Hindered or restricted predominance of the diffusion weighted signal function of the diffusion time at ultra-high magnetic field.

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Introduction:

The exact origin of water diffusion anisotropy in brain white matter is not fully understood. Several modeling have been proposed to explain the biophysical mechanisms but it is still not clear whether the observed diffusion anisotropy arises from the intra-axonal compartment (primarily restricted diffusion) or the extra-axonal compartment (primarily hindered diffusion) or some combination thereof. The CHARMED model [1] is a framework that combines contribution of hindered and restricted diffusion compartments arising from the extra- and intra- axonal space assessed by multi-diffusion time DWI measurements. Through the increased sensitivity, the use of ultra-high magnetic field likely yields new information about the exact origin of this signal. Here we propose to assess the effect of the diffusion times on DTI derived parameters in the rat brain white matter at two different ultra-high magnetic fields: 9.4T and 14.1T.

Materials and Methods:

Experiments were performed on two different magnets: 9.4T/31cm and 14.1T/26cm (Varian/Magnex) both equipped with 12-cm gradient coils (400mT/m, 120µs). Two different quadrature transceive surface RF coils were used with diameter of 20 and 21 mm for 9.4T and 14.1T, respectively. For each magnetic field strength, exactly the same following protocol was used. The rat (n = 5 for each B_0) was lying prone, its head secured via ear bars and continuously anesthetized under a flow of 1.5-2% isoflurane in oxygen. Body temperature was maintained at 37±0.5°C using thermoregulated water circulation. After automatic adjustment of first and second order shims (FASTMAP [2] - water half-height linewidth ranged between 16 and 20 Hz), 6 repeated Diffusion Tensor Echo Planar Images (4 shots) were performed with t_d = 9, 11, 13, 15, 17 and 24 ms, respectively. A semi-adiabatic double spin echo sequence was used [3] and diffusion gradients were applied around the first 180° with the same polarity resulting in a *b*-value fixed to 1000 s.mm^{-2} over all the 6 DT-EPI acquisitions. Diffusion gradients were applied along 42 spatial directions: Icosahedral 21 directions as well as the 21 opposite directions to cancel *b*-value cross terms [4]. DT-EPI parameters were: FOV = 23 × 15 mm^2, matrix size = 128 × 64 zero-filled to 256 × 168, 10 slices of 0.8 mm thickness in the axial plane, 8 averages with TE = 50 ms. A TR of 2s was used and as a result T_1 effect was assumed to be the same for both B_0. Using homemade Matlab (Mathworks, Natick, MA) software, diffusivity values (ADC, $D_{//}$ and $D_{\perp}$) as well as fractional anisotropy (FA) was derived from the tensor. On the direction encoded color maps, ROIs were drawn in the corpus callosum for the 10 different slices of the rat brain and averaged two by two to obtain 5 different image-planes of measurement (fig. 1). Collected data were submitted to a Friedman non-parametric test.

Results:

Overall, the cortical SNR was found equal to 59±12 and 57±16 for 9.4T and 14.1T, respectively. The expected increase in SNR at higher B_0 is offset by the T_2 decrease at 14.1T: 29 ms compared to 42 ms at 9.4T, in the cortex. At a TE of 50 ms, this amounts to a reduction in relative signal by 42%.

In the corpus callosum, independently of t_{diff} and B_0, the rear part of the body (image-planes 2 and 3 in fig. 1) exhibited significantly higher $D_{\perp}$ and lower $D_{//}$ values than splenium, front part of the body as well as genu (image-planes 1, 4 and 5 in fig. 1, respectively) resulting in a lower FA.

At 9.4T, FA values were found significantly lower for t_{diff} = 9 ms than the values obtained with t_{diff} = 24 ms independently of the image-plane analyzed (fig. 1). This lower FA was predominantly due to an increase of $D_{\perp}$. Nevertheless, no significant difference in FA was found at other t_{diff} used.

At 14.1T, FA values were found significantly lower for t_{diff} = 9 ms and 11 ms than the values obtained with t_{diff} = 24 ms independently of the image-plane analyzed and was also found significantly lower with t_{diff} = 13 ms only at levels 2 and 3 (fig. 1).

9.4T vs. 14.1T: FA values were significantly lower at 14.1T than at 9.4T only with the shortest t_{diff} (= 9 ms). At longer t_{diff}, (≥ 11 ms) FA values were found similar between 9.4T and 14.1T. This low FA at 14.1T for t_{diff} = 9 ms was predominantly due to a larger $D_{\perp}$. The characteristic diffusion time (t_{hr}) from which the signal pass from predominantly hindered to predominantly restricted was longer at 14.1T than at 9.4T and depending on the axonal structure (at 14.1T, longer in region with lowest FA).

