Quantifying Non-Gaussian Diffusion in Brain Tissue at High b-Factors

F. Grinberg[1], E. Farrher[1], J. Kaffanke[1], A-M. Oros-Peusquens[1], and N. J. Shah[1,2]
[1]Institute of Neuroscience and Medicine - 4, Forschungszentrum Juelich GmbH, 52425 Juelich, NRW, Germany, [2]Department of Neurology, Faculty of Medicine, RWTH Aachen University, JARA, 52074 Aachen, Germany

Introduction

Attenuation of the water NMR signal by molecular diffusion in brain tissue provides valuable information with respect to microstructural environment of water molecules [1]. Conventional diffusion tensor imaging (DTI) methods are based on a simplified Gaussian model and designed to retrieve diffusion characteristics only in the low range of diffusion weightings. However, diffusion behaviour beyond this range is more complex and cannot be adequately quantified in the framework of the Gaussian model [2]. The aim of this work was to examine approaches capable of capturing more detailed information on the propagation mechanisms and underlying tissue microstructure in comparison to the conventional methods. We report an *in vivo* diffusion study of the brain based on the Biexponential Diffusion Tensor Analysis (BEDTA) performed in the range of very high *b*-values on the voxel-by-voxel basis [3].

Materials and Methods

In vivo diffusion studies were carried out on 14 healthy volunteers, with a whole-body 3T Siemens MAGNETOM Tim-Trio scanner (Siemens Medical Systems, Erlangen, Germany). DW images were acquired using a bipolar gradient double spin-echo echo-planar imaging pulse sequence provided by the manufacturer. Fifteen *b*-values and 6 non-collinear directions of the diffusion-encoding gradients were used. The voxel size was 2×2×2 mm^3. The echo/repetition time was 113/1000 ms. Between 16 and 32 averages were acquired. Mono- and biexponential functions were fitted to the acquired diffusion attenuations on the voxel-by-voxel basis in the range of $b \leq 1000$ s mm^{-2} and $b \leq$ 7000 s mm^{-2}, respectively. The eigenvalues of the "mono", "fast" and "slow" diffusion tensors (in the following referred to as MDT, FDT and SDT, respectively) were reconstructed using standard DTI procedures. The fractions of the FDT and SDT were constrained to be independent of the gradient orientation. In the following, the subscripts "m", "f", and "s" will refer to the MDT, FDT and SDT, respectively.

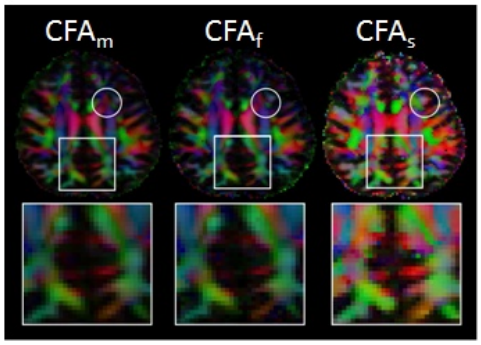

Figure 1. The CFA maps related to MDT, FDT, and SDT.

Results and discussion

Several parameter maps were evaluated based on the BEDTA such as the maps of mean apparent diffusivities and fractional anisotropies (FA) related to the MDT, FDT and SDT. We constructed, for the first time, novel colour-coded FA maps (CFA) related to the SDT, the ACPhi map (absolute *cosine* of the angle between the major eigenvectors of the FDT and SDT), and new *alpha*-maps quantifying the degree of non-exponentiality of the attenuation curves. Figure 1 shows, as an example, the CFA maps of a representative volunteer. While CFA_m and CFA_f maps are very similar to each other, the maps of CFA_s visualise more structural details in white matter (WM) regions, compare the patterns at the level of frontal gyrus, the anterior cingulate and the cuneus. A comparison of the colour codes in the CFA_f and CFA_s maps shows that fibre tract orientations derived from the FDT and SDT appear largely correlated in most parts of WM. However, in a few regions the fibre tract orientations as depicted by the CFA_m/CFA_f and CFA_s maps were different, see, for instance, regions marked by circles. The maps of FA_s were found to exhibit considerably higher values than that of FA_m and FA_f. This finding was substantiated by the analysis of the corresponding histograms averaged over 14 subjects, Figure 2. Characteristic of all three histograms in Figure 2 is the presence of a relatively narrow peak in the range of values below 0.25 attributed to non-WM. Related to WM regions, the histogram of FA_s appears considerably shifted towards the larger values. Besides, it exhibits an additional peak in the range of values between 0.7 - 0.75.

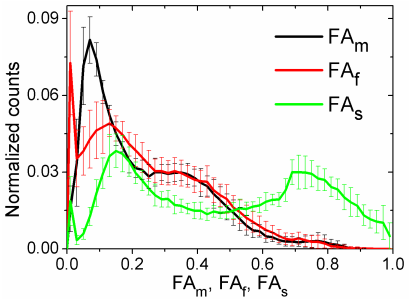

Figure 2. The histograms of the maps of FA_m, FA_f , and FA_s averaged over 14volunteers.

Our results demonstrate that FA_s/CFA_s maps are capable of essentially improving WM mapping and of revealing otherwise hidden tiny microstructure. Due to this feature and a more favourable shape of the histogram a potentially higher sensitivity of FA_s/CFA_s in brain diagnostics was hypothesised. The ACPhi and *alpha*-maps were shown to provide valuable information which cannot be accessed via standard DTI.

Conclusions

By application of the advanced BEDTA approach we have attained a comprehensive description of non-Gaussian diffusion in brain tissue and illustrated the benefits of studying diffusion at high *b*-factors. The range of *b* factors typically used in conventional DTI was exceeded by a factor of seven. Several new map parameters were proposed as potential novel biomarkers of developmental and pathological changes in WM.

References

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