In vivo measurement of T_2 relaxation times in mouse brain at 17.6 Tesla

F. Kara[1], F. Chen[1], J. Matysik[1], and A. Alia[1]
[1]Leiden Institute of Chemistry, Leiden University, Leiden, South holland, Netherlands

Introduction: Transverse (T_2) proton (^{1}H) magnetic resonance (MR) relaxation time plays an important role in clinics since it has a potential to distinguish different tissue types such as healthy tissue from pathological tissue [1, 2, 3]. Mice are routinely used as models for studying human brain disorders and the present trend in *in vivo* mouse brain MRI is to move toward ultra-high magnetic field, which can provides greater signal to noise ratio (S/N), increased resolution, sensitivity and specificity [4]. While the values for T_2 relaxation time in different parts of the mouse brain have been published in different field strength, there are no established values of T_2 relaxation times in mouse brain at 17.6T magnet. In this study, we aimed to establish the values of regional T_2 relaxation time for mouse brain *in vivo* at 17.6 T and to determine whether the T_2 value shows any changes at different magnetic field strengths. Phantom solutions were used to validate changes in T_2 at different field strengths and to explore sources of errors when using a multi slice multi echo sequence (MSME) to measure T_2.

Methods:

Mice: For *in vivo* scans 10-month-old wild type B6;SJL (n=8, 4 male) mice were used. The experiments were performed on 9.4 T and 17.6 T vertical 89-mm bore magnets equipped with a 1 Tm-1 actively shielded imaging gradient insert (Bruker, Germany). RF transmission and reception was performed with a volume coil, with an inner diameter of 20 mm. Bruker ParaVision 5.0 was used for scan control and image acquisition. MSME method based on Carr-Pucell-Meiboom-Grill sequence has been used to produce images for T_2 relaxation measurements. Imaging parameters were: NA = 2; FOV = 2.0 x 2.0 cm; matrix size= 256 x 256; NS=10. For 9.4 T imaging parameters were: echo time (TE) = 8.5, 17, 25.50, 34, 42.50, 51.0, 59.50, 68, 76.5, 85, 93.5, 102 ms and repetition time (TR) = 1500 ms. For 17.6 T imaging parameters were TE = 6.06, 12.13, 18.19, 24.26, 30.32, 36.38, 42.45, 48.51, 54.58, 60.64, 66.70 and 72.77 ms; TR= 2000 ms. While inside the probe, respiration rate of the mouse was constantly monitored. To calculate T_2 relaxation times, region of interests (ROIs) were drawn manually on the images by using image sequence analysis (ISA) tool package (Paravision 5, Bruker), which uses T_2vtr fit function (y= A+C*exp (-t/T_2) for T_2 evaluation. A= Absolute bias, C= signal intensity, T_2= spin-spin relaxation time.

Phantom: Phantom tubes consisting of different concentration of Gadolinium-complex (Gd-DOTA) (Dotarem; the Netherlands) were prepared in PBS (pH=7.50). T_2 relaxation times were determined both by MRI (at 9.4T and 17.6T) and by high resolution NMR (2.35 T, 9.4 T and 17.6 T) using same phantom solutions. For NMR experiments a broadband 5-mm solution-state NMR probe were used. Radiation damping was minimized by using a restricted sample volume in low-Q probes. The pulse sequence used for T_2 measurements is based on Hahn-echo scheme. The pulse lengths of 90 and 180 degree at all fields were 9.6 and 19.2 µs, respectively. A variable list of 16 duration times between 90 and 180 degree pulse were changed approximately to the expected T_2 value of each sample. Both the recycle delay and the longest duration time were kept at larger than 10 times of the expected T_2 value of each sample.

