The relationship between "axial" and "radial" diffusivities and the eigenvectors of the diffusion tensor in the brain.

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Introduction: Axial and radial diffusivities reflect the water diffusion coefficients along and across white matter fibre-bundles and are particularly interesting in the brain as potential biomarkers of axonal integrity and myelination. In recent years the principal eigenvalue of the diffusion tensor (DT) has been associated with the axial diffusivity and the average of the second and third eigenvalues with the radial diffusivity[1]. Here we challenge this assumption and underline the importance of analysing the eigenvalues of the DT together with the corresponding eigenvectors. We present results of several simulations to illustrate the effect. We also compare the eigenvalues of the DT between two healthy controls and two MS patients, using non-linear registration and the preservation of principal direction (PPD) algorithm[2].

Methods: (i) Simulations - Synthetic data were obtained by simulating the superposition of two tensors (A and B; see table) representing white matter tracts, either crossing at 90° or at 60° using Camino (http://www.camino.org.uk). SNR was assumed to be equal to 16, typical value of in vivo DT data. A hundred voxels with random Rician noise were generated. A single tensor model was fitted and radial diffusivity, axial diffusivity and FA were estimated from its eigenvalues. In order to simulate demyelination or axonal loss in one of the tracts, one of the components of either A or B was altered and the single diffusion tensor fitting procedure was repeated. (ii) In vivo data - Two healthy controls (females, 35 and 37 years old, respectively) and two patients with relapsing remitting Multiple Sclerosis (MS) (a female, aged 34 disease duration = 1.5 years, EDSS (Expanded Disability Status Scale) = 2.5 and a male, aged 55 disease duration = 7 years, EDSS = 5.5) were scanned on a 1.5T GE Signa MRI scanner (General Electric, Milwakee, WI, USA) with a maximum gradient strength of 33 mT m^{-1}. An 8-channel phased-array coil was used as receiver, while the whole body coil was used as transmitter. A cardiac gated Diffusion-Weighted Spin-Echo Echo Planar Imaging (DW-SE-EPI) sequence was used to acquire data with 61 distributed diffusion weighting directions and b-factor = 1200 s mm^{-2}, interleaved with 7 non-diffusion weighted b ≈ 0 acquisitions, 60 axial slices prescribed parallel to the anterior commissure - posterior commissure (AC-PC) line, FOV = 220mm, acquisition matrix = 96×96 (reconstructed to 128×128), in-plane resolution = 2.3×2.3mm^2 (reconstructed to 1.71×1.71mm^2), sl. thickness = 2.3mm, TR = 20RRs≈20s (depending on the cardiac cycle rate), TE = 84.8ms, total acquisition time ≈20min. The in vivo data were processed as follows: eddy-current induced distortions and small head motion were corrected using an algorithm that applies affine 3D registration to a reference volume (the first b ≈ 0 volume of the dataset) (see eddycorrect, FMRIB Diffusion Toolbox (FDT) - http://www.fmrib.ox.ac.uk/fsl/fdt/index.html); The corrected dataset was fed to a DT fitting procedure and FA was computed for each subject. In order to minimize registration errors, inter-subject registration was achieved using a non-linear algorithm (FNIRT, part of the FSL package) on the FA maps, with one of the healthy controls as target. The transformations were then applied to each component of the DT followed by the PPD algorithm for appropriate reorientation and the rotated DT was diagonalised to determine the eigenvalues and eigenvectors of the registered datasets. The angle between the principal eigenvector of each subject and that of the reference subject was computed to highlight areas of misalignment between corresponding eigenvectors of corresponding areas of different subjects.

Results and conclusions: (i) Simulations - The table shows the results of the simulations. Changes in the "axial" or "radial" components of either tensor A or B affects not only the eigenvalues of the single tensor fitting, but also the direction of its eigenvectors, with a mean change in the direction of the principal eigenvector as large as 76.5° when simulating a reduced axial component of tensor B (see table). (ii) In vivo data – Changes in the direction of the principal eigenvectors happen both in normal tissue as well as in tissue affected by pathology. An effective increase or decrease of one of the eigenvalues of the DT may be related to a complicated biophysical process, not necessarily related to the most straightforward explanation. Without checking the direction of the eigenvectors and without knowing the tissue structure, one can wrongly compare eigenvalues representing diffusivities along directions that are not aligned with the underlying fiber bundle but that may deviate from such a direction by a significant angle. The figure shows an example of FA map overlaid with voxels characterised by an increase in the "radial" diffusivity and a significant misalignment of the principal eigenvector between one of the patients and one of the controls.

