Fractional Anisotropy Assessment of Early-Stage Diabetic Nephropathy

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Introduction: Currently-available clinical indicators of kidney disease such as serum creatinine and albuminuria lack the sensitivity and specificity to identify early-stage diabetic nephropathy (DN).[1] Diffusion weighted imaging (DWI) techniques have been used to assess renal Apparent Diffusion Coefficient (ADC) in both healthy and diseased subjects[2,3], while Diffusion Tensor Imaging (DTI) methods have been used to assess diffusivity changes in an experimental model of DN.[4] We have also previously reported that diffusion fractional anisotropy (FA) may provide a sensitive assessment of kidney microstructural changes associated with human DN in comparison to healthy controls.[5] However, a thorough investigation into the capability of DTI anisotropy assessments to identify *early-stage DN* has yet to be completed.

Methods: High quality coronal DTI renal images were obtained for on 16 diabetic subjects (40-65 years of age) and 5 age-matched healthy control subjects using a Siemens Espree 1.5T scanner. The diabetic subjects were divided two groups: i) early stage DN (eGFR ≥ 60, n=10); and ii) later stage DN (eGFR < 60, n=6). eGFR values were calculated from recent serum creatinine measures. A respiratory-gated, single-shot, DTI–EPI acquisition was used to acquire diffusion weighted images of the left and right kidneys (b = 0 and 400 s/mm^2, 6 directions + null, TR/TE = 2000 ms / 75 ms, imaging slice thickness = 6 mm, 10 imaging slices / subject). Six imaging averages were acquired to obtain images with a sufficient signal-to-noise ratio (SNR) to ensure an accurate FA assessment. Co-registered, coronal HASTE images were used for medullary and cortical kidney ROI selection (32 ROIs over 4 central slices for each subject) as previously reported.[5] Medullary and cortical FA along with eGFRs of early-stage and late-stage diabetics and healthy control subjects were compared using a two-tailed student's t-test.

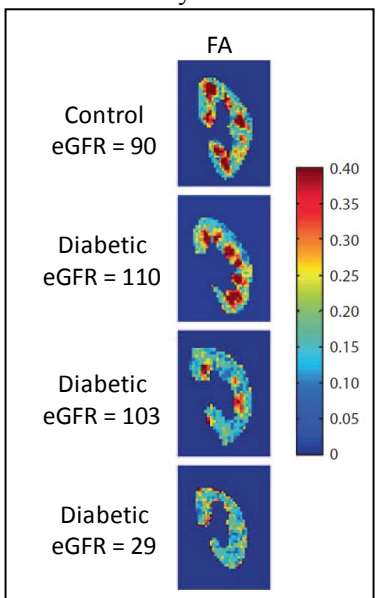

Fig 1: Fractional anisotropy (FA) maps of kidneys from non-diabetic control (top panel) in comparison to diabetics.

Results: Representative FA maps of a control (non-diabetic) and 3 diabetic subjects are shown in **Fig. 1**. Note the large differences in medullary FA for the early-stage DN subjects (panes 2 and 3) despite minimal difference in eGFR (110 and 103, respectively). A comparison of eGFR for all three groups is shown in **Fig. 2**. As expected, eGFR meaasures distinguish between early and late-stage DN ($p < 0.0005$). However, eGFRs for control and early-stage DN subjects were not significantly different. In contrast, mean medullary FA for early-stage diabetics is significantly lower than for controls (P = 0.001, **Fig. 3**). Medullary FA was also significantly lower in diabetics with eGFR<60 compared to controls.

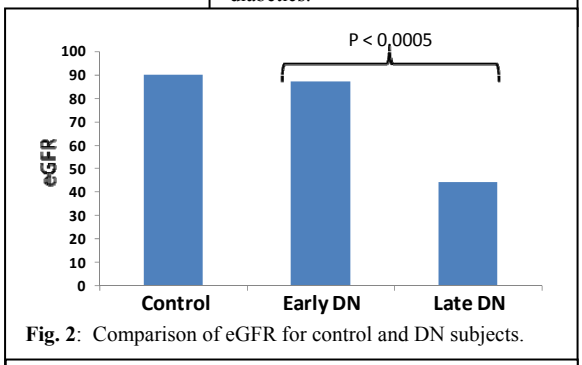

Fig. 2: Comparison of eGFR for control and DN subjects.

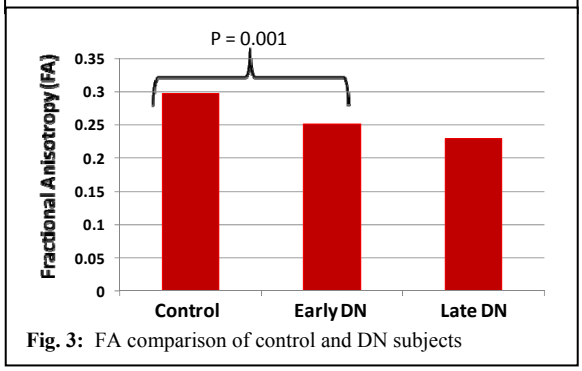

Fig. 3: FA comparison of control and DN subjects

Discussion and Conclusions: These preliminary results are highly suggestive that FA may be able to detect early-stage DN better than current clinical measures (eGFR). Even with limited number of early-stage diabetic subjects, the data suggest significant medullary FA differences between healthy individuals and mild DN subjects. This pilot study suggests that changes in medullary DTI assessments may be a sensitive indicator of early DN. Further studies are needed to determine if this finding could serve as a predictive biomarker to identify diabetics at risk for progression to clinically overt DN. Additional studies are also required to directly compare biexponential ADC assessments with the FA measures described here.

References: [1] Dronavalli S, Nat Clin Pract Endoc. Metab 2008. [2] Thoeny HC, Radiology 2005. [3] Ries M JMRI 2001. [4] Ries M, JMRI 2003. [5] Lu L, ISMRM 2010.

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