Assessment of motor impairment in acute/subacute stroke patients with diffusional kurtosis metrics

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Introduction A major complication after stroke is often motor function impairment (1). A robust biomarker for predicting a patient's recovery of motor function, which would ultimately benefit clinicians' decision making on rehabilitation planning (2), would be useful. Several studies (3-5) have used diffusion tensor imaging (DTI) to assess the structural integrity of the corticospinal tracts and correlate with chronic stroke patients' motor outcome. However, a fundamental restriction of DTI is that it cannot resolve crossing fibers on a voxel level (6), thus confounding the assessment of white matter tract integrity. One of the potential techniques that can overcome this limitation is diffusional kurtosis imaging (DKI) which quantifies non-Gaussian diffusion thereby allowing a more complete characterization of tissue microstructures (7). Specifically, the apparent diffusional kurtosis (K) measures tissue complexity due to the presence of cell membranes and organelles, and water compartments with differing diffusion properties. The central hypothesis of this study is that diffusional kurtosis metrics would provide for an improved assessment of the motor impairment of acute/subacute stroke patients as compared to conventional DTI measures.

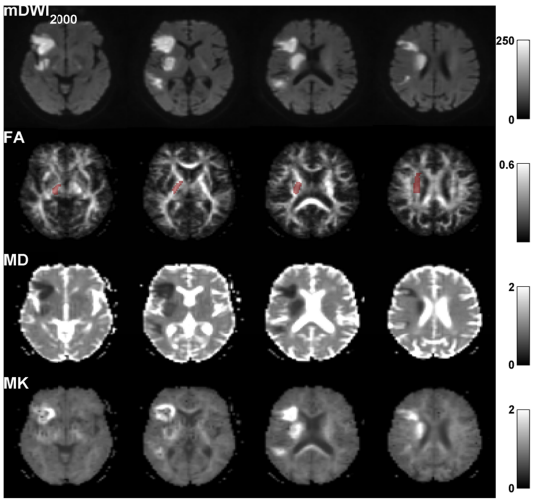

Fig.1 Mean of all DWI with b-value of 2000 s/mm^2 ($mDWI_{2000}$), and parametric maps of diffusion metrics of an acute stroke patient with a Fugl-Meyer Motor Scale (FMMS) of 16. ROIs (red) covering the corticospinal tracts were overlaid on the FA maps.

Methods N=10 patients (mean ± SD of age: 58 ± 13, time after onset: 11.25 – 53 hours) presenting with acute ischemic stroke symptoms were recruited. The degree of motor impairment was measured one day after DKI scan using the upper and lower limbs movement section of the Fugl-Meyer Motor Scale (FMMS) (8). The full scale is 100 with 66 and 34 points for upper and lower extremities, respectively. A lower FMMS indicates more motor impairment. MRI experiments were performed using a 1.5 T Avanto Siemens MR scanner. DKI acquisition was performed with 3 b-values (0, 1000 and 2000 s/mm^2) along 30 diffusion encoding directions using single-shot twice-refocused-EPI with NEX=1 (NEX=10 for b=0). Other imaging parameters were: acquisition matrix = 74 x 74, image resolution = 3 x 3 x 3 mm^3, TR/TE = 5500/99 ms, BW/pixel = 1325 Hz. Fractional anisotropy (FA), mean (MD), axial ($\lambda_{//}$), radial diffusivity ($\lambda_{\perp}$), mean (MK), axial ($K_{//}$) and radial kurtosis ($K_{\perp}$) were computed using the in-house DKE software (9). All images were normalized to a T1-weighted template obtained from elderly volunteers and subsequently segmented into grey (GM) and white matter (WM) masks using a spm8 (http://www.fil.ion.ucl.ac.uk) toolbox by Chris Rorden (http://www.cabiatl.com/CABI). Since ischemia changes the contrast of T1-weighted images (reference image of the brain normalization), mirror images of the WM/GM masks in the normal hemisphere were used to estimate those in the ischemic lesion. The corticospinal tracts, comprising of superior corona radiate, posterior limb of internal capsule, cerebral peduncle and corticospinal tract, on the lesional hemisphere were segmented using the JHU DTI-based WM atlas (http://cmrm.med.jhmi.edu/) for each patient (see example in FA maps in **Fig.1**). Measurements were then performed by averaging all pixels within the corticospinal tracts. Pearson correlations between diffusion metrics and FMMS were performed.

