Contrast/SNR optimization for the Imaging of Cationized-Ferritin labeled Glomeruli at 9.4T

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Target Audience

Scientists involved or interested in performing glomerular imaging using MRI for the quantification of glomeruli could benefit from this work. This work could also be of interest to scientists and clinicians performing kidney imaging at ultra-high-fields and/or using cationized-ferritin (CF) as a contrast medium.

Purpose

In this work we present a method for contrast enhancement between glomeruli labeled with CF and the kidney cortex, where they are embedded. This facilitates the glomerular imaging, and the possible glomerular segmentation and quantification. An estimation of the effective transverse relaxation time (T_2*) of the kidney cortex at 9.4 T is given. For practical purposes we use the term cationized-ferritin labeled glomeruli (CFgl) to describe the net apparent effect of the CF in glomeruli in the case of perfused in vitro kidneys. This T_2* estimation is presented as well.

Introduction

Glomeruli are networks of capillaries in the kidney cortex where the blood is filtrated and purified from waste produced during cell metabolism. A reduction in the number of glomeruli is not only linked to a lower efficiency in the purification of the blood but also diverse kidney diseases [1]. Therefore, by monitoring the number of glomeruli in the kidney the condition of the kidney could be diagnosed.

MRI has been used in studies to image CFgl in the kidney using small rodents. In vitro and even some in vivo experiments have been performed [2-4]. The imaged glomeruli of in vitro samples have also been counted using image post-processing techniques. The main challenge of imaging glomeruli with MRI is that long acquisition times are required (reported to be at least 4 hours [2]) even when using ultra-high-fields ($\geq$ 7 T) in high-end preclinical scanners. Optimization of the imaging protocols can reduce the scanning times and improve the accuracy and efficiency of possible glomerular quantifications.

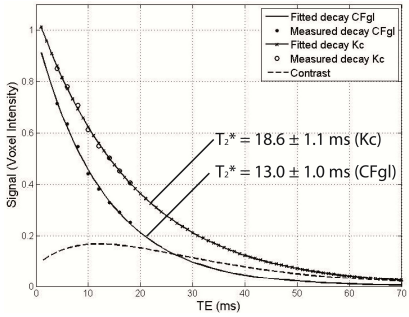

Figure 1 *T_2* decays of the kidney cortex (Kc) and CF labeled glomeruli (CFgl). Contrast between them is presented for the optimal selection of TE*

Methods

Two mouse kidneys were labeled with CF (Sigma-Aldrich, St. Louis, MO), perfused and dissected following the protocol presented in [2,3]. Imaging was performed using a 9.4 T Bruker BioSpec 94/20USR small animal scanner (Bruker BioSpin GmbH, Ettlingen, Germany). 1st and 2nd degree order shimming and a purpose-built volumetric Alderman-Grant resonator [5] were used to maximize the homogeneity of B_0 and B_1 respectively, thus reducing the variability of the signal intensity across the image profile. 3D datasets of the whole kidneys were acquired using a standard GRE unbalanced sequence with a repetition time TR = 50 ms, flip angle = 15°, isotropic resolution = 100 µm³, field of view = 16.1x10x7.5 mm³, number of averages = 2, zero-filling = 1.5 and acquisition time = 5m46s. TE was varied from 4 to 18 ms in incremental steps of 2 ms to obtain a total of 8 datasets per kidney.

Image reconstruction and post-processing were performed with MATLAB (The Mathworks, Natick, USA). To estimate the T_2* of the kidney cortex two samples (41x41x6 voxels) were taken of the kidney cortex without medulla and background. A morphological algorithm was applied to fill the "valley" (low signal pixels) caused by the CF. The mean intensity values of the two samples were averaged and taken as the signal of the kidney cortex for every TE. The T_2* value of the CFgl was estimated by using the same samples in the calculation of the T_2* of the cortex. Those samples of the original volume (containing cortex and CFgl) subtracted from the filled volume gave the depth of the valley, which were the glomeruli. We obtained a mean of the depths and subtracted them from the mean cortex value of each selection. The average of the two samples was considered the signal in the CFgl. These signal values were verified by taking manual samples of the cortex and the glomeruli.

