SUSCEPTIBILITY TENSOR IMAGING REVEALS REDUCED ANISOTROPY IN RENAL NEPHROPATHY

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Target Audience: Scientists and clinicians interested in renal nephropathy and susceptibility tensor imaging (STI)

Purpose

The nephron structure and epithelial organization are essential for kidney function. Diffusion tensor imaging (DTI) can assess the integrity and architecture of the nephron tubules (1). Susceptibility tensor imaging (STI) has recently demonstrated sensitivity in additional layers of the kidney and can be complementary to DTI (2). In disease models, DTI revealed some changes in anisotropy (1). The purpose of this study is to determine whether STI can be more sensitive to kidney disease or nephropathy. Two models were used including angiotensin receptor knockout AT1a -/- AT1b -/- and diabetic nephropathy model Akita. Kidneys from these mice exhibit hypertrophy, tubular damage, and a loss of cellular organization, which leads to reduced structural anisotropy. In the present study, we found that DTI displayed some injury in the inner medulla of the kidney, while STI exhibited significantly reduced anisotropy. STI may offer a powerful method to study renal pathophysiology.

Methods

Perfusion & fixation: Studies were performed on kidneys from wild type C57Bl/6, Akita, and AT1a -/- AT1b -/- mice. Animals were perfusion fixed with 10% formalin. Kidneys were immersion enhanced with 2.5 mM ProHance to decrease T_1 and improve SNR (3). Kidneys were imaged 48 hours after fixation. MRI: MRI was performed in a vertical bore 9.4T Oxford magnet (Agilent Direct Drive console). The specimen was placed in a sphere to facilitate multiple orientations for STI. The holder was placed in a high Q loop gap resonator. STI data were acquired using 3D multi-echo gradient echo sequence (12 directions total). DTI data were acquired using a 3D diffusion-weighted spin echo sequence. One b_0 image and 12 diffusion weighted (1500 s/mm^2) images were acquired at 55×55×55 μm^3. STI and tractography: Registered phase images were used to solve for the 6 independent elements of the susceptibility tensor (χ_{11}, χ_{12}, χ_{13}, χ_{22}, χ_{23}, and χ_{33}) following (4). Eigenvalue decomposition was performed on the tensor to define the 3 principal susceptibilities and eigenvectors. Tractography was performed on major diamagnetic eigenvector, seeded by mask images, and filtered by renal regions and track lengths (TrackVis). Angle threshold was 60°. DTI fractional anisotropy (FA) and STI susceptibility anisotropy (SA) were set a threshold of 0.15 to 0.9.

Results

Fig. 1 compares DTI and STI from normal and diseased kidneys. Mean diffusivity (MD), fractional anisotropy (FA), mean susceptibility (MS), and susceptibility anisotropy (SA) are displayed. In the center of the inner medulla, we found the following DTI FA: 0.22 in wild type, 0.21 in Akita, and 0.17 in AT1a -/- AT1b -/-. In contrast, we found the following STI SA: 0.29 in Wild type, 0.03 in Akita, 0.04 in AT1a -/- AT1b -/-. This is equivalent to a SA reduction of 86-90% in diseased kidneys compared to normal. On the other hand, FA was reduced by 5-23%. Similar trends can be found in mean susceptibility and mean diffusivity images. Fig. 2 shows tractography results. DTI reveals some reduced tracks in the inner medulla of diseased kidneys. STI virtually did not track any tubules in the same area.

