

MRI QUANTIFICATION OF SINGLE GLOMERULAR FUNCTION

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A fundamental problem in clinical nephrology is the lack of specific, quantitative information describing kidney function at the level of single glomeruli. Early-stage renal disease often presents in small regions of the kidney, and is not detected by bulk measurements of glomerular filtration. It is thus imperative to develop a method for detecting single glomerular function. We have developed a nanoparticle MRI contrast agent to detect glomerular structure and function. We have also developed a 3D method to quantify functional glomeruli in the whole kidney, and have validated the method in a rat model.

Rats were injected by tail-vein with 3.3mg/100g of cationic horse spleen ferritin (CF, Sigma Aldrich), in a bolus repeated at 1.5-hour intervals. Rats were sacrificed by perfusion and the kidneys were placed in a 2% glutaraldehyde buffer within a syringe. The left kidneys were imaged with an 11.7T Bruker MRI scanner (3D GRE pulse sequence, TE/TR=12/30ms, resolution=50x50x50 μ m). Image data were reconstructed and segmented with Mimics software (Materialise). Segmentation was performed using parametric thresholding and region-growing operations. Segmented data were then reconstructed into 3D meshes to represent both the kidney and the glomeruli within. Raw segmented data were used to count the number of glomeruli and to quantify both collective and average glomerular volumes.

CF was found to accumulate specifically in kidney glomeruli and single glomeruli were detectable with MRI. 3D reconstruction enabled whole-organ views of the kidney and the glomerular cloud within. 68,830 distinct glomeruli were found to occupy a total volume of 14.49mm³ within a 988.22mm³ kidney for a test case, corresponding to 2.11x10⁵ μ m³ per glomerulus. Data gathered using different amounts of contrast agent in both healthy and diseased cases will be presented.

The number of glomeruli detected for the test case was consistent with values from the literature. These results indicate that MRI is capable of quantifying glomeruli with molecular agents. This methodology could be clinically valuable in detecting distinct glomeruli for functional assessment of focal kidney disease, and for quantifying contrast agent uptake in numerous related applications.