# Diffusion Kurtosis Imaging of Fibrotic Mouse Kidneys

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**Introduction:** Renal fibrosis is considered a major factor in the progression of chronic kidney disease. The diagnosis and monitoring of kidney fibrosis is therefore important. Typically, kidney fibrosis is diagnosed from a biopsy and a reliable non-invasive method is therefore of great interest. Diffusion weighted MRI is sensitive to tissue microstructure and ADC/mean diffusivity (MD) has previously been shown to correlate with renal fibrosis in patients[1]. However, more sensitive microstructural markers may be offered by diffusion kurtosis imaging (DKI). In the past, both acquisition and post processing in DKI have been very time consuming, which has held back its clinical utility. Recently, a fast DKI method based on Ref. 2 was proposed, allowing estimation of MD, fractional anisotropy (FA), mean kurtosis ($\overline{W}$) and fractional kurtosis anisotropy (FKA) from 19 diffusion weighted images with a postprocessing time of seconds[3,4]. The fractional kurtosis anisotropy (FKA)[2,5] measures the degree of directional variability of the observed kurtosis and is expected to reflect tissue microstructure differently than the traditional diffusional FA. The aim here is to investigate if the diffusion metrics estimated with this method can detect renal fibrosis in a mouse model of progressive kidney disease.

**Method:** 3 wildtype mice (WT), BalbC, and 3 genetically modified (GMO, TGF-β inserted next to renin-coding gene) mice were perfusion fixated and both kidneys removed. High resolution anatomical scans [60 µm x 60 µm x 120 µm] (FLASH) and diffusion tensor MRI data were acquired on Bruker Biospin 9.4T animal system. The kidneys hereafter underwent histology with reticular staining. The diffusion metrics were calculated from a diffusion MR protocol with 19 images (1 b=0, b=1 ms/µm$^2$ and b=2.5 ms/µm$^2$ along the nine distinct directions described in Ref. 2). In some data sets a few pixels had signal dropout at high b-values causing numerical outliers in the calculated parameter images. The histology indicated that these low signal pixels occur in tissue areas where the tissue has pores allowing almost free diffusion. We therefore omitted these points in the further analysis. ROIs were drawn covering the cortex and medulla of the kidneys, and in those the mean and standard deviation of the diffusion metrics were calculated for each kidney. The calculated diffusion metrics of GMO and WT mice were compared and a two-tailed t-test was performed.

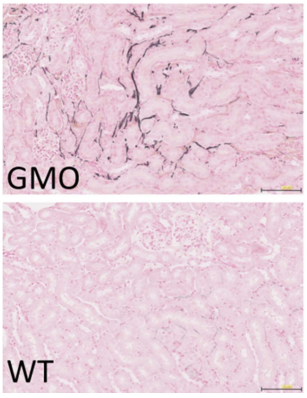


*Figure 3. Reticulin Stain of kidney tissue on the border between cortex and medulla.*

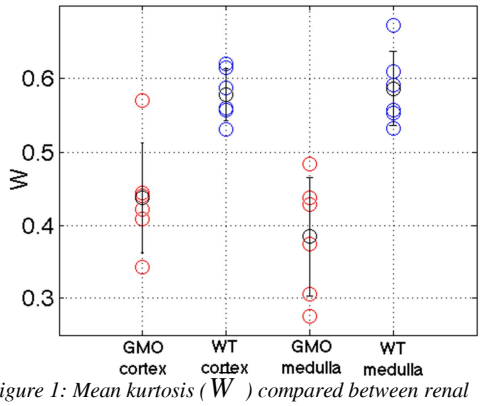


*Figure 1: Mean kurtosis ($\overline{W}$) compared between renal cortex and medulla in GMO and WT p<<0.01 for both cortex and medulla*

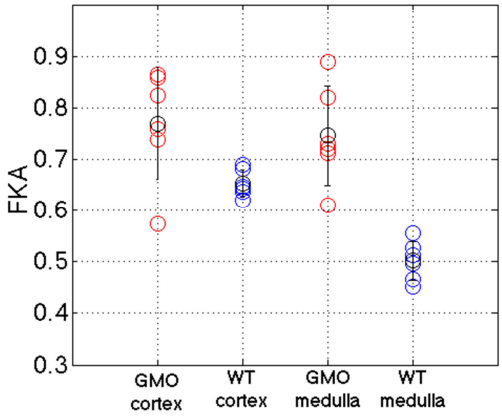


*Figure 2 FKA is seen to differ significantly between WT and GMO kidneys. p=0.03 for cortex, p=0.0002 for medulla*

**Results:** We found a significant difference in $\overline{W}$ and FKA between the GMO and WT mice, figure 1 and 2 see text below figures. However, no significant difference in FA was observed (p = 0.6/p = 0.1 for cortex/medulla. Mean in cortex 0.29±0.06 and medulla 0.26±0.05). MD was not significantly altered in cortex (p = 0.3. mean was 0.71±0.09 µm$^2$/ms in GMO and 0.8±0.1 µm$^2$/ms in WT) but a weak significant difference was found in medulla (p = 0.047, mean was 0.8±0.1 µm$^2$/ms in GMO and 0.97±0.09 µm$^2$/ms in WT). Histology of the kidneys confirmed a higher amount of fibrillar reticulin in GMO mice as compared to WT mice, which indicates increased fibrosis (figure 3).

**Discussion:** As expected, the fibrotic tissue appears much less homogenous than the WT kidneys (fig 3). This is reflected in the observed (within ROI) variation in $\overline{W}$ and FKA, which is larger for GMO than WT (fig 1 and 2). The kurtosis metrics $\overline{W}$ and FKA are both significantly different between WT and GMO kidneys. No clear correlation was found between MD and fibrosis, although this was observed in Ref. 1. In conclusion we find that the DKI metrics $\overline{W}$ and FKA are able to detect the microscopic changes in the fibrotic kidney tissue better than conventional DTI metrics. The tested protocol for fast acquisition and post processing of kurtosis data will be available for clinical systems (Siemens c2p) and in vivo tests are planned for the near future. These initial tests indicate that the method might be useful for both diagnosing and monitoring of patients with renal fibrosis in the future.

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**References: 1.** Inoue et al, J Am Soc Nephrol 22:1429–1434, 2011. **2.** Hansen et al, MRM, 69:1754-1760, 2013, **3.** ISMRM poster #2606, 2014, **4.** Hansen et al, in review **5**: Jespersen SN: NMR in biomed 25(6), 2012.