Magnetic resonance BOLD and diffusion tensor imaging for diagnosis of histopathological changes in a rat model of diabetic nephropathy

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Introduction: Diabetic nephropathy is characterized by decreasing renal function and specific structural changes including kidney hypertrophy, thickening of the glomerular basement membrane, glomerulosclerosis, tubular atrophy and interstitial fibrosis. So far, diagnosis of diabetic nephropathy is mainly based on laboratory parameters such as albuminuria and glomerular filtration rate (GFR). The purpose was to evaluate whether magnetic resonance (MR) BOLD and diffusion tensor imaging (DTI) can provide additional information about presence and, more importantly, progression of renal pathologies in diabetes.

Methods: Twenty-one male Sprague-Dawley rats were divided into three groups (n=7 each): control, diabetes (DM), and diabetes with uninephrectomy (DM UNX) to accelerate renal impairement. Eight weeks after diabetes induction with streptozotocin animals underwent MRI (1.5 T Magnetom Avanto, Siemens Healthcare, Erlangen, Germany) using an 8-channel wrist coil. Coronal proton density, BOLD (TR 184 ms; 12 TE, 6.2-53.0 ms) and echo-planar DTI (b=0, 300 s/mm^2, 6 diffusion directions) images were acquired. T2*-values, Apparent Diffusion Coefficient (ADC) and Fractional Anisotropy (FA) were calculated separately for renal cortex (CO), outer stripe (OS) and inner stripe of the outer medulla (IS) and inner medulla (IM). ROIs were placed on T2*-maps and trace weighted images, respectively (Figure 1A) and copied to ADC and FA maps. MRI parameters were compared to laboratory parameters and histopathological findings.

Figure 1: Trace weighted image with clear differentiation of anatomical layers of the kidney (A). Tractography overlaying trace image visualizes preferred diffusion direction radial to the renal pelvis (B).

Results: In streptozotocin-treated animals serum glucose and urinary output were significantly increased (p<0.001) and insulin was decreased (p<0.001) as expected in diabetics. Uricemia, albuminuria and renal pathologies were more pronounced in DM UNX than in DM alone. T2*-values were not significantly different between groups and no significant correlation to histopathological changes was observed. However, FA was significantly reduced in DM UNX in all anatomical layers except for the IS when compared to controls and in the IM also when compared to DM group (Figure 2A). In DM without UNX only cortical FA was significantly reduced in comparison to controls (p<0.001). Furthermore, MR DTI demonstrated renal architecture (Figure 1). The degree of glomerulosclerosis negatively correlated with cortical FA (p=0.003) and FA of the OS (p=0.022), whereas the degree of interstitial fibrosis inversely correlated with FA of the IM (p=0.028) and tubular damage significantly correlated with FA in CO and IM (p=0.015 and p=0.006, respectively). When dividing animals according to the presence and absence of albuminuria and interstitial fibrosis, FA values were significantly reduced in animals with those pathologies (Figure 2B+C).
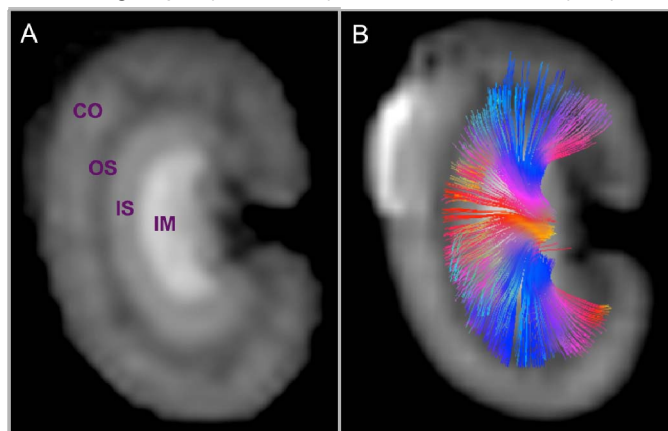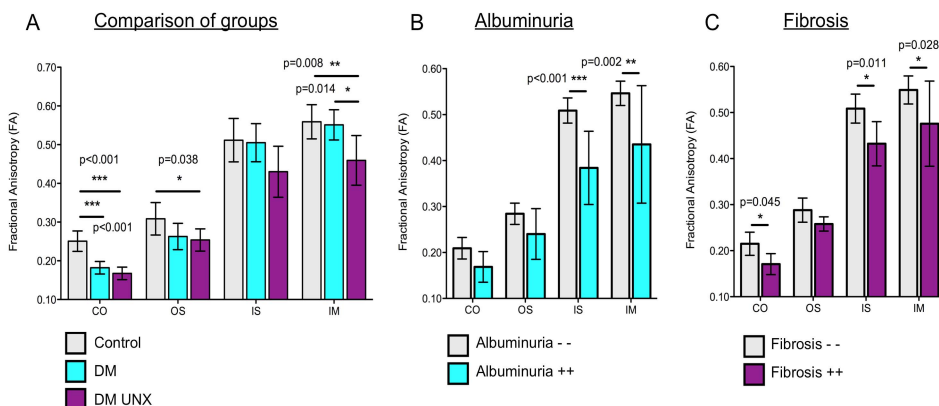
Discussion: Renal pathologies in a rat model of diabetic nephropathy such as glomerulosclerosis, interstitial fibrosis and tubular damage are associated with a reduction of FA at MR DTI. DM and DM UNX animals that represent different disease stages could be differentiated. In contrast to BOLD imaging, which did not reveal any differences, MR DTI may be valuable for noninvasive detection and monitoring of renal involvement in diabetic patients.

Figure 2: FA of different anatomical layers was significantly reduced in DM UNX group (A). Presence of albuminuria and fibrosis were defined as >mean+2SD in relation to the control group and animals, which were positive (pathologic) for those findings were compared to healthy animals (negative). FA of IS and IM were significantly reduced in animals with albuminuria (B). Renal fibrosis was accompanied by significant FA reduction in different layers (C).