Imaging Glomeruli in a Clinical MRI System at 3 T

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Introduction

Kidneys with reduced number of glomeruli (Nglom) have been associated with kidney diseases, hypertension and other conditions in past studies [1,2]. Obtaining the Ngloms of patients and monitoring their changes according to diseases and/or conditions would help foresee or prevent the need for dialysis or a transplant but the current gold-standard (Stereology) involves the dissection of the kidney and is not suitable for clinical applications. Using animal/research scanners at ultra-high-fields (B_0 = 7 T [3], 11.7 T [4], 9.4 T [5], and 19 T [6]), cationized-ferritin (CF) labeled glomeruli have been imaged and quantified from in vitro mouse, rat, and even human transplant kidneys. Based on these successful results, there is the hypothesis that obtaining glomerular numbers and sizes using MRI in vivo could not only be possible, but it could also be used in the future as a clinical routine. In order to prove that hypothesis, as a first step it is important to consider and evaluate the current limitations in the clinical area.

Compared to the preclinical animal scanners used so far for the glomerular imaging, average clinical scanners typically have lower main magnetic fields strengths e.g. 1.5 T to 3 T and rarely 7 T. Decreasing the main magnetic field reduces the effect of cationized-ferritin [6]. It also produces images with lower SNR for the same protocols and increases the relaxation times (T2 and T2*) of the tissues. Clinical scanners have also lower gradient strengths and slew rates. This limits the minimum field-of-view (FOV), resolution, minimum echo and repetition times (TE/TR). Finally, there are specific absorption rate (SAR) limitations in the clinical scanners for patient protection. SAR regulations restrict the use of saturation slices which could be used to reduce the FOV and therefore the scanning times.

To take a first step towards human applications, we used rat kidneys as proof of concept to demonstrate the feasibility of imaging CF-labeled glomeruli using a clinical scanner at 3 T. Furthermore, we assessed the current standing position on the way towards possible human trials.

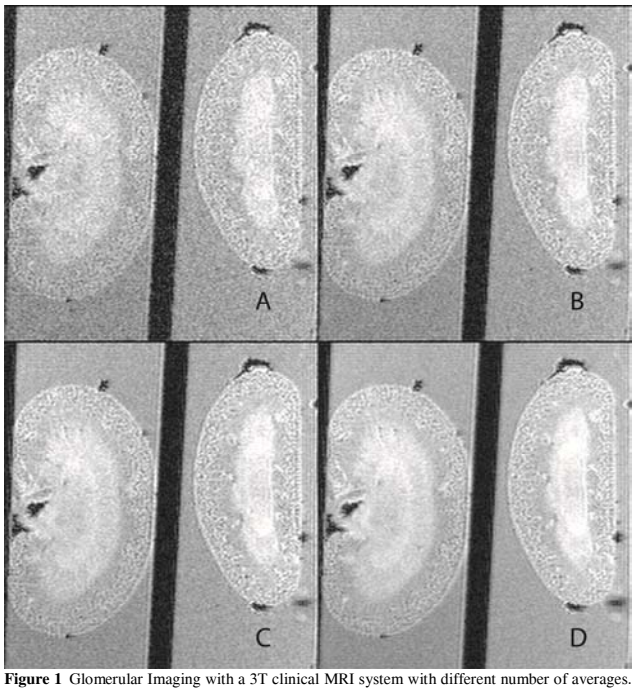

Figure 1 Glomerular Imaging with a 3T clinical MRI system with different number of averages. A) 8 averages B) 16 averages C) 24 averages D) 48 averages. Voxel size ≈ 86x78x100 µm³ after zero filling.

Materials and Methods

Two rat kidneys were labeled with CF and perfused as described in [4]. The kidneys were then embedded in agarose gel and imaged in vitro. The glomerular imaging was performed in a clinical Magnetom Skyra 3 T MR Scanner (Siemens Healthcare, Erlangen, Germany) with XQ gradients that deliver: maximum amplitude = 45 mT/m, minimum slew time = 225 µs and maximum slew rate = 200 T/m/s per axis. The coil used was an 8-channel rat volumetric resonator (RAPID Biomedical, Rimpar, Germany). A standard 3D gradient-echo sequence using Cartesian k-space sampling was used with the following parameters: TE/TR = 40/52 ms, FOV = 33x28.7x16 mm³, matrix size = 192x186x80, number of averages = 8, 16, 24 and 48 (Fig. 1 A-D) and scan time ≈ 12.5 min per average. The volume was zero-filled to 384x372x160 with MATLAB (The Mathworks, Natick, USA), resulting in a voxel size of ~86x78x100 µm³. A segmentation of the glomeruli was attempted using an algorithm based on morphological filling [8] in each dataset.

