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Diffusion tensor parameters and principal eigenvector coherence: Relation to *b*-value intervals and field strength

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ABSTRACT

Diffusion-weighted MRI images acquired at *b*-value greater than 1000 s mm^{-2} measure the diffusion of a restricted pool of water molecules. High *b*-value images are accompanied by a reduction in signal-to-noise ratio (SNR) due to the application of large diffusion gradients. By fitting the diffusion tensor model to data acquired at incremental *b*-value intervals, we determined the effect of SNR on tensor parameters in normal human brains, *in vivo*. In addition, we also investigated the impact of field strength on the diffusion tensor model. Data were acquired at 1.5 and 3 T, at *b*-values 0, 1000, 2000 and 3000 s mm^{-2} in twenty diffusion-sensitised directions. Fractional anisotropy (FA), mean diffusivity (MD) and principal eigenvector coherence (κ) were calculated from diffusion tensors fitted between datasets with *b*-values 0–1000, 0–2000, 0–3000, 1000–2000 and 2000–3000 s mm^{-2}. Field strength and *b*-value effects on diffusion parameters were analysed in white and grey matter regions of interest. Decreases in FA, κ and MD were found with increasing *b*-value in white matter. Univariate analysis showed a significant increase in FA with increasing field strength in highly organised white matter. These results suggest there are significant differences in diffusion parameters at 1.5 and 3 T and that the optimal results, in terms of the highest values of FA in white matter, are obtained at 3 T with a maximum $b = 1000$ s mm^{-2}.

1. Introduction

Magnetic resonance diffusion tensor imaging (DTI) provides quantitative measures to capture the diffusive properties of water molecules, *in vivo*. The three dimensional diffusivity of water in tissue such as brain white matter can be characterised using the diffusion tensor, D [1]. Measurement of the three orthogonal, principal directions of diffusion (principal eigenvectors, $\boldsymbol{\varepsilon}$) and the three corresponding magnitudes of diffusivity in these directions (eigenvalues, λ) can be calculated from D [1]. Further parameters derived from a tensor are indicative of the underlying brain microstructure as the diffusivity measured is governed by the structural architecture within the voxel. Parameters quantifying bulk water molecular motion within a voxel (mean diffusivity, MD) and its degree of diffusion anisotropy (fractional anisotropy, FA) are two common scalars that have been used to investigate changes in brain structural integrity in a number of pathological diseases such as multiple sclerosis [2,3], epilepsy [4,5], brain tumours [6] and Alzheimer's disease [7]. Another index is the principal eigenvector coherence, κ, which measures the level of alignment for a number of estimates of the principal direction of diffusion, $\boldsymbol{\varepsilon_1}$, in a voxel [8]. Multiple estimates of $\boldsymbol{\varepsilon_1}$ can be made by using a statistical sampling method, known as bootstrapping, to produce many replicates of the diffusion-weighted datasets from which to calculate $\boldsymbol{\varepsilon_1}$.

Most diffusion MRI studies use a maximum *b*-value of approximately 1000 s mm^{-2}. Studies using higher *b*-values (where *b*-value>2000 s mm^{-2}) on both healthy adults [9–11] and neonates [12] have shown that the signal decay is non-monoexponential and leads to marked contrast between white and grey matter tissue on MD maps. High *b* diffusion-weighted imaging has also been found to give improved lesion-to-normal contrast in Alzheimer's patients [13] and better identification of deep grey matter injury from acute asphyxia in neonates [12]. A number of approaches have been used to fit the non-monoexponential decay including bi-exponential fitting which assumes two compartments in slow exchange: one is a rapidly diffusing component and the other a more slowly diffusing component [9,10]. A comparison between 'fast' and 'slow' diffusion tensors (calculated from diffusion-weighted data fitted at low and high *b*-values, respectively) have also shown white/grey matter contrast in MD and increases in FA at high *b* that may be due to the movement of a more restricted, or slower diffusing pool of protons

Abbreviations: CS, centrum semiovale; D, diffusion tensor; DTI, diffusion tensor imaging; FA, fractional anisotropy; MD, mean diffusivity; ROI, region of interest; SNR, signal-to-noise ratio.

