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

Y. van de Looij1,2, N. Kunz1,2, P. S. Hüppi1, R. Gruetter1,2, and S. V. Sizonenko1

1Division of Child Growth & Development, University of Geneva, Geneva, Switzerland, 2Laboratory for Functional and Metabolic Imaging, Ecole Polytechnique Fédérale de Lausanne, Lausanne, Switzerland, 3Department of Radiology, Universities of Lausanne and Geneva, Lausanne and Geneva, Switzerland

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, 120 μs). 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 B0) 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 tD = 9, 11, 13, 15, and 24 ms, respectively. A semi-adiabatic double spin echo sequence was used [3] and diffusion gradients were applied around the first 180° pulse. The same for both B0. Using homemade Matlab (Mathworks, Natick, MA) software, diffusivity values (ADC, D parallel and D perpendicular) were 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 B0 is offset by the T2 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 tD and B0, the rear part of the body (image-planes 2 and 3 in fig. 1) exhibited significantly higher D parallel and lower D perpendicular 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 tD = 9 ms than the values obtained with tD = 24 ms independently of the image-plane analyzed (fig. 1). This lower FA was predominantly due to a significant increase in D parallel. Nevertheless, no significant difference in FA was found at other tD values used.

At 14.1T, FA values were found significantly lower for tD = 9 ms and 11 ms than the values obtained with tD = 24 ms independently of the image-plane analyzed (fig. 1). The characteristic diffusion time 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).

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, T2 = 36 and 23 ms at 9.4T and 14.1T, respectively. In white matter, by increasing T2 (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 T2 decreases when experimenting B0 increases is not the same in intra- and extra-axonal space: T2 reduction is expected to be more important in a more confined compartment. As a result, at 14.1T, the weight of species with short T2 is lower than at 9.4T and the characteristic diffusion time t90 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 characterize for the first time, the characteristic diffusion time along the corpus callosum at ultra-high magnetic field (t90 ~ 9-11 ms). Furthermore, we show that t90 was increasing with B0, which might be explained by a shortening of the intra-axonal T2 more pronounced than the one of the extra-axonal T2. 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 T2.

References:

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.