Blood oxygen level dependent (BOLD) and diffusion tensor (DTI) imaging of the kidneys in patients with Type 1 diabetes: preliminary clinical experience with reference to healthy control subjects

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Purpose: Diabetic kidney disease (DKD) is the primary cause of end stage renal disease (ESRD) in many countries. DKD remains incompletely understood, with traditional clinical markers of declining renal function (albuminuria, declining glomerular filtration rate [GFR]) not reliable in type 1 diabetics (T1DM)[1]. Changes to renal parenchymal R2* and diffusion metrics have been reported in Type 2 diabetic patients using blood oxygen level dependent (BOLD) MRI and diffusion tensor imaging (DTI) respectively, but have not previously been assessed in T1DM human subjects. The purpose of this study was to evaluate changes in medullary and cortical R2* in BOLD MRI, fractional anisotropy (FA) and apparent diffusion coefficient (ADC) in DTI comparing T1DM with a spectrum of DKD to healthy controls.

Methods: 25 T1DM were prospectively recruited (17 M, 8 F, mean 46 y, range 29 – 73 y) with renal disease (mean eGFR 82, range 24 - 91) and were compared with 10 healthy controls (5 M, 5 F, mean 43 y, range 27 – 63 y). After an overnight fast with controlled water intake, subjects underwent 3T MRI (Skyra, Siemens, Erlangen, Germany) including BOLD and DWI. BOLD parameters were: TR/TE = 85/ (4.3-56.7) ms, interecho spacing 4.8ms, FA 30°, FOV 420 x 420mm, 1 slice, sl thickness 7mm, breath-hold acquisition (11.6s). Respiratory-navigated DWI parameters were: TR/TE = 1800/ 81ms, FA 90°, FOV 400 x 400mm, slice thickness 3mm, number of slices 7, b 0 and 500s/mm^2, 12 directions. A single radiologist obtained cortical and medullary R2* (CR2*, MR2*) values from BOLD T2* maps selecting multiple regions of interest (ROIs) on an offline workstation (MultiModality Workplace, Siemens), avoiding focal lesions, vessels and regions of artifact. Multiple ROIs were obtained in similar fashion from FA and ADC maps automatically generated by the scanner to measure cortical and medullary FA (cFA, mFA) and ADC (cADC, mADC). Median CR2*, MR2*, medullary to cortical R2* ratio (MCR2*), cFA, mFA cADC, and mADC values were compared between 3 groups: a) T1DM with eGFR <90 (n=9); b) T1DM with eGFR ≥90 (n=16); and c) healthy controls (n=10). Parameters were compared between groups with the Mann-Whitney test, with $p<0.05$ considered statistically significant.

Results: All subjects completed MRI and had normal renal morphology. BOLD-derived parameters and cortical/ medullary ADC were not significantly different between groups (Table 1). DTI however demonstrated significantly lower medullary FA in the T1DM eGFR <90 group compared to T1DM eGFR≥90 (p= 0.037) and to controls (p= 0.021). Cortical FA was also significantly lower in T1DM eGFR <90 than T1DM eGFR ≥90 (p= 0.037).

Table 1. Median values (IQR) for eGFR, medullary to cortical R2* ratio (MCR2*), medullary and cortical FA (mFA, cFA) and ADC (mADC, cADC), stratified by group. Significant differences were observed in median mFA and cFA values as presented in bold font.

	eGFR ml/min/1.73m^2	MCR2*	mFA µm^2/ms	cFA µm^2/ms	mADC µm^2/ms	cADC µm^2/ms
T1DM eGFR < 90	68 (58.7 – 76.75)	1.51 (1.39 – 1.55)	**0.369** (0.331 – 0.406)	**0.145** (0.124- 0.16)	2.246 (2.118 – 2.491)	2.385 (2.276 – 2.509)
T1DM eGFR ≥ 90	91 (91 – 91)	1.52 (1.43 – 1.6)	**0.417** (0.369 – 0.448)	**0.156** (0.14 – 0.19)	2.354 (2.118 – 2.533)	2.548 (2.322 – 2.681)
Controls	91 (80 – 91)	1.42 (1.32 – 1.57)	**0.443** (0.393 – 0.472)	0.162 (0.153 – 0.172)	2.205 (2.09 – 2.392)	2.445 (2.363 – 2.550)