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than is seen with $b=1000$ s mm^{-2} acquisitions [11]. It would therefore appear that high b diffusion-weighted imaging has potential in providing further information on the underlying tissue structure. The disadvantage of high b is the decrease in the signal-to-noise ratio (SNR) of the diffusion-weighted image due to the application of larger diffusion gradients. Reducing SNR has a detrimental effect on diffusion parameters, causing an upward bias in FA, particularly if the true FA is low, as in grey matter [14–16], and reduces the certainty in the principal direction of diffusion [15,17]. Therefore one of the aims of this study is to determine the effect of b-value range on diffusion parameters in healthy adults.

To further assess the effect of SNR on diffusion parameters, comparisons are made between acquisitions at 1.5 and 3 T magnetic field strengths. As 3 T MRI technology is becoming more clinically available, diffusion tensor parameters obtained at this field strength need to be determined as most previous diffusion tensor imaging studies have been made at 1.5 T. It is noteworthy that the few studies which compare 1.5 and 3 T diffusion tensor parameters have differed in their findings; one study reported no significant differences with increasing field strength [18], whereas others found a significant increase in FA and decrease in MD [19,20].

In summary, the aim of this study is to determine the effect of b-value (in the range 0 to 3000 s mm^{-2}) and field strength on FA, MD and principal eigenvector coherence in healthy adult subjects, for white and grey matter regions of interest (ROI) in human brain.

2. Materials and methods

2.1. Subjects and imaging protocol

Eight healthy subjects (three women, five men; age range, 23–27 years; median age 26) with no history of neurologic or other systemic diseases were scanned on a 1.5 T (Avanto, Siemens, Erlangen, Germany) and 3 T MRI scanner (Trio, Siemens, Erlangen, Germany). Both systems have a maximal gradient strength of 40 mT m^{-1}. Subjects were scanned according to local ethics approval and all gave written informed consent. On each MRI system, images were acquired with a double refocused pulsed diffusion-weighted echo-planar sequence [21]. Scan parameters were: repetition time 4100 ms; echo time 112 ms; matrix size 96×96; field of view 240 mm^2; number of averages 2. Voxel dimensions were 2.5×2.5×5 mm, with 25 axial slices for full brain coverage. Diffusion gradients were applied in twenty non-collinear directions at b-values 1000, 2000 and 3000 s mm^{-2}, following a single non-diffusion-weighted acquisition. Increasing diffusion-weighting was achieved with increasing gradient amplitude whilst the diffusion time remained unchanged. Four repeats of the acquisition protocol were performed for each volunteer within the same scanning session (i.e. four $b=0$ s mm^{-2} acquisitions and 240 diffusion-weighted volumes). This imaging protocol was identical for both 1.5 and 3 T. T1-weighted images were also acquired with a 3D FLASH sequence and parameters are as follows: For 1.5 T – TR/TE = 11/5 ms, flip angle 15°, matrix = 256 × 224, 256 sagittal slices, voxel dimensions 1 mm^3. For 3 T – TR/TE = 1500/2.9 ms, flip angle 10°, field of view = 211 mm^2, matrix = 192 × 192, 208 sagittal slices, voxel dimensions 1.1 mm^3.

2.2. Data pre-processing

Diffusion-weighted data was registered to $b=0$ s mm^{-2} space using the following protocol [22]: for each of the four repeats, the acquired twenty directions of diffusion data were averaged on a per b-value basis (thus giving an averaged volume of diffusion-weighted images at $b=1000$, 2000 and 3000 s mm^{-2} i.e. a total of three volumes for each repeat). These averaged b volumes were registered to the $b=0$ image [23] and the relevant transformation matrices applied to the original, corresponding b-value diffusion-weighted volume. The $b=0$ volume from three acquisitions were registered to the first acquired $b=0$ volume and the transformation matrices applied to corresponding diffusion-weighted volumes. The four acquisitions were then averaged to produce a 'master' diffusion dataset. This registration protocol was applied on each subject's data at 1.5 and 3 T.