Exponentials were fitted to the signal intensities to find an estimate T_2* relaxation for both the cortex and the CFgl using the approximation $S_0 = \exp(-TE/T_2^*)$. The fitted T_2* exponential curves were subtracted from each other to find a contrast at the given echo times (see Fig. 1).

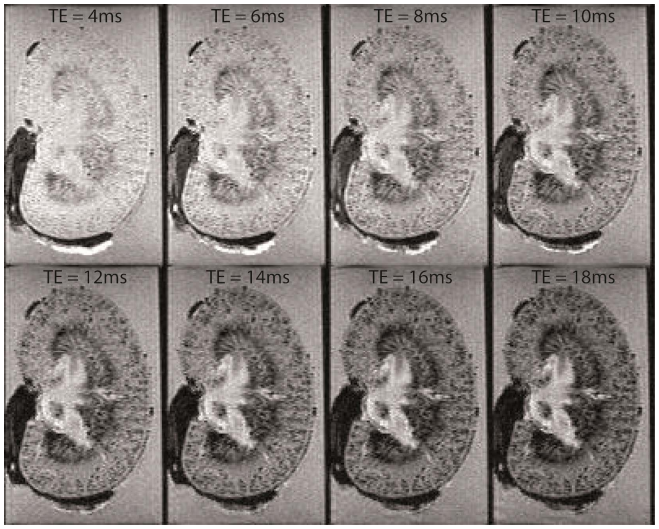

Figure 2 *CF-labeled mouse kidneys imaged at different echo times. Glomeruli can be observed as darker pixels in the cortex of the kidney.*

Results

Using a total acquisition time of ~46 minutes we acquired eight 3D datasets imaging whole mouse kidneys. Glomeruli in those kidneys were visible upon the optimization of the TE. This can be seen in Fig. 2 where very short TE values (e.g. TE = 4 ms) reduce or even impede the visibility of the glomeruli but as the TE increases, it becomes easier to distinguish the glomeruli from the cortex until the SNR becomes too low to distinguish them with certainty.

For this particular MRI system and imaging parameters, the maximum contrast between the kidney cortex and the CFgl was found at TE = 12 ms. The average T_2* value of the kidney cortex was found to be 18.6 ± 1.1 ms. We obtained an average T_2* value of the CFgl of 13.0 ± 1.0 ms both with 95% confidence in the exponential fit.

Discussion and Conclusion

There is an increase in apparent size of the glomeruli as the TE increases due to dissipative relaxation mechanisms [6] induced by the CF in its surroundings. This and possible geometric distortion effects [7] will be investigated into more detail in our future work. Nevertheless, the possible advantage provided by the increase in apparent size of the glomeruli (while segmenting or quantifying them) is diminished by the decay of the signal e.g. there is 27.6 % less signal at TE = 18 ms compared to TE = 12 ms. This produces a decrease in the overall SNR and longer scanning times could be required to visualize the glomeruli, especially as the resolution is increased. Considering the limited contrast between the cortex and the glomeruli and the overall decay of the signal, an optimum compromise was found at TE = 7 ms where we have ~95% of the contrast and a 55% increase of the signal calculated from the cortex at TE = 12 ms. Other compromises can be defined focusing on specific parameters: contrast, SNR and/or apparent glomerular size.

The T_2* values vary depending on the field strength and homogeneity of the scanner used. It could be a good practice to repeat this experiment in order to optimize the imaging parameters before performing glomerular imaging with higher resolutions. For the case of MRI systems with $B_0 < 7$ T where the experiment cannot be simulated due to a low SNR, Figure 2 can be useful as a visual reference for the parameter optimization of glomerular imaging i.e. by matching the contrast of cortex and medulla to the ones presented here where the glomeruli are visible. In conclusion, the information obtained from this simple and quick experiment can increase the efficiency of the glomerular imaging by optimizing the selection of TE, which has great impact on the SNR and contrast between the objects of interest.

References

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