR of BOLD signals acquired at 1.5T; (2) motion artifact for all acquisitions; (3) susceptibility artifact in some BOLD data sets; (4) misregistration between ROIs in different maps, and (5) limited number of subjects. These limitations could be overcome in future study by performing the measurements at higher field (3T instead of 1.5T), applying better shimming technique and so on. It is also highly possible that BOLD and MR renography parameters are related in a nonlinear way, because of their respective nonlinear relationship with our target parameter, tissue pO₂.

In conclusion, we observed significant correlations between regional BOLD and MR renography parameters in healthy kidney, suggesting that BOLD could be a promising tool for functional assessment of kidney. Absolute quantification of tissue pO₂ from BOLD signals will require further technical improvements and better understanding of BOLD effect.

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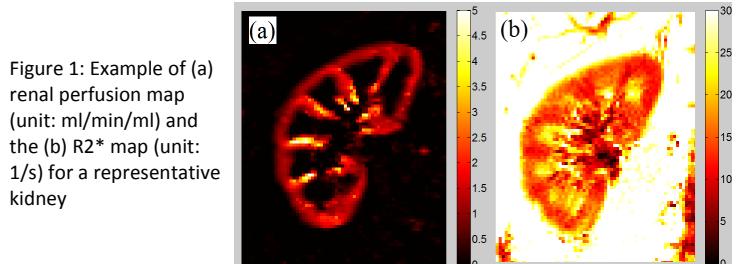


Figure 1: Example of (a) renal perfusion map (unit: ml/min/ml) and the (b) R2* map (unit: 1/s) for a representative kidney