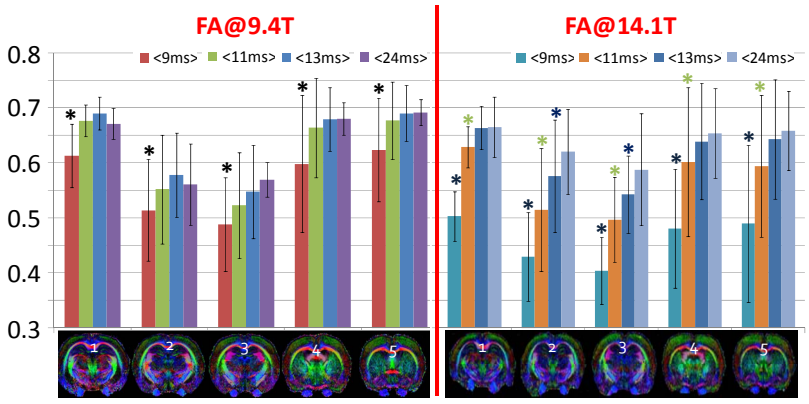

Figure 1: Histograms of FA±SD function of t_{diff}: 9, 11, 13 and 24 ms at 9.4T (left) and 14.1T (right) for the 5 slices analyzed (1 to 5). *:p<0.05, FA @ t_{diff} = 9, 11 or 13 ms *vs.* t_{diff} = 24 ms for each B_0. For clarity, non significant results (t_{diff}= 15 and 17 ms) have been removed from the fig.

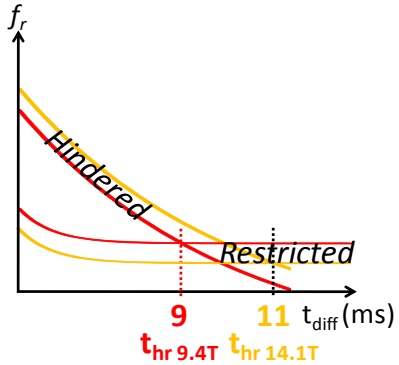

Figure 2: fraction of the diffusion weighted signal (*fr*) function of the diffusion time (t_{diff}) at 9.4T (red) and 14.1T (yellow). t_{hr}: the characteristic diffusion time from which the signal pass from predominantly hindered to predominantly restricted is longer at 14.1T.

Discussion:

The FA changes reported along the different slices are due to the well known non-uniform axonal structure along the CC: the axonal diameter is changing throughout the CC in the front-rear direction [5]. Since the SNR was roughly the same between 9.4 and 14.1T, this cannot explain the differences between the two magnetic field strengths. However, in the corpus callosum, T_2 = 36 and 23 ms at 9.4T and 14.1T, respectively. In white matter, by increasing t_{diff} (fig. 2), the diffusion weighted signal is increasingly dominated by restricted diffusion processes (high FA). Based on the CHARMED theory, it is thus likely that the T_2 decreases when experimenting B_0 increase is not the same in intra- and extra-axonal space: T_2 reduction is expected to be more important in a more confined compartment. As a result, at 14.1T, the weight of species with short T_2 is lower than at 9.4T and the characteristic time t_{hr} is reached later (fig. 2). In region with higher axonal diameter this characteristic time is a bit longer probably due to differences in the structure of the hindered space.

Conclusion:

We characterized, for the first time, the characteristic diffusion time along the corpus callosum at ultra-high magnetic field (t_{hr} ~ 9-11 ms). Furthermore, we show that t_{hr} was increasing with B_0, which might be explained by a shortening of the intra-axonal T_2 more pronounced than the one of the extra-axonal T_2. The results of this study are in very good agreement with a two compartment model (e.g. CHARMED model) giving a new insight into the understanding of the diffusion signal origin and suggesting differences in intra- and extra-axonal T_2.

References: [1] Assaf Y et al. MRM 2004; [2] Gruetter R et al. MRM 2000; [3] van de Looij Y, Kunz N et al. MRM 2010; [4] Madi S et al. MRM 2005; [5] Barzany D et al. Brain 2010.

Acknowledgements: Supported by NEOBRAIN, the Fond National Suisse (N° 31003A-112233), the Centre d'Imagerie Biomédicale (CIBM) of the UNIL, UNIGE, HUG, CHUV, EPFL, the Leenards and Jeantet Foundation.