Results: As clear from Fig. 1, T_2 times, measured using different concentration of Gd-DOTA complex, are significantly shorter at 17.6 T as compared to those at 9.4 T. Fig. 2 depicts relaxation rate (R_2= 1/T_2) constants and relaxivity of phantom solutions, which were determined at different field using MRI and NMR. NMR results in Fig. 2 show that R_2 relaxivity at 17.6 T is ~9% higher than at 9.4 T and ~12% higher than at 2.35 T. While, R_2 relaxivity at 9.4 T was slightly higher than at 2.35T, the R_2 relaxivity at 17.6 T was moderately higher than at 9.4 T, clearly suggesting that T_2 relaxation times decreased at higher field strength. Table 1 demonstrates the differences in the relaxation times between 9.4 T and 17.6 T at different regions of the mouse brain *in vivo*. The selected mouse brain regions (ROI) are depicted at Fig. 3. The T_2 results at 17.6 T indicate a moderate decrease (>25 %) in values over those at 9.4 T. Shortening of T_2 at higher magnetic field might be due to faster chemical exchange between the hydration layer water and the bulk water [5]. Another mechanism for shorter T_2 values at higher field might be related with diffusion of tissue water through the increased susceptibility gradients (e.g. due to surrounding blood vessels and around the sinuses and bone) [6]. In summary, we show that T_2 relaxation times at ultra high field strength (17.6 T) can be accurately measured using MSME sequence and our results validate that T_2 decreases with increasing magnetic field strength. Furthermore we establish for the first time the T_2 relaxation time constants in different regions of mouse brain at 17.6 T. These estimates of *in vivo* T_2 relaxation of mouse brain will be useful to optimize sequence for optimal image contrast and sensitivity in mouse brain at 17.6 T.

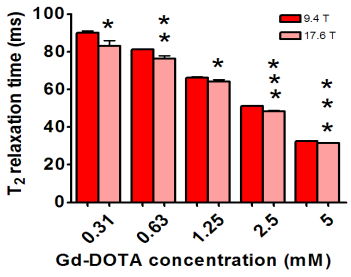

Fig. 1. T_2 relaxation time of Gd-DOTA dilutions estimated at 9.4T and 17.6T by using MRI.

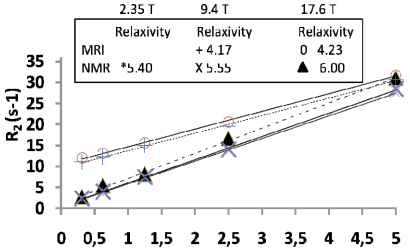

Fig. 2. Plot of relaxation rate (R_2) versus Gd-DOTA concentration estimated at 2.35 T, 9.4T and 17.6T magnet by using MRI and high-resolution NMR. Mean R_2 in s^{-1} ± error bars (SD). Relaxivity in mM^{-1} s^{-1}± SD. Relaxivity: slope of linear regression line

***Table 1**: In vivo T_2 relaxation times in different regions of mouse brain at 9.4 and 17.6T**

	Structure								
	HC	CX	TH	HT	CC	Cpu	OB	GI	M
9.4 T	37,60 ± 0,97	37,20 ± 1,01	33,90 ± 0,86	34,83 ± 1,55	33,91 ± 0,77	35,45 ± 0,74	36,98 ± 0,71	36,98 ± 0,77	24,95 ± 1,04
17.6 T	27,47 ± 0,95	27,04 ± 1,07	25,51 ± 1,18	26,07 ± 2,10	27,77 ± 0,92	26,55 ± 0,58	27,24 ± 0,58	27,21 ± 0,81	24,41 ± 1,57
Factore decrease	1,37	1,38	1,33	1,34	1,22	1,34	1,36	1,36	1,02

*Mean relaxation times (ms ± SD). HC = Hippocampus, CX = Cortex,TH = Thalamus, HT = Hypothalamus, CC = Corpus collosum, M = Muscle, Cpu = Caudate putamen, OB = Olfactory Bulb, GI= Glomerular layer olfactory bulb

References: [1] Damadian, Science 1971;171:1151.
[2] Weidensteiner et al. Magn Reson Med 2009;62:35.
[3] Braakman et al, J Magn Reson Imaging 2006.
[4] de Graaf et al. Magn Reson Med 2006; 56:386.
[5] Zhong et al. Magn Reson Med 1989;11:295.
[6] Jezzard et al Radiol 1996; 199:773.

Acknowledgement: This work was supported by grants from Internationale Stichting Alzheimer Onderzoek (ISAO), Centre for Medical Systems Biology (CMSB).

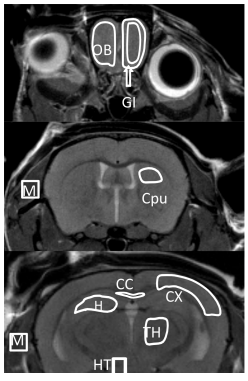

Fig. 3. Regions of interests depicted on images acquired with RARE sequence (TR: 6000 ms; ET:15 ms). Three representative MRI coronal slices showing different ROIs in brain regions: hippocampus (HC), cortex (CX), thalamus (TH), hypothalamus (HT), corpus callosum (CC), caudate putamen (Cpu), olfactory bulb (OB), glomerular layer of OB (GI) and muscle (M). Scale bar: 500µm