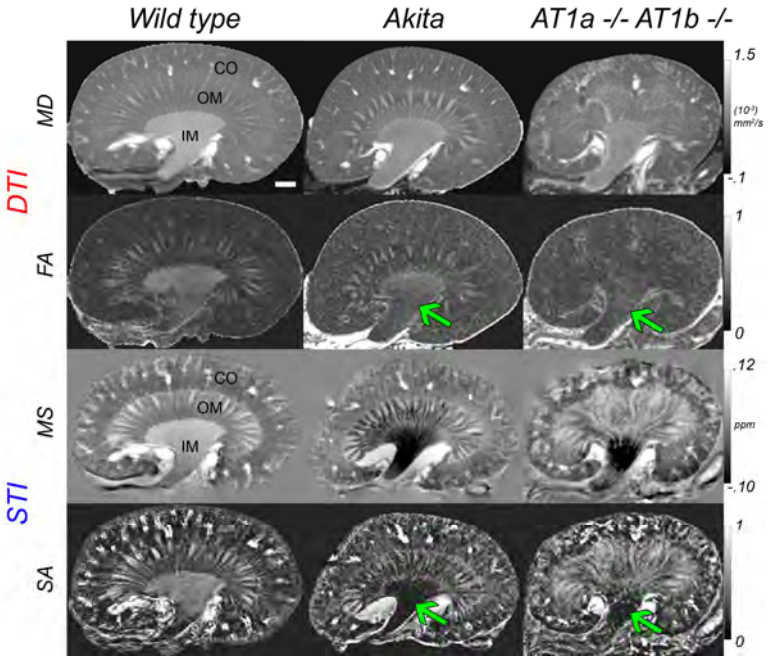

Fig. 1. Comparison of DTI and STI. Columns left to right: wild type, Akita, and AT1a -/- AT1b -/-. Rows top to bottom: MD from DTI, FA from DTI, MS from STI, and SA from STI. CO=cortex, OM=outer medulla, and IM=inner medulla. Green arrows point to IM of diseased kidneys. Scalebar =1 mm.

Discussion and Conclusion

DTI provided excellent reconstruction of the normal nephron tubules, however it was limited to the inner medulla while STI detected additional layers. In disease models, DTI failed to exhibit significant changes in diffusion anisotropy. STI demonstrated a near disappearance of susceptibility anisotropy in the inner medulla of Akita and AT1a -/- AT1b -/- models. Consequently, the presence of diffusion anisotropy and the performance of DTI tractography demonstrate that the straight tubular segments are intact. This rules out the potential contribution of tubular damage to the significant reduction of susceptibility anisotropy. The coherent tubular structures are also visible in the magnitude images of all kidneys. Similar to the model of cellular structures creating anisotropy in white matter tracts (5), the origins of susceptibility anisotropy in the kidney are most likely due to the cellular content in the epithelial cells. In the case of hypoplasia in the AT1a -/- AT1b -/- model and cellular abnormality in the Akita model, the cellular structures, organelle direction, and lipid orientation are disrupted. We believe STI is very sensitive in detecting these epithelial cells and walls of the nephron tubules, while DTI is mostly limited to the anisotropic water diffusion inside the tubules. In conclusion, we demonstrated that the susceptibility anisotropy in coherent tubules of diseased kidneys nearly disappears, while diffusion anisotropy remains similar. Our results suggest that the cellular content and organization may contribute to the observed susceptibility anisotropy when the nephron tubules remain intact. STI can be very sensitive in detecting diseases with subtle microstructural damages.

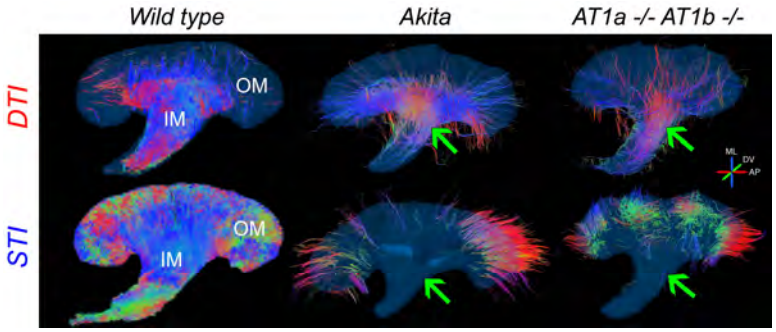

Fig. 2. Tractography of DTI and STI. Columns left to right: wild type, Akita, and AT1a -/- AT1b -/-. First row: DTI. Second row: STI. OM=outer medulla and IM=inner medulla. Green arrows point to IM of diseased kidneys. Color axis: red=anteroposterior, green=dorsoventral, and blue=mediolateral.

References

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