T1 relaxation in mouse brain at 9.4 and 17.6 Tesla

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Introduction - Increasing knowledge of the mouse nervous system and the availability of a large number of transgenic models has made the mouse a very popular species to study neurological disorders. MRI has shown great potential to study brain pathology in these models. However, the small size of the mouse brain has considerable implications for obtaining images comparable to those generally obtained with MRI in patients. To obtain acceptable spatial resolution and signal to noise ratios (SNR), higher magnetic field strengths (up to 17.6 T) are used. The application of higher field strengths requires knowledge of the relaxation rates at these field strengths for proper adjustment of image acquisition parameters. Reports on T₁ relaxation times for mouse brain are limited mainly to systems up to 9.4 T [1,2]. Also, with increasing field strength, chaotic spin dynamics may interfere with intrinsic relaxation. Therefore we first validate quantitative T₁ imaging at high fields using phantoms. We provide the first in vivo T₁ relaxation maps of mouse brain at 17.6 T and compare those with measurements at 9.4 T. The results are discussed in terms of SNR and contrast.

Methods - Phantom tubes containing different concentrations of Gd[DOTA] (Dotarem, Guerbet, Netherlands) in phosphate buffered saline were prepared. To validate the MRI method, T₁ relaxation times were determined both by MRI and by high resolution NMR at field strengths of 9.4 and 17.6 T.

In vivo imaging was performed on 6 female C57BL/6j mice aged 3 months (Charles River, Maastricht, the Netherlands). Mice were anaesthetized with 4% isoflurane in air (50%) and O₂ (50%) and maintained with ~1.5% isoflurane during all procedures. The respiratory rate was monitored via an air-pressure cushion connected to a laptop using Biotrig software (Bruker, Rheinstetten, Germany).

MRI: The experiments were performed on two vertical 89-mm-bore magnets (Bruker BioSpin, Rheinstetten, Germany) with field strengths of 9.4 T and 17.6 T. A Bruker Minishield gradient system of 200 mT/m and a transmit/receive birdcage radiofrequency coil with an inner diameter of 38 mm was used on both systems. Bruker ParaVision 3.0 software was used for image acquisition. T₁ data were acquired with a saturation recovery method with variable repetition time (TR). Slices excitation and refocusing were accomplished by three-lobed sinc pulses of 1.0 and 0.81 ms, respectively. Imaging parameters were: echo time (TE) = 3.5 ms; TR-array at 9.4T = 0.1, 0.12, 0.15, 0.3, 0.5, 0.9, 1.5, 3, 6, 12 and 20 s; TR-array at 17.6T = 0.1, 0.12, 0.15, 0.3, 0.5, 0.9, 1.5, 3, 6, 10 and 30 s; matrix = 128 × 128; FOV = 25.6 mm; slice thickness = 1 mm. All images were acquired as single slices to avoid interslice modulation effects, and unwanted stimulated echoes were suppressed by spoiler gradients in the slice direction. The slice was positioned through the centre of all phantom tubes or dorsally through the middle of the cerebellum and rostrally through the olfactory bulb (Fig. 2).

Data processing: Eight regions of interest (ROIs) for cortex, corpus callosum, caudate putamen, hippocampus, periaqueductal grey, ventricle and cerebellar grey and white matter were defined for each individual mouse (Fig. 1A). Phase correction was performed on the entire complex data matrix before image reconstruction. For the T₁ fits, eleven TR values with a fixed TE of 7 ms (second echo) were used. The T₁ values of the various ROIs were determined using a three-parameter fit function $M(t) = M_0 \exp(-t/T_1)$.

Results - Measurement of phantoms showed that at 17.6 T the imaging method yields T₁ relaxation times consistently 10% shorter than the high resolution NMR method. Despite these differences, a plot of $1/T_1$ vs. concentration Gd[DOTA] for the five phantoms with physiologically relevant T₁ values yields straight lines with comparable slopes for the two methods, validating our T₁ imaging method at high magnetic fields. The T₁ relaxation times of T₁-weighted mouse brain regions in six 3-month-old wildtype C57BL/6j mice were determined in vivo at 9.4 and 17.6 T. Figure 1D shows the T₁ relaxation times of the different ROIs and their relative changes with field strength. The gray/white matter T₁ difference is reduced at high fields, and this leads to inversion of the apparent T₁w image contrast. Even with optimised TE/TR, the observed image contrast is dominated by proton density (Fig. 2).

Discussion - Here we provide for the first time T₁ relaxation times of mouse brain at 17.6 T. In addition, at data 9.4 T are extended. Although the increase in SNR is one of the most important advantages of high field MRI, due to the increasing dependence of T₁w signal intensity on proton density and the resulting change in gray/white matter contrast, one has to take caution when interpreting T₁-weighted high field images. Special sequences such as MDEFT may be of use to regain part of the T₁ contrast.

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