Intravoxel Incoherent Motion Imaging of Renal Fibrosis: A Murine Model Study of Unilateral Ureteral Obstruction

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Target Audience: Radiologists and Scientists interested in renal imaging and intravoxel incoherent motion imaging

Purpose: Intravoxel incoherent motion (IVIM) modelling of diffusion-weighted imaging (DWI) data separately accounts for water diffusion and perfusion in the tissue[1]. The purpose of this study was to explore possible alterations in IVIM diffusion and perfusion parameters with the development of fibrosis in the kidney, using a murine model of unilateral ureteral obstruction (UUO).

Methods: This study was approved by the institutional animal care and use committee. UUO was created in 6 male C57/BL6 mice (8 weeks old, 20-30g) by ligating the ureters of their right kidneys only, while the left kidneys were undisturbed to serve as controls. The mice were scanned using a 7T microMRI scanner (Bruker ClinScan) 1 day before ligation and 7 days after ligation; afterwhich the kidneys were harvested for histology, which included staining with Sirius Red and Podocin for quantification of collagen as a marker of fibrosis and glomerulus counting, respectively. DW images were acquired using a multishot spin-echo echo-planar imaging sequence with the following scan parameters: TR = 3000 ms, TE = 41 ms, and *b* values of 0, 50, 100, 200, 400, 800, 1200 s/mm^2. Fitting of the IVIM model to voxel-level DWI data was performed using the approach proposed by Luciani et al[2] to yield parameters that reflect blood flow (*D**), perfusion fraction (*f*) and tissue diffusivity (*D*). Regions of interest were drawn over the renal parenchyma (cortex and medulla). Median parameter values before and after ligation, as well as between ligated (right) and non-ligated (left) kidneys were compared using the paired t-test. A $p<0.05$ was considered statistically significant.

Results: Histological analysis confirmed the development of fibrosis in all the ligated kidneys at Day7. Renal parenchyma *D* value was significantly lower in the ligated kidneys at Day7 ($0.958\pm0.101\times10^{-3}$mm^2/s, p=0.014) compared with the same kidneys before ligation (1.035 ± 0.055). Similarly, *f* values at Day7 after ligation (0.103 ± 0.040, p=0.046) was significantly lower than those before ligation (0.168 ± 0.034). No significant difference was found for *D** before ($7.026\pm1.244\times10^{-3}$mm^2/s) and after ligation (7.564 ± 0.906, p=0.386). Comparing between left (non-ligated) and right (ligated) kidneys within the same mouse at Day7, significantly lower *D* values were observed in the ligated kidneys as compared with the non-ligated ones (1.136 ± 0.055, p=0.012), while no significant difference was found for *f* and *D**, although the values of *f* are generally lower in the ligated kidneys. No significant difference was observed for all parameters when comparing left and right kidneys within each mouse before ligation. Similarly, no significant difference was observed for all parameters in the non-ligated (left) kidneys before and at Day7 after ligation procedures.

Discussion: Previous studies have shown that the apparent diffusion coefficient (ADC) decreases with the development of renal fibrosis[3]. This has been commonly attributed to an increase in cells, including fibroblasts, which hinder the diffusion of water in the interstitium. However, ADC reflects a combination of water diffusion and perfusion, thus possible microvascular contribution to ADC reduction in renal fibrosis cannot be ruled out. The present results suggest that apart from a reduction in tissue diffusivity *D* due to the increase in interstitial cells/fibroblasts with the development of renal fibrosis, there may also be a reduction in vascularity, which can be assessed using *f*. Histologically, this is supported by a general reduction of Podocin staining in the ligated kidneys, which is indicative of the decrease in glomerulus counts.

Conclusion: IVIM analysis revealed a decrease in both *D* and *f* in the renal parenchyma with the development of fibrosis, and suggested possible microvascular contribution to the reduction in ADC.

References: [1] Koh et al, AJR 2011;196:1351-61. [2] Luciani et al, Radiol 2008;249;891-899. [3] Togao et al, Radiol 2010;255:772-780.

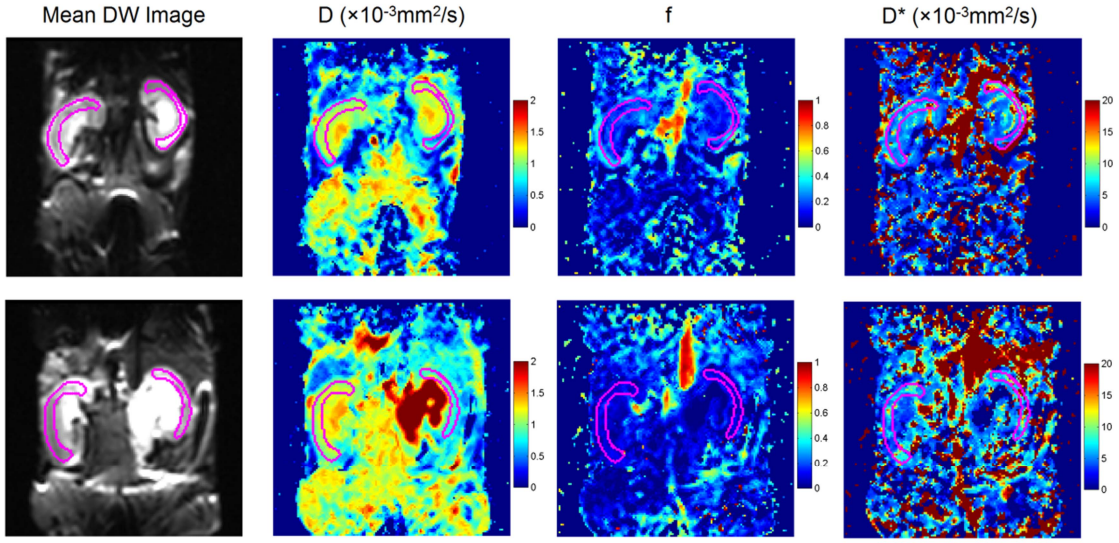

Fig.1. Mean DW image together with the various IVIM parameter maps are shown for a mouse study case 1 day before ligation of the right kidney (top row) and 7 days after ligation (bottom row). Regions of interest manually drawn on both kidneys are shown in magenta. Parameter maps show decrease in *D* and *f* in the ligated (right) kidney on Day7.