

Non-invasively Quantitative Measurements of Intrarenal R2' in Human Using an Asymmetric Spin Echo EPI Sequence

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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]. However, R2* is a summation of irreversible (R2) and reversible (R2') relaxation rates (R2* = R2 + R2'). It has been suggested that R2 is sensitive to many physiological perturbations, including tissue water content, inflammation and the change of tissue oxygenation. According to the biophysical analytical model [2], R2' is dependent on tissue oxygenation in a linear and direct manner. R2' is, therefore, able to provide a more specific and direct evaluation of renal oxygenation. In this study, an asymmetric spin echo (ASE) single shot echo planar imaging (EPI) sequence [3] was implemented to estimate R2' as a direct indication of the renal oxygenation level in normal volunteers. Renal R2' measurements were repeated over a course of three days to assess the reproducibility of the method. Furthermore, we evaluated whether the ASE-EPI approach can reliably detect renal oxygenation changes under a physiological/pharmacological condition induced by a loop diuretics, furosemide.

Method

This study was approved by the Ethics Committee. In total, two groups of healthy young subjects (Group 1, n = 9 and Group 2, n = 10) were studied with informed consent. In group 1, the reproducibility of measurements with ASE EPI sequence in the intrarenal R2' was evaluated in nine healthy young subjects (three men, six women, age range, 20-32 years) and the baseline ASE-EPI sequence was repeated three times on three consecutive days. In group 2, ten healthy young human subjects (six men, four women; age range, 22-39 years) were studied and ASE images were acquired before and after the administration of furosemide. The ASE-EPI images were acquired at the end of expiration with breath-holding. For group 2, furosemide (20mg, IV) was injected intravenously. Then, the same ASE-EPI sequence protocol was repeated 5 minutes after the furosemide injection. All of the experiments were conducted on a 3.0 T whole-body MR scanner (Signa ExciteTM; GE Medical Systems, Milwaukee, Wisconsin, USA). The ASE-EPI protocol included one spin echo and 19 asymmetric spin echoes. The 19 ASE images were acquired using different 180° pulse offset time (τ) ranging from 10.75 ms to 24.25 ms with an increment of 0.75 ms, and one SE image at $\tau = 0$ ms. The reversible R2' decay time is 2τ . Other parameters were TE = 65ms, TR = 1000ms, Field of View = 240mm*240mm, matrix size = 96*64, slice thickness =

Figure 1. Representative anatomical Spin-Echo images acquired pre (a) and post (b) Furosemide administration. The free hand ROIs in cortex and medulla region are marked in (c).

6mm, number of slices = 8, and the total data acquisition time for the ASE-EPI sequence was 20s. To examine the impact of the presence of intravascular signal on the measurement of intrarenal R2', different levels of flow dephasing gradients ($b = 0$, $b = 40$, and $b = 80$ s/mm²) were applied to suppress intravascular signal. An analytical signal model [2] was employed to estimate renal R2'. Regional renal R2' was calculated by means of region of interest (ROI) analysis. The acquired spin echo EPI image ($\tau = 0$) was used to manually define ROIs. Free hand ROI that cover at least 20 pixels was placed in multiple slices (Figure 1.c demonstrates the ROIs overlay on the spin echo image). The reproducibility of ASE-EPI sequence was evaluated using the coefficient of variance (CV). Paired student t test was employed to test whether measurements of renal R2' was significantly different before and after the administration of furosemide.

Results

Representative SE anatomical images from the same slice pre and post furosemide administration are shown in Fig. 1. In the absence of flow dephasing gradients in the ASE EPI sequence ($b = 0$), in medulla region, the computed coefficient of variation (CV) was $21.31\% \pm 4.52\%$, and furosemide induced a slight decrease in R2' without statistical significance ($p > 0.05$).

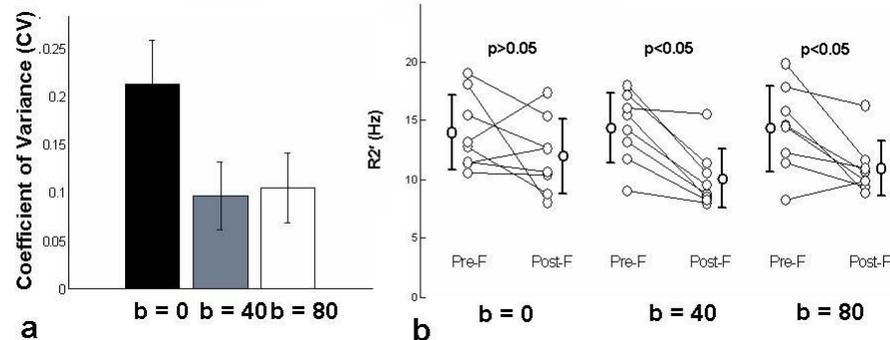


Figure 2. Comparison of changes in coefficient of Variance (CV) in response to different levels of flow dephasing gradient (a). Individual changes in medullary R2' in response to different levels of flow dephasing gradient pre and post furosemide administration (b).

ASE-EPI method can provide quantitative measurements of renal R2' rapidly (within 20 seconds) in human under both normal and pharmacological altered conditions. This method is highly reproducible and is sensitive to detect the R2' changes induced by renal oxygenation changes under pharmacological conditions. Our results also suggest that small flow dephasing gradients, e.g. $b = 40$, should be applied to suppress intravascular signal for a reliable measurement of renal tissue R2' measurements.

Reference

- [1] Prasad PV, et al, Circulation 1996; 94:3271-3275.
- [2] Yablonskiy DA and Haacke EM. MRM 1994; 32:749-763.
- [3] An H, et al, MRM 2003; 50:708-716.

On the other hand, CV was reduced to $9.68\% \pm 3.58\%$ ($b = 40$) and $10.50\% \pm 3.62\%$ ($b = 80$), respectively, after using flow dephasing gradients in the ASE EPI sequence. As shown in Fig. 2, significant reductions of R2' in the renal medulla were obtained ($b = 40$, R2' = 14.56 ± 2.38 pre-furosemide vs. 10.16 ± 1.81 post-furosemide, $P < 0.05$; $b = 80$, R2' = 14.31 ± 3.67 pre-furosemide vs. 10.93 ± 2.32 post-furosemide, $P < 0.05$), after the administration of furosemide, suggesting an increase of oxygen tension in the medullary region. Moreover, R2' measurements did not differ much between $b = 40$ and $b = 80$ scans, suggesting small diffusion gradients were sufficient to minimize the effects from intravascular signal.

Discussion and Conclusions

Our preliminary results demonstrated that a single shot