Quantitative 3D molecular imaging of kidney glomeruli

D. H. Frakes[1], A. Elvikis[2], J. Plasencia[1], S. Beeman[1], and K. M. Bennett[1]

[1]Harrington Department of Bioengineering, Arizona State University, Tempe, Az, United States, [2]Partnership for Research in Spatial modeling, Arizona State University, Tempe, Az, United States

Introduction: Smart and targeted molecular imaging agents have been developed for MRI to detect molecules and cellular processes *in vivo* (1). Molecular targets are abundant for detecting pathology, and switchable smart contrast agents have been developed to be change contrast upon activation *in situ*. The goal of this work was to quantify the three-dimensional distribution of a contrast agent at a molecular target throughout an organ. Cationic iron oxides (cationic ferritin, CF) accumulate with high specificity on anionic glycosaminoglycans in kidney glomeruli, and are highly MRI-visible (2). Here we studied whether the three-dimensional accumulation of CF in the kidney glomeruli, as detected with T2*-weighted MRI, could be used to determine the number of kidney glomeruli and their spatial distribution.

Methods: A rat was injected by tail-vein with 3.3mg/100 g of cationic horse spleen ferritin (CF, Sigma Aldrich), in a bolus repeated two times in 1.5 hour intervals. The rat was sacrificed by perfusion, and the kidneys were placed in 2% gluteraldehyde buffer in a syringe. The left kidney was imaged in a Bruker 11.7T scanner, with a 3D GRE sequence with TE/TR = 12/30 ms, and resolution of 50 x 50 x 50 µm. Image data were segmented and reconstructed with Materialise Mimics software to isolate, quantify, and display glomeruli. Segmentation was performed with thresholding and region growing operations. Segmented data were then reconstructed from isotropic resolution to form 3D triangular meshes, using grey value interpolation to minimize partial volume effects. All quantitative calculations were based directly on the segmented image data.

Results and Conclusions: CF accumulated in kidney glomeruli, and not in the peri-glomerular space, seen in Fig 1a.Three-dimensional reconstruction allowed whole-organ views of the kidney, as seen in Fig 1b-c. Glomeruli throughout kidney were observed in 3D (Fig 1d), and placed in the context of the organ (Fig. 1e). Glomeruli were found to occupy a cumulative volume of 14.49 mm^3 within the 988.22 mm^3 kidney. A total of 68,830 distinct glomeruli were detected. This is consistent with number of kidney glomeruli reported in healthy rats in the literature (3). These results demonstrate the capability of MRI to quantify both the number of labeled kidney glomeruli and cumulative glomerular volume with the use of molecular imaging agents. This capability could be of significant clinical value in detecting single glomeruli for functional assessment in focal kidney disease, and could be used to quantify contrast agent uptake throughout the body.

References: (1) Querol M et al. Handb Exp Pharm. 2008; (185 Pt 2): 37-57. (2) Bennett KM et al. Magn Reson Med. 2008; 60:564-574. (3) Menini S et al. J Hyptertens. 2004; 22(11): 2185-2192.

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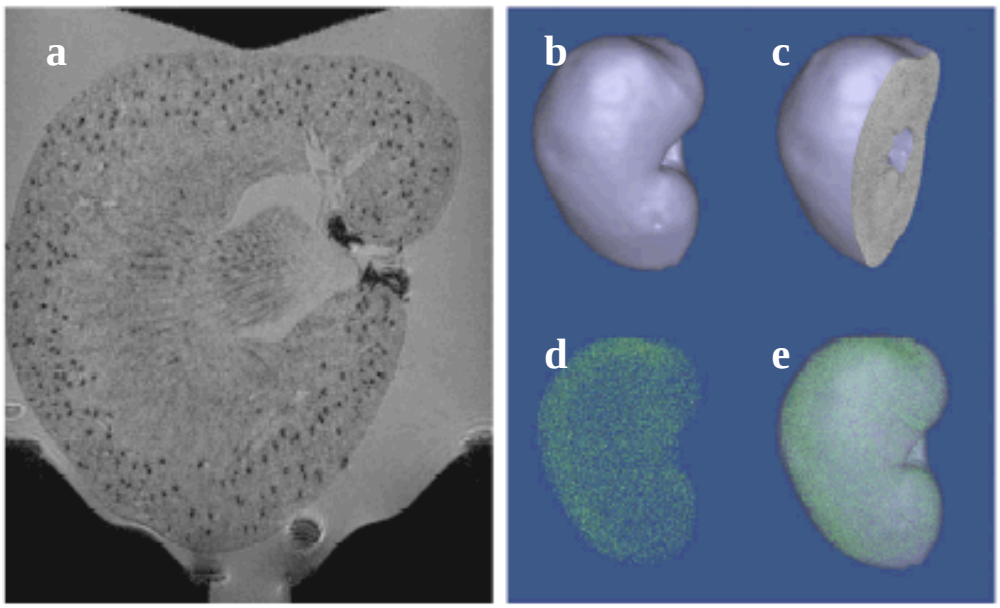

Figure 1: (a) 3D GRE-MRI showing a perfused, fixed kidney after intravenous injection of cationic ferritin (CF) nanoparticles. CF accumulated in glomeruli due to anionic proteoglycans. (b-c) 3D-reconstructed kidneys, showing surface, cortex, medulla, and pelvis. (d) Reconstructed map of labeled kidney glomeruli (deep glomeruli are not shown in the view), and (e) projected onto the kidney surface maps.