In vivo DTI parameter choice using Monte-Carlo diffusion simulations in a model of brain white matter

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Introduction

Diffusion Tensor Imaging (DTI) has been proposed to visualize the fibres of brain white matter (WM) based on the selectivity of the maximal apparent diffusion coefficient (ADC) which correspond to the water diffusion along the axons. DTI potentially provides more detailed information about tissue organization but significant questions remain concerning different relations between tissue microstructure, brain water compartments, the connectivity of cerebral areas with ADC values and experimental DTI parameters. In this study, simulated diffusion-weighted signal in a model of WM was developed [1-3] in order to study the relationship between diffusion time (tdif) and ADC values. *In vivo* water diffusion experiments on rat brain were performed and compared to the simulated data.

Methods

Simulations: The WM fibres were modelled by adjacent, longitudinal and hexagonally spaced cylinders [1-3]. Fig.1 shows a transverse scheme of the model composed of intra-axon, myelin and extra-axon compartments defined by axon diameter, spacing between axon centres (SPC) and water volume fraction. The signal diffusion was simulated using a 3D random walk Monte-Carlo method with 10 µs time step. Each simulation run calculated signal from 10^5 particles distributed with a defined compartment volume fraction V_f (see Fig.1). The free diffusion coefficient D_0 was set to 2.0×10^{-3} mm²/s. The pulsed-field-gradient spin-echo NMR experiment was computed with a varying diffusion time in the range of [10-100 ms], 5 ms gradient duration and 20 different b-values in the range of [0, 4000 s/mm^2]. The program allowed the maximal and minimal ADC calculations which correspond to the ADC parallel and perpendicular to the axon axis respectively. All programs were developed on Matlab®.

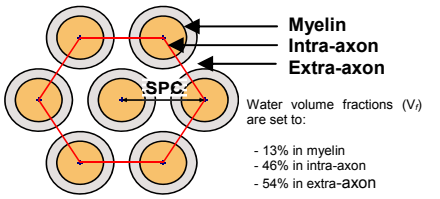

Fig.1: Transverse scheme of the model of WM fibers.

In vivo experiments were performed at 7.0 T on a Bruker Avance III console with 600 mT/m maximum gradient strength. Wistar rats were anaesthetized using isoflurane (2%) in air. A volume/surface cross RF coil was used for all acquisitions. Spectroscopic diffusion-weighted stimulated-echo sequence with squared gradients was used. Elimination of unwanted coherences was performed by the application of a 5 ms spoil gradient during the mixing time interval and by using an eight-step phase cycling scheme. Echo time and repetition time were set to 18 ms and 800 ms respectively. A volume of interests (VOI = 2 mm x 2 mm x 1.1 mm) was positioned in the white matter in the corpus callosum as shown in Fig.2. In the VOI, water diffusion measurements were made using 8 distinct b-values (500, 800, 1000, 1500, 1800, 2000, 2500, 3000 s/mm²). For each b-value, diffusion gradients were applied in 30 directions according to Jones et al [4]. 1024 data points per scan were collected during 410 ms with a 4 kHz spectral window. Peak integrals of the water spectra were measured and fitted to exponential model. Maximal and minimal ADC values were extracted from the diffusion tensor.

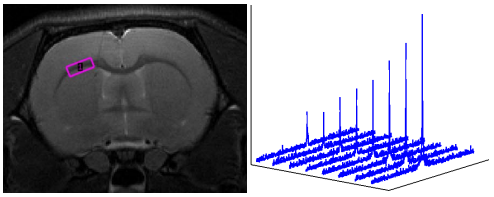
Fig.2: Left: Volume of interest for the diffusion-weighted stimulated-echo sequence. Right: Exponential decay of water spectra vs b-values in one direction.

Results

Fig.3 and Fig.4 show results from *in vivo* and from two simulated geometries (SPC = 6 µm and SPC = 20 µm). Maximal and minimal ADC values are plotted versus tdif from 10 ms to 100 ms. In Fig.3, the simulated maximal ADC values are constant and equal to D_0 for the both geometries, showing that water diffusion is free in the direction of the fibre bundles. The *in vivo* results show a maximal ADC lower than D_0 and independent of tdif as simulated data.
Fig.4 shows different behaviour of minimal ADC values for the two simulated geometries. At short tdif (< 40 ms) and in the case of SPC = 20 µm, minimal ADC decreases from 0.9×10^{-3} mm²/s to 0.4×10^{-3} mm²/s. In this case, and in opposite to SPC = 6 µm, water diffusion is probably more free. *In vivo*, minimal ADC values show a similar behaviour to simulated data with SPC = 6 µm according to the known micro-architecture of WM. However *in vivo* results are lower than simulated data.

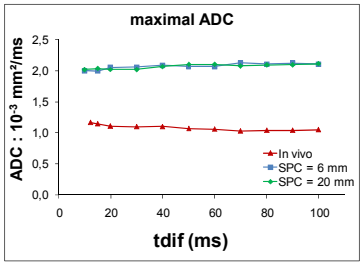

Fig.3: Maximal ADC in WM. Simulated (SPC = 6 µm and SPC = 20 µm) and *in vivo* data.

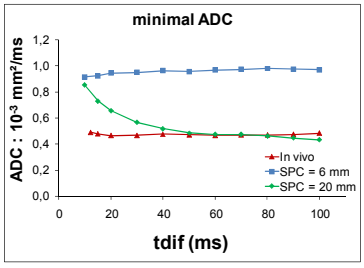

Fig.4: Minimal ADC in WM. Simulated (SPC = 6 µm and SPC = 20 µm) and *in vivo* data.

Discussion

All the results show that in order to better distinguish minimal from maximal ADC values, signal acquisitions for fibre-tracking imaging by DTI, do not necessitate large diffusion time. Therefore in order to have a high Signal to Noise Ratio, *in vivo* measurements would rather be acquired with short tdif than with larger tdif.
The difference between simulated and *in vivo* ADC values are probably due to the viscosity and to the tortuosity of the WM medium, as well as to the intra/extra axons water exchange which are not yet considered in the model. Moreover, up to now, WM models described in literature underestimate the intracellular compartment volume fraction. An improved model which fit better *in vivo* microstructure might match better simulation results to experimental data.

A flexible tool for diffusion NMR signal simulation has been developed. Here we present our first results from the simulator computed in a WM model compared to *in vivo* data. The perspective of this work is to model fibres when they cross gray matter to better establish a relationship between DTI parameters and minimal and maximal ADC values.

References

[1] Sen and Basser, Biophys J, 2005. [2] S. Peled, IEEE Trans Med Imaging, 2007. [3] Mauconduit and Lahrech, ESMRMB, 2009. [4] D.K. Jones, MRM, Magn Reson Med, 1999.