Discussion/Conclusion

We found no significant differences between BOLD derived parameters for T1DM and controls. However, medullary FA was found to be significantly lower in T1DM eGFR <90, compared with T1DM with normal renal function and healthy controls, possibly reflecting disruption of medullary tubular architecture with progressive DKD. Similarly, cortical FA was observed to be significantly lower in T1DM eGFR <90 compared to T1DM eGFR ≥90, but not to controls. Relatively small sample size and large proportion of T1DM patients with normal renal function by eGFR are limitations of the study, with further experience in a larger population required. BOLD imaging during a diuretic challenge might uncover differences between groups with regard to tissue oxygenation and further evaluation is planned.

Fig 1. Control coronal A)T2 multiecho GRE, B)T2* map, C)FA map, D)ADC map. Note the excellent cortical (arrow) and medullary (arrow head) differentiation.

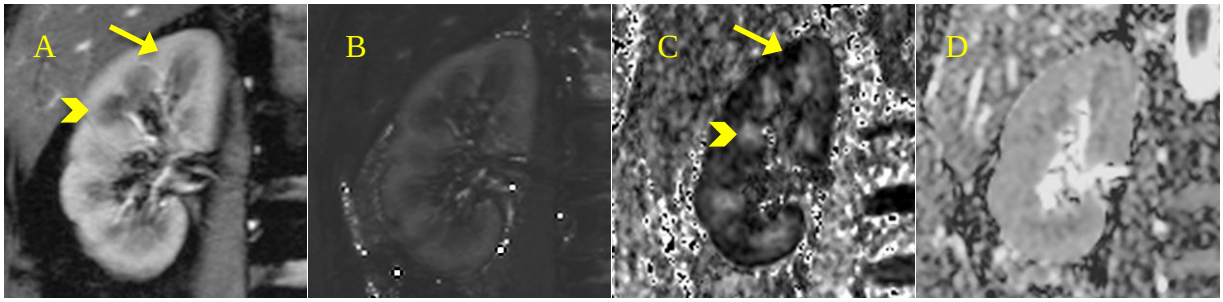
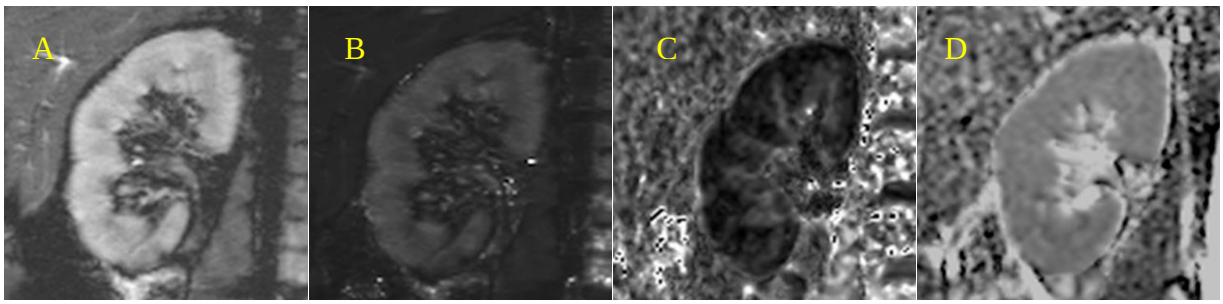


Fig 2. T1DM with DKD coronal A) T2 multiecho GRE, B) T2* map, C) FA map, D) ADC map. Note the reduced corticomedullary differentiation.



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