Table: Results of simulations. Mean values of % changes are averaged over 100 voxels.

	90° crossing	60° crossing	90° crossing	60° crossing
Original tensor A	$0.5\begin{bmatrix}15&0&0\\0&3&0\\0&0&3\end{bmatrix}$	$0.5\begin{bmatrix}12&5.196&0\\5.196&6&0\\0&0&3\end{bmatrix}$	$0.5\begin{bmatrix}15&0&0\\0&3&0\\0&0&3\end{bmatrix}$	$0.5\begin{bmatrix}12&5.196&0\\5.196&6&0\\0&0&3\end{bmatrix}$
Original tensor B	$0.5\begin{bmatrix}3&0&0\\0&15&0\\0&0&3\end{bmatrix}$	$0.5\begin{bmatrix}3&0&0\\0&15&0\\0&0&3\end{bmatrix}$	$0.5\begin{bmatrix}3&0&0\\0&15&0\\0&0&3\end{bmatrix}$	$0.5\begin{bmatrix}3&0&0\\0&15&0\\0&0&3\end{bmatrix}$
Alteration	Increase "radial" component of B	Increase "radial" component of B	Reduce "axial" component of B	Reduce "axial" component of B
Resulting tensor A	$0.5\begin{bmatrix}15&0&0\\0&3&0\\0&0&3\end{bmatrix}$	$0.5\begin{bmatrix}12&5.196&0\\5.196&6&0\\0&0&3\end{bmatrix}$	$0.5\begin{bmatrix}15&0&0\\0&3&0\\0&0&3\end{bmatrix}$	$0.5\begin{bmatrix}12&5.196&0\\5.196&6&0\\0&0&3\end{bmatrix}$
Resulting tensor B	$0.5\begin{bmatrix}5&0&0\\0&15&0\\0&0&5\end{bmatrix}$	$0.5\begin{bmatrix}5&0&0\\0&15&0\\0&0&5\end{bmatrix}$	$0.5\begin{bmatrix}3&0&0\\0&12&0\\0&0&3\end{bmatrix}$	$0.5\begin{bmatrix}3&0&0\\0&12&0\\0&0&3\end{bmatrix}$
Effect of the tensor's alterations on DT indices estimates by fitting a single tensor				
Mean % change in RADIAL DIFF	↑ (+9.3±2.9%)	↑ (+27.8±2.18%)	↓ (-6.6±1.83%)	↓ (-54.1 ± 3.75%)
Mean % change in AXIAL DIFF	↑ (+13.7±4%)	↔ (+0.98±.37%)	↓ (-5.32±2.43%)	↓ (-25.9 ± 3.70%)
Mean % change in FA	↓ (-9.6±3.3%)	↓ (-10.93±1.05%)	↓ (-3.4±1.63%)	↑ (+23.6±7.82%)
Mean change in the direction of principal eigenvector	57.3°	2.63°	42.9°	76.5°

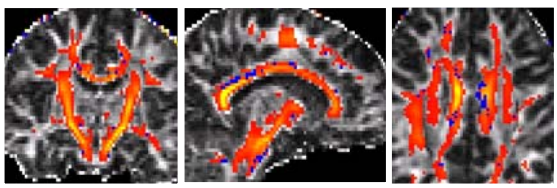

Figure: FA maps overlaid with voxels with FA>0.3 in all four subjects (hot-colours). Blue voxels represent a change in the radial diffusivity of one of the patients with MS of more than 10% compared to the healthy control used as reference and an angle between the principal eigenvectors of > 45°.

Referernces: [1]. Song et al. Neuroimage. 20, 1714 (2003); [2] Alexander et al. IEEE Trans. Med. Imaging 20, 1131 (2001).

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