High non-linear diffusion fraction correlates with histological fibrosis in allograft kidneys

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Target Audience: Nephrology, radiologists, kidney transplant

Introduction: Percutaneous ultrasound guided needle biopsy is the current gold standard for monitoring progression of renal interstitial fibrosis. However, this invasive procedure has limited sample volume as well as poor patient acceptance with the risk of major complications. MRI has the ability to provide a non-invasive evaluation of this transplant kidney. One of the major pathways of kidney dysfunction begins with alteration of the kidney microvasculature. Due to poor renal clearance, these patients are not suitable for gadolinium perfusion studies. However, signal acquired in a diffusion weighted sequence has been shown to be sensitive to both perfusion and diffusion components. Low b- value gradients preferentially attenuate signal from flow and microcirculation, whereas higher b-value gradients attenuate signal due to purely diffusive motion[1,2]. We sought to find the degree to which flow and microcirculation are present by measuring the non-linear fraction of the diffusion curve in patients with transplant kidneys.

Methods: Diffusion weighted imaging was acquired on a cohort of 10 patients undergoing biopsy of their transplanted kidney. All patients were consented under local REB approval. Multi b value, diffusion weighted imaging of the kidney using respiratory navigator was acquired. Pertinent sequence parameters were TR/TE=3500/68ms, 7 b values: 0, 50, 100, 300, 600, 800, 1000, GRAPPA x 2, and a 1.5x1.5x5mm voxel size. Total imaging time was 2:47 with a navigational efficiency of ~50%. Data were taken off line and reconstructed in Matlab 2013b. Standard ADC calculation was performed using the b=0 and 1000 values. In addition, f, the non-linear fraction was calculated using two separate linear fits, one using the data acquired with low b-value diffusion data (b<100), and another using the high b-value data (>300) (See Figure 1). Patient's biopsy samples were stained with Masson's Trichrome and evaluated by a trained pathologist for the amount of fibrosis and assigned a Banff score between no fibrosis and severe fibrosis. f-maps were calculated on a pixel by pixel basis over all the diffusion data. The area affected by non-linear behavior was quantified by calculating the area of the kidney with elevated non-linear f components.

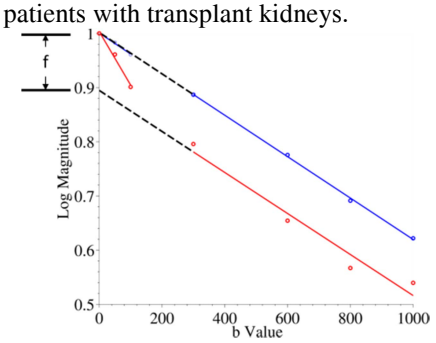

Figure 1: Calculation of "f" from diffusion
The non-linear component is calculated as the difference in the intercept between the data acquired with b-value <=100 and the data acquired for b>=300. In blue is shown actual data for a pixel with f=0%; and in red below is data for f=10%.

Results: Figure 2 shows two example f-maps from two patients, one with histologically severe fibrosis and one with no histological evidence of fibrosis. Elevated non-linearity, suggesting an increase in organized microstructure, is evident on the patients with severe fibrosis compared with those patients with less severe fibrosis. On those with mild fibrosis, elevation is only depicted in the medullary regions of the kidney. Non-linear fraction was calculated for different f thresholds and plot in figure 3. Patients with mild fibrosis have much lower fraction of their kidney occupied by this non-linear diffusion behavior than do those with severe fibrosis. These differences are not observed with standard ADC calculations which masks the non-linear behavior.

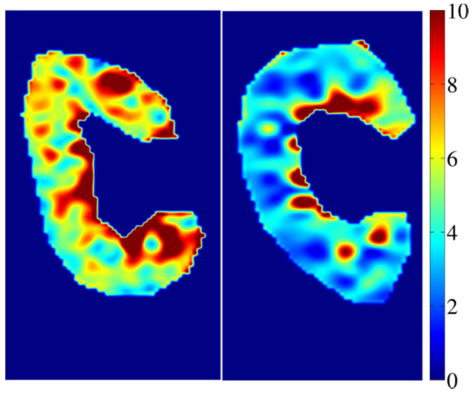

Figure 2: f-maps from 2 patients
The panel left above is an f-map from a patient with histologically severe biopsy results, whereas the image right was taken from a patient with no histologically fibrosis. Elevation in non-linear diffusion behavior is observed in the case of severe fibrosis.

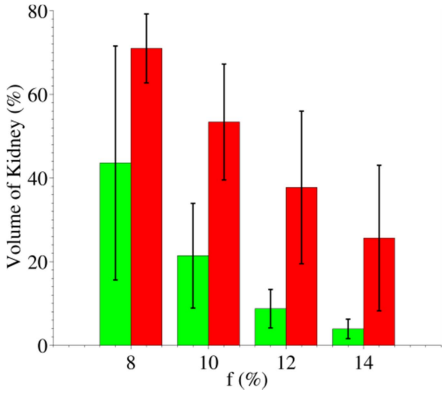

Figure 3: Volume with elevated f
Plot above is the mean percentage of segmented kidney voxels with an f score greater than the value denoted on the horizontal axis for mild (green) and severe (red) patients. One standard deviation of the mean is plot.

Discussion: We demonstrate an increased non-linear diffusion fraction in patients with pathologically proven fibrosis. Previously, investigators have demonstrated a decreased ADC[3–5] in patients with chronic kidney disease. We fail to detect this difference in this group of patients. We hypothesize that this increased f-fraction may be due to either an increase in perfusion to compensate for reduced filtration caused by fibrosis, or caused by increased tubular volume to compensate for the decrease in function due to early fibrosis. This may predate changes to ADC. Further investigation of the pathological specimens are warranted to verify these findings.

References: 1.Le Bihan, D. *et al.* *Radiology* 168, 497–505 (1988).**2.** Le Bihan, D. *Radiology* 249, 748–752 (2008). **3**. Thoeny H. C., , *Radiology* 235, 911–917 (2005). **4.** Thoeny, H. C. *Radiology* 259, 25–38 (2011) **5.** Xu, X., *Eur Radiol* 20, 978–983 (2010).