2.3. DTI post-processing and bootstrapping

All $b=0$ s mm^{-2} volumes were skull stripped using FSL's Brain Extraction Tool [24], and the brain masks applied to all registered diffusion-weighted images. The Wild bootstrap was implemented as defined by Davison and Hinkley [25] and performed on one of the four whole brain diffusion-weighted acquisitions, creating 1000 replicate datasets at $b=0$, 1000, 2000 and 3000 s mm^{-2}. A diffusion-weighted bootstrap dataset, $\mathbf{S_B}$, is computed by randomly perturbing the residuals, e (where e_i is the residual in the ith diffusion gradient and residuals are calculated from fitting D to the original signals, $\mathbf{S}$), using a two-point distribution:

$$e_i^* = \begin{cases} e_i\left(1-\sqrt{5}\right)/2, probability = \pi \\ e_i\left(1+\sqrt{5}\right)/2, probability = 1-\pi \end{cases}$$

where $\pi = \left(5+\sqrt{5}\right)/10$
and adding e_i^* back to the original diffusion-weighted signals (i.e. $\mathbf{S_B} = \mathbf{S} + \mathbf{e^*}$). Using a linear least squares fit to the log of the measured signals, the diffusion tensor [1] was fitted on all bootstrapped datasets, two b-value datasets at a time. That is, for b interval (0, 3000), only bootstrapped diffusion-weighted data at $b=0$ and $b=3000$ are used to calculate D. For b interval (2000, 3000), only bootstrapped diffusion-weighted data at $b=2000$ and $b=3000$ are used. For every bootstrapped dataset, a diffusion tensor was calculated at each of the following five b intervals: (0 and 1000), (0 and 2000), (0 and 3000), (1000 and 2000) and (2000 and 3000) s mm^{-2}. In order to calculate coherence, a mean of all bootstrapped principal eigenvectors is first defined. This is achieved by calculating the dyadic tensor for each voxel:

$$\left\langle \varepsilon_1^j \varepsilon_1^{j\,T} \right\rangle = \left\langle \begin{pmatrix} (\varepsilon_{1x})^2 & \varepsilon_{1x}\varepsilon_{1y} & \varepsilon_{1x}\varepsilon_{1z} \\ \varepsilon_{1y}\varepsilon_{1x} & (\varepsilon_{1y})^2 & \varepsilon_{1y}\varepsilon_{1z} \\ \varepsilon_{1z}\varepsilon_{1x} & \varepsilon_{1z}\varepsilon_{1y} & (\varepsilon_{1z})^2 \end{pmatrix} \right\rangle = \frac{1}{n}\sum_{j=1}^{n} \varepsilon_1^j \varepsilon_1^{j\,T}$$

where $\boldsymbol{\varepsilon^j_1}$ is the principal eigenvector for the j^{th} bootstrap, and n is the total number of bootstraps. The coherence, κ, is then determined from the eigenvalues (β_1, β_2, and β_3) of the dyadic:

$$\kappa = \left(1 - \sqrt{\frac{\beta_2+\beta_3}{2\beta_1}}\right)$$

when κ is equal to zero, all bootstrapped $\boldsymbol{\varepsilon_1}$ are equally distributed on a sphere (thus $\beta_1=\beta_2=\beta_3$). Coherence has a maximum value of 1 when all $\boldsymbol{\varepsilon_1}$ are aligned in the same direction [8].

2.4. Defining regions-of-interest

MD and FA maps [16] were calculated using the master dataset from tensors fitted between b intervals (0, 1000), (0, 2000), (0, 3000), (1000, 2000), and (2000, 3000). White matter ROI were drawn in the genu and splenium of the corpus callosum, and bilaterally in the centrum semiovale (CS). These regions were identified for each subject on the master $b=0$ volume separately on both 1.5 and 3 T data. Grey matter ROI were defined on T1-weighted images using FSL's FIRST [26] to automatically segment bilateral