Effects of diffusion time on diffusion tensor derived parameters measured on the rat brain at ultrahigh magnetic field

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Introduction:

Over the last decade, Diffusion Tensor Imaging (DTI) became an MR technique routinely used in clinical environments. The importance of preclinical studies at ultrahigh magnetic field resulted in an increasing number of publications focused on the rodent brain. Several studies have shown that the choice of sequence parameters (diffusion gradient sampling scheme, number of directions, diffusion gradient duration, diffusion time, region of interest) as well as the intrinsic specifications of the system (magnetic field strength) can have a huge impact on the derived tensor quantifications [1-3], but this work has never been done at ultrahigh magnetic field. In this context, the aim of this work was to study the influence of t_d and brain microstructures on diffusion tensor derived parameters in the rat brain at 9.4T.

Materials and Methods:

All experiments were performed on an actively-shielded 9.4T/31cm magnet (Varian/Magnex) equipped with 12-cm gradient coils (400mT/m, 120µs) with a quadrature transmit-receive 18-mm surface RF coil. The rat (n = 4) 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 [4] - water half-height linewidth ranged between 18 and 22 Hz), 3 repeated Diffusion Tensor Echo Planar Images (4 shots) were performed with t_d = 10, 25 and 39 ms respectively. A semi-adiabatic double spin echo sequence was used [5] and diffusion gradients were applied around the first 180° with the same polarity for short t_d or around the two 180° with inverted polarity for long t_d, resulting in a *b*-value set to 1000 s.mm^{-2}. Diffusion gradients were applied along 42 spatial directions: Icosahedral 21 directions as well as the 21 opposite directions to cancel *b*-value cross terms [6]. For the three measurements, image parameters were: FOV = 23 × 15 mm^2, matrix size = 128 × 64 zero-filled to 256 × 168, 8 slices of 0.8 mm thickness in the axial plane, 18 averages with TE/TR = 50/2000 ms. Note that, both TE and the *b*-value were kept constant (50 ms and 1000 s.mm^{-2} respectively) for the three different t_d, allowing an accurate assessment of the effects of the diffusion time only. 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 and in the cortex for the 8 different slices of the rat brain (fig. 1) in order to evaluate the variation of diffusion tensor derived parameters function of the t_d and along the rat brain. Collected data were submitted to a Friedman non-parametric test.

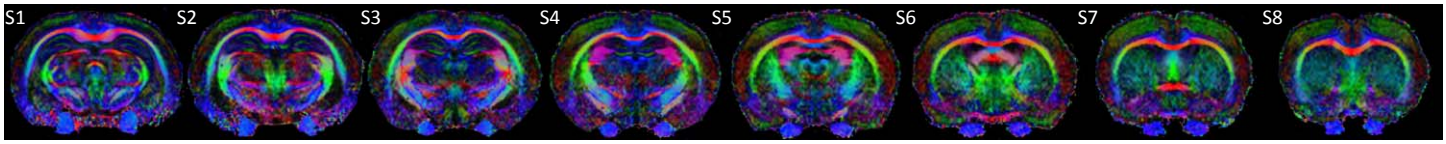

Fig. 1: Direction encoded color maps of a typical rat brain with a t_d = 39 ms at different slices of the brain (S1 to S8).

Results:

Effects of t_d: In the cortex FA values remained constant for all the t_d (fig. 2), but all diffusivity values (ADC, $D_{//}$ and $D_{\perp}$) were significantly lower at t_d = 25 and 39 ms compared to t_d of 10 ms (fig. 3). In the corpus callosum, on 7 to 8 slices $D_{//}$ remained stable whereas $D_{\perp}$ was significantly decreased at longer diffusion times (25 and 39 ms compared with 10 ms - fig. 3), resulting in a significantly larger FA (fig. 2). We measured, in the cortex as well as in the corpus callosum, no significant difference on diffusion tensor derived parameters between the acquisitions performed at the two longer diffusion times (25 and 39 ms - fig. 2 and 3).

Effects of the position: At short t_d (10 ms) derived tensor parameters remained stable along the cortex, whereas at longer t_d (25 and 39 ms) $D_{//}$ appeared significantly different as a function of the slice (essentially increasing from S5 to S8). In the corpus callosum, independently of the diffusion time, $D_{\perp}$ values were found to be significantly higher at slices 3 and 4 compared with the others, resulting in a lower FA (fig. 2).

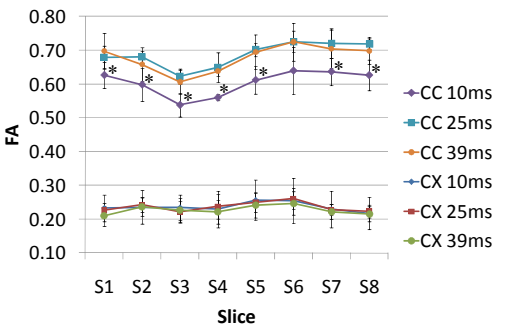

Fig. 2: Plot of the FA values (mean ±SD) function of the slice in the CC and in the CX for each t_d (10, 25 and 39 ms). *: $p<0.05$ between t_d = 10 and t_d = 25 or 39 ms.

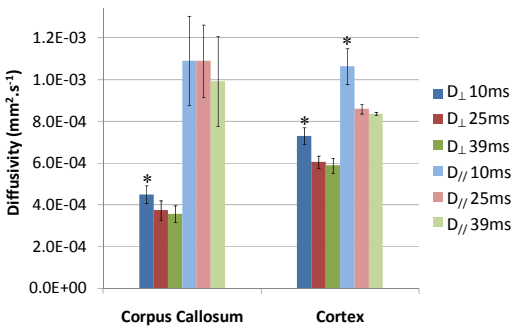

Fig. 3: Histogram of the diffusivity values (mean ±SD) for a typical slice in the CC and in the CX for each t_d (10, 25 and 39 ms). *: $p<0.05$ between t_d = 10 and t_d = 25 or 39 ms.

Discussion and conclusion:

In the gray matter, at longer t_d, the increasing interactions between water molecules and surrounding cellular structures due to restricted diffusion result in lower diffusivity values. Nevertheless, an asymptotic value seems to be reached before t_d = 25 ms, according to the absence of difference between the two longer diffusion times. On the other hand, a longer t_d appears to be more sensitive to the microstructure because diffusivity values vary along the cortex ($t_d \geq 25$ ms), which is a cellular structure with low FA. In white matter, by increasing t_d, the greater restriction to water diffusion across axons is observed, which corresponds with the decrease of $D_{\perp}$ and the increase of FA. The thinner parts of the corpus callosum showed lower FA values independently of the diffusion time, most likely due to the intrinsic differences along the white matter structure. We conclude that this study proposes an accurate measurement of the effect of the diffusion time on the diffusion tensor derived parameters at 9.4T with high resolution and a 21 directions diffusion gradient sampling scheme. We have shown a dependence of diffusion tensor derived parameters on diffusion time from 10 ms to 25 ms in white matter as well as gray matter, whereas previous studies, at lower magnetic field, reported an absence of dependence with a typical t_d of 8 ms or higher [2,3]. Long diffusion times appear more sensitive to the differentiation of white/gray matter (due to the higher FA in white matter) as well as to the effect of cellular microstructure (variation of diffusivity values along the cortex).

References: [1] Qin W. MRM 2009; [2] Niendorf T. et al. MRM 1996; [3] Clark CA. MRM 2001; [4] Gruetter R. et al. MRM 2000; [5] Kunz N. et al. Proc ISMRM 2008; [6] Madi S. et al. MRM 2005.

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