Diffusion MRI of crossing fibers combining double pulsed field gradient (dPFG) eccentricity and q-ball imaging

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Target audience: Neuroimaging scientists and clinicians interested in diffusion imaging and advanced acquisition/reconstruction.
Purpose: It has been shown that the diffusion metric of fractional anisotropy (FA) is, amongst many other things, sensitive to orientation dispersion in the voxel [1,2]. This leads to reduced or sometimes very low FA values in regions of strong fiber crossings, and since the FA value is often used as threshold in tractography this can potentially lead to suboptimal tractography results, for the FA threshold has to be low enough to accommodate strong crossings, which at the same time leads to false positives in other regions [4]. Recently new measures of micro-anisotropy have been proposed which are not influenced by the macroscopic orientation dispersion in the voxel, the rotationally invariant eccentricity metric or the qMAS derived uFA. In this abstract we use the rotationally invariant eccentricity approach to generate an eccentricity metric which is insensitive to macroscopic orientation dispersion and combine the data with a conventional q-ball acquisition with matching imaging parameters to demonstrate this metric's independence from the underlying crossing structure.
Methods: All data was acquired using the Magnetom Connectom A scanner with the AS302 body gradient coil (Gmax=300 mT/m, Smax=200 mT/m/ms). The data for the rotationally invariant eccentricity measurement where acquired using a cardiac-gated fully balanced twice-refocused dPFG sequence [3], where each diffusion block had an equal magnitude of **q** (δ =6 ms, Δ=13 ms, G=226.23 mT/m, q=0.0395 μm^{-1}, b=800 s/mm^2) and the diffusion blocks where separated by a mixing time of 15 ms. The readout module was a 2mm iso-tropic EPI with 220 mm FOV and a matrix size of 110, 1966 Hz/px bandwidth, partial Fourier 6/8 resulting in TE=107 ms. Since no acceleration was used, we limited the coverage to a single-hemisphere, sagittal slab of 35 slices. A total of 72 directions was acquired following the dPFG-5 scheme [1] (12 axes of an icosahedron followed by 5 perpendicular directions for a total of 60 perpendicular encodings and 12 parallel encodings along these axes) as well as 12 interspersed b=0 images. The cardiac gating was accommodated with a TR of 600 ms and 7 concatenations. Depending on the subjects heart rate the acquisition time was about 8 minutes. In order to improve SNR, the scan was repeated three times. Following gradient non-linearity correction the rotationally invariant eccentricity εq^4 was calculated by subtracting the logarithm of the mean of the perpendicular encodings from the logarithm of the mean of the parallel encodings [1]. The 12 parallel encodings were additionally processed by FSL dtifit to generate a matching FA map from the same data.
The q-ball acquisition was performed with a matching resolution and slice prescription, but acquiring 128 directions on a single b=5000 s/mm^2 shell without the use of cardiac gating. The TE and TR of the q-ball acquisition where 63ms and 4300ms respectively. After gradient non-linearity and eddy-current correction the q-ball data was reconstructed using DSI studio and tracts seeded in the crossing fiber region of the centrum semiovale where visualized. The FA and eccentricity values along the tracts are visualized by the fiber pseudo color code.

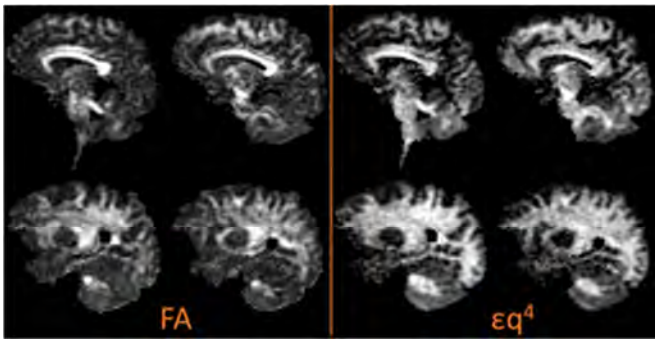

Figure 1: FA and eccentricity maps of 4 slices. Scale is 0-0.6 for both.

Results: In figure 1 it can be seen that the calculated eccentricity maps depict the known white matter structure and are qualitatively more uniform in the white matter than the FA maps.. In particular areas in the centrum semiovale, brainstem, cerebellum and prefrontal white matter show improved uniformity. The absolute values of eccentricity ε are in the range of a few $10^5 \mu m^4$, while the non-normalized map εq^4 has values ranging from 0 to 1. In figure 2 we show the centrum semiovale area as example of a strong fiber crossing area, confirming the premise of this abstract that the eccentricity map is less sensitive to crossing fiber structures than FA.
Discussion: FA metrics are commonly used as indicator of the presence of anisotropic structures in the tissue, however they are very sensitive to spatial coherence of the underlying anisotropic structures, were the presence of multiple orientations of a perfectly anisotropic microstructure could lead to very low FA values. Here we use a rotationally invariant measure of eccentricity to provide a measure of microscopic anisotropy independent of the structures multiple orientations. It is interesting to note that in healthy white matter a mix of multiply oriented cylinders would be an appropriate model, however the measured ε values of this approach are several orders of magnitude smaller than expected for cylinders of voxel-size length and less than 10 μm diameter. One reason for this is the relatively short diffusion time used in this measurement compared to the long axis of the cylinders. It does however indicate the presence of non-spherical restricted diffusion in the voxel, which is a more general measure than FA and may prove more suitable for a number of applications. The technique is quite feasible to implement and can be substantially improved in SNR by shortening the TE via accelerated image acquisition. The scan-time can be further reduced by utilizing the simultaneous multi-slice technique [5]. The only additional effort in the acquisition of the dPFG data is the cardiac gating, which is required to reduce dropouts due to brain pulsation during the mixing time. Forthcoming work will incorporate the eccentricity maps into tractography techniques to investigate improved specificity and reduced threshold sensitivity when using eccentricity maps to guide tractability rather than FA maps.

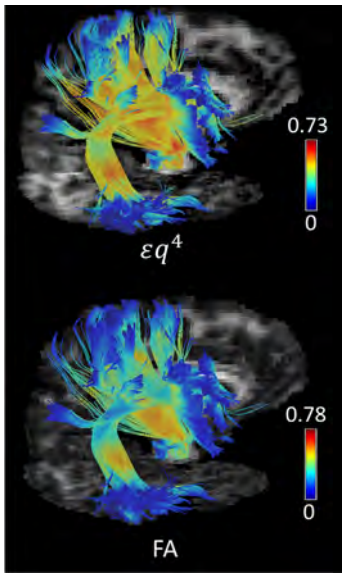

Figure 2: FA and eccentricity values mapped onto tracts seeded in the centrum semi-ovale..

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Refererences: [1] Jespersen SN et.al. NMR Biomed. 2013 Dec;26(12):1647-62. [2] Szczepankiewicz F. et.al. Proc. ISMRM 22 (2014) 0098. [3] Callaghan TD&MR Oxford 2011 [4] Thomas et.al. PNAS 2014 [5] Setsompop K. et. al. Magn Reson Med. 2012 May;67(5):1210-24.