Results and Discussion The mean of all DWI with b-value of 2000 s/mm^2 ($mDWI_{2000}$) and the parametric maps of diffusion metrics of an acute ischemic stroke patient with FMMS of 16 are shown in **Fig.1**. Notice that the extent and contrast of the ischemic signal abnormality are different between DTI and DKI diffusion metrics, with DKI metrics showing a more extensive and heterogeneous ischemic lesion. **Fig. 2** shows the correlation between mean of FA, $\lambda_{//}$ and $K_{//}$ in the corticospinal tracts versus the motor impairment score. It is evident that $K_{//}$ correlates strongly (r=-0.89, p=0.001) with motor impairment, while conventional DTI metrics do not show significant correlations. The results from the current study suggest that diffusional kurtosis metrics may provide a better characterization of structural integrity in the acute/subacute phase compared with DTI metrics, possibly because the sensitivity of DTI metrics is compromised due to complex fiber architecture (6). By measuring diffusional non-Gaussianity, DKI is, for example, better able to characterize tissue with intersecting fiber bundles (10). In order to investigate whether DKI can benefit rehabilitation planning, longitudinal DKI data will be acquired in future studies to examine whether diffusional kurtosis metrics can also predict recovery of motor function. In summary, the current study shows for the first time that measurement of structural integrity of corticospinal tracts using diffusional kurtosis metrics significantly correlates with acute/subacute stroke patient motor impairment.

References 1. MMWR Morbidity and mortality weekly report 2008;57(18):481-485. 2. Stinear C. Lancet neurology 2010;9(12):1228-1232. 3. Jang SH et al. Annals of neurology 2008;64(4):460-465. 4. Lindenberg R et al. Human brain mapping 2011. 5. Stinear CM et al. Brain 2007;130(Pt 1):170-180. 6. Zhan W, Yang Y. J Magn Reson 2006;183(2):193-202. 7. Jensen JH et al. Magn Reson Med 2005;53(6):1432-1440. 8. Fugl-Meyer AR et al. Scand J Rehabil Med 1975;7(1):13-31. 9. Tabesh A et al. Magn Reson Med 2011;65(3):823-836. 10. Lazar M et al. Magn Reson Med 2008;60(4):774-781.

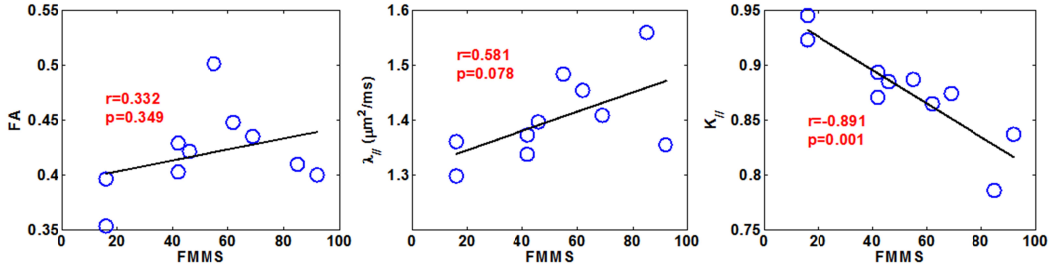

Fig.2 Correlation between the measurements of FA, $\lambda_{//}$ and $K_{//}$ in the corticospinal tracts versus the FMMS. Lower score indicates more severe motor impairment.