To assess the current standing point on glomerular imaging for humans, the average size of a human kidney was taken from the literature [7] and used as the FOV necessary to obtain a 3D dataset of the whole kidney. With this FOV and the imaging parameters from the glomerular imaging in rat kidneys, an estimated scan time was calculated. The average human right kidney dimensions used were: Length = 108.5 mm, Width = 51.3 mm and Thickness = 57.7 mm (FOV = 108.5x51.3x57.7 mm³). To provide an initial estimation of the minimum time it would take to scan a human kidney and visualize glomeruli using a clinical MR scanner, an initial calculation was made for an in vitro sample i.e. neglecting motion artefacts and aliasing problems. Once the FOV is estimated, the number of phase encoding steps necessary to cover a whole human kidney in each dimension is calculated and multiplied by the repetition time to find a scan time per average (Tacq = TRxPE1xPE2xNoAverages).

Results

3D volumes containing two CF-labelled rat kidneys were acquired using the minimum achievable FOV for the given parameters. The two kidneys were imaged entirely and simultaneously. The results of the segmentation when 48 averages were used can be observed in Figure 2. Glomeruli were identified by the segmentation algorithm but many 3D objects outside of the kidney were mistakenly segmented as glomeruli. Due to this inaccuracy of the segmentation, quantification of the segmented 3D objects was not achieved.

For the theoretical extrapolation of the same glomerular imaging protocol to a human kidney, a matrix size ≈ 631x332x289 was calculated. The multiplication of this matrix size times the repetition time (TR = 52ms) provided the acquisition time per average. This acquisition time in the case of a human kidney would be Tacq ≈ 1h23m per average.

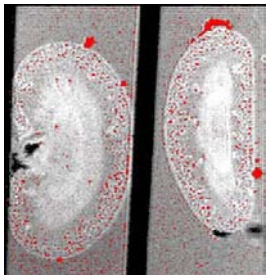

Figure 2 Results of the glomerular segmentation algorithm for the 48 averages' experiment. Tacq = 6h36m

Discussion and Conclusion

To our knowledge, this is the first time that glomeruli of any type of animal are shown using a clinical human MR system and at a B_0 of less than 7 T. This was achieved despite the restrictions in B_0, gradient amplitude and performance, and SAR. The glomeruli were visible using as few as 8 averages but the SNR is not enough to identify them clearly from the noise. The quantification of glomeruli was not possible for the combination of the resolution utilized and the SNR obtained. This means that if glomerular quantification is desired, the resolution has to be increased with a high impact on SNR that would have to be compensated via averaging with repercussions on the total scanning times. This is also yet to be proven feasible and is in the scope of our future work.

The experiment is a proof of principle to show that the echo times and repetition times, as well as the resolution that some clinical scanners can provide would be enough to image CF-labeled glomeruli. It is estimated that glomeruli in humans are ~7 times larger than the glomeruli in rats based on the average individual glomerular volume (IGV) in human (~4.48×10^{-3} mm³ [2]) and in rat kidneys (~6.62×10^{-4} mm³ [1]). This suggests that the parameters used here are enough to image glomeruli in human kidneys; moreover, the actual resolution needed to quantify glomeruli in human kidneys at 3 T using a clinical MRI scanner is expected to be in the order or lower than the one used in this study but it is yet to be determined by future experiments. However, due to the high acquisition times used in this experiment and considering patient motion and possible aliasing issues arising from the size of the human abdomen, it is unrealistic to expect successful human in vivo experiments with the current technology used in the clinical area and/or using the these imaging methods. Scanners with higher magnetic fields and improved imaging techniques could make this possible in the future. This makes glomerular imaging and quantification a challenging project with vast research opportunities.

References

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