MEG-guided diffusion kurtosis imaging in patients with refractory epilepsy

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BACKGROUND: In patients with refractory epilepsy, diffusion tensor imaging (DTI) can non-invasively provide valuable information on the microstructure and architecture of brain tissue in vivo and can be used to detect and evaluate microstructural alterations of white matter, even beyond the visually abnormal area. However, DTI has an important limitation because it incorrectly assumes that water diffusion in biological tissues occurs in an unrestricted manner and follows a Gaussian distribution in which the diffusion weighted signal attenuates monoexponentially with the strength and duration of the diffusion gradient (i.e. b-value). Diffusion kurtosis imaging (DKI) is an extension of the DTI technique which takes the deviation of restricted water diffusion in biological tissues from the Gaussian distribution (i.e. excess kurtosis characterizing the non-monoexponential signal decay) into account, thereby offering a more sensitive method of detecting subtle microstructural changes in neural tissue, both in the predominantly anisotropic white matter and the more isotropic grey matter [1]. In this study, DKI was used in patients with refractory epilepsy and unknown seizure focus to examine both the region indicated by a preceding magnetoencephalography (MEG) exam (i.e. magnetic dipole cluster) and, if present, the grey matter abnormality visible on anatomical MRI scans.

METHODS: Eighteen patients with refractory epilepsy who were included in the presurgical evaluation protocol and in whom the MEG exam had shown a magnetic dipole cluster indicating the potential seizure focus, subsequently underwent a DKI exam on a 3 Tesla system using 3 b-values (0, 1000 and 2000 s/mm^2) and 30 gradient directions. TR = 5900 ms, TE = 96 ms, voxel size = 2.7 mm x 2.7 mm x 2.7 mm. Seven maps were calculated from the diffusion weighted images, namely the mean, radial and axial kurtosis maps, the mean, radial and axial diffusivity maps and the fractional anisotropy (FA) map. On previously acquired structural MRI at 3 Tesla, 11 patients showed a visible abnormality located nearby or in the dipole cluster, whereas 7 patients had a negative MRI. Using the high resolution anatomical scans (FLAIR3D and MPRAGE), regions of interest were defined: three three-dimensional spherical shaped ROIs of varying sizes (5, 10 and 20 mm radius) were drawn at the location of the magnetic dipole cluster designated by the MEG exam, one ROI delineated the abnormality (if present) and three (no visible abnormality) or four (in case of a visible abnormality) ROIs of similar size were drawn in the corresponding normal-appearing regions on the contralateral side. Each of the ROIs was segmented in grey and white matter. All ROIs were subsequently transposed to each of the seven maps and values of the corresponding ipsi- and contralateral ROIs were analyzed with a paired samples t-test.

RESULTS: Preliminary results show significant differences between ipsi- and contralateral signal intensity in the grey matter for the ROIs delineating the visual abnormality in FA (p = .035), mean, radial and axial kurtosis (p = .008, p = .008, p = .017, respectively), for the ROIs with 5 mm radius in mean kurtosis (p = .018), for the ROIs with 10 mm radius in mean kurtosis (p = .037) and for the ROIs with 20 mm radius in mean and axial kurtosis (p = .037, p = .009, respectively). In the white matter, significant differences between ipsi- and contralateral sides were found for the ROIs delineating the visual abnormality in mean and radial kurtosis (p = .010, p = .041, respectively), for the ROIs with 5 mm radius in mean, radial and axial diffusivity (p = .006, p = .027, p = .010, respectively) and axial kurtosis (p = .013), for the ROIs with 10 mm radius in FA (p = .011), mean and radial diffusivity (p = .023 and p = .014 respectively) and mean, radial and axial kurtosis (p = .004, p = .010 and p = .030, respectively) and for the ROIs with 20 mm radius in FA (p = .006), mean and radial diffusivity (p = .014 and p = .006, respectively) and mean, radial and axial kurtosis (p = .004, p = .006 and p = .020, respectively).

DISCUSSION: In patients with refractory epilepsy, preliminary results suggest that when using MEG to locate the potential seizure focus, diffusion kurtosis imaging is able to identify microstructural changes in both grey and white matter. Mean, radial and axial kurtosis values in the ROI containing the grey matter abnormality were significantly decreased with respect to the normal-appearing contralateral side.
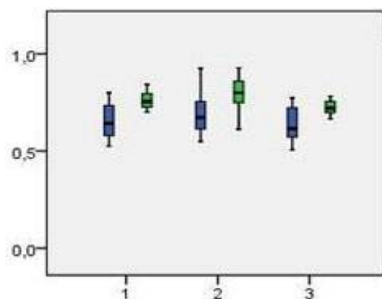
Box plot showing mean (1), radial (2) and axial kurtosis (3) of the the grey matter abnormality (blue bars) and the contralateral normal appearing side (green bars). Box = 25th–75th percentile, horizontal line = 50th percentile. There is a significant reduction in mean, radial and axial kurtosis in the grey matter abnormality compared with the contralateral normal-appearing side.

Reference 1. Cheung M, Hui E, Chan K, Helpern J, Qi L, Wu E, Does diffusion kurtosis imaging lead to better neural tissue characterization? A rodent brain maturation study, NeuroImage 2009;45:86-392