Diffusion Tensor Imaging as a Biomarker of Diabetic Nephropathy

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Introduction

Chronic Kidney Disease (CKD) is a major complication of diabetes mellitus (DM) characterized by initial hyperfiltration followed by a steady, slow decrease in glomerular filtration rate (GFR) [1]. The development of successful treatments for CKD associated with DM requires a non-invasive means to detect early-stage CKD. Recent studies using diffusion-weighted imaging (DWI) and diffusion tensor MRI (DTI) have shown promise in studying renal disease [2-5]. In this study, we used DTI to quantitatively assess renal diffusion changes relative to estimated GFR (eGFR) in diabetic subjects. Our initial results suggest that medullary fractional anisotropy (FA) decreases with GFR. Further, FA may differentiate subjects with mild CKD (eGFR = 60-89) from healthy subjects (eGFR > 90), suggesting an opportunity for early detection of CKD and progression as well as therapeutic intervention.

Methods

High quality coronal DTI renal images were obtained on five diabetic subjects presenting with either normal (n=1), mildly decreased (n=3), or severely decreased (n=1) eGFR. Six normal subjects were also scanned for comparison. A respiratory-triggered single-shot DTI-EPI sequence (coronal acquisition, TR/TE=2000/75ms, NA=6, NS=10, TH=6mm, FOV=384x200mm, 6 directions) was optimized on a 1.5T Siemens Espree scanner. A b-value of 400 sec/mm^2 was selected to provide reasonable SNR while still limiting capillary perfusion effects [4]. Image maps of fractional anisotropy (FA), apparent diffusion coefficient (ADC), and diffusion eigenvalues ($\lambda_1,\lambda_2,\lambda_3$) were computed offline in Matlab for the left and right kidneys of each subject. T_2-weighted images were used to select multiple medullary and cortical regions of interest for each kidney of all subjects to ensure a robust assessment (Fig.1,T2W-I). Medullary ROIs were focused primarily on renal pyramid regions with aligned nephrons.

Results

Representative images from a healthy subject (eGFR>90), and 2 diabetic subjects with mild CKD (eGFR=76) and advanced CKD (eGFR=32) are shown in Fig. 1. An ROI analysis from these diffusion maps are shown in Table 1 for all subjects. The FA maps from the healthy volunteer show clear differentiation between the renal cortex and medulla. However, the medullary FA decreases significantly (p<0.05) with CKD severity and preliminary data suggest a linear relationship between GFR and FA (Fig. 2). No discernable FA difference was observed in the renal cortex of these subjects. Cortical and medullary ADC values also showed a trend towards decreased diffusivity with CKD progression (Table 1). However, these results are not statistically significant suggesting greater sensitivity of FA to CKD-induced changes in eGFR. In addition, the parameters we measured on healthy subjects are consistent with the previous findings [3-4].

Fig. 1: T_2-weighted image as well as FA, ADC, and λ_1 map for a healthy volunteer (eGFR>90) (I), subject with mild CKD (eGFR=76) (II), and subject with advanced CKD (eGFR=32) (III). Representative ROIs of medulla and cortex are shown in T2W image for subject I.

		Control	Patient
Medulla	FA	0.31±0.02	0.23±0.03*
	ADC	2.40±0.09	2.20±0.21
	λ_1	3.25±0.19	2.73±0.28*
	λ_2	2.20±0.07	2.14±0.20
	λ_3	1.75±0.07	1.74±0.17
Cortex	FA	0.20±0.02	0.20±0.03
	ADC	2.67±0.13	2.49±0.23
	λ_1	3.24±0.16	3.02±0.26
	λ_2	2.63±0.15	2.46±0.23
	λ_3	2.15±0.13	2.01±0.23

Units for ADC and $\lambda_1, \lambda_2, \lambda_3$ are 10^{-3} mm^2/s

Table 1: Mean diffusion results for diabetic patients and healthy controls. (* = p<0.05)
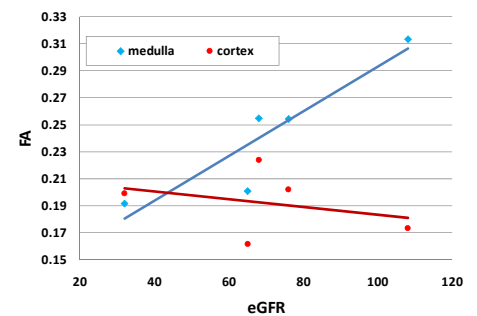
Fig. 2: Plot of mean FA in medullary renal pyramid (blue diamonds) and outer cortex (red circles) as a function of eGFR for diabetic subjects.

Discussion

These preliminary results are highly suggestive that FA may be a viable imaging biomarker for CKD disease progression. Even with limited number of subjects, the data suggest significant medullary FA differences between healthy individuals (eGFR>90) and mild CKD subjects (60<eGFR<90). Further, little or no change in cortical and medullary ADC was observed. Medullary FA changes were focused primarily in the renal pyramids, suggesting vascular and/or tubular changes downstream from glomerular degradation associated with CKD. The decreased medullary FA is primarily due to decreased medullary λ_1 suggesting a change in vascular/tubular flow rate. Overall, FA may predict if diabetic subjects will progress to advanced CKD before changes in eGFR are observed.

References

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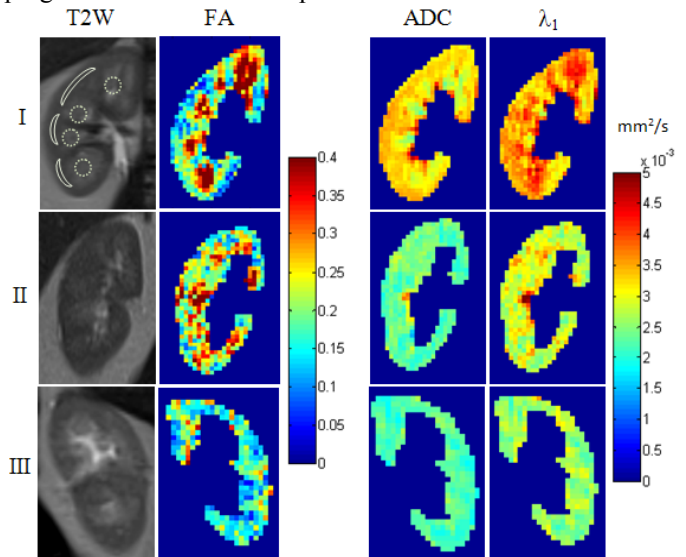[5] Chandarana H,AJR Am J Roentgenol. 2009, 192(6):1550-1557.