

High-Resolution T₁ mapping of the mouse brain using MP2RAGE at 14.1T

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Target Audience: Researchers interested in high-Resolution T₁ mapping in rodent models at high field strengths

Introduction: There has been a growing interest for the development of MR quantitative T₁ mapping techniques in the human brain since *in-vivo* applications in many neurological disorders (Parkinson's disease, gray and white matter diseases) have shown their usefulness¹. Recently, MP2RAGE² of the human brain was introduced allowing both high spatial resolution MR imaging and T₁ mapping at high field (>3T)³. With the increasing number of transgenic mouse models available and the need to assess very small structures (<100μm) with high signal-to noise ratio developing MP2RAGE techniques in mice represents an interesting challenge. In the present work, the in-plane spatial resolution of MP2RAGE images acquired at 14.1T was increased (<80x80μm²) and T₁ mapping was performed in the *in-vivo* mouse brain before and after injection of manganese.

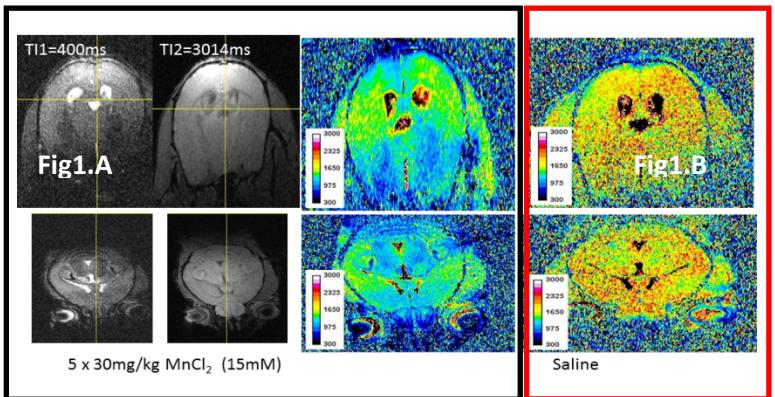


Table1: Mean (±SD) T₁ times (ms) for different structures of the mouse brain

Anatomy	T ₁ ± SD (ms)	T ₁ (ms) (5x30mg/kg MnCl ₂) ± SD	P value
Cortex	1771.6±171	1300±86	<0.008
Hippocampus	1930.3±36	1330±26	0.002
Hypothalamus	1480.6±237	1033.0±189	0.05
Cerebellum	1652±248	1151.8±15	0.1
CPu	1700.3±211	1343.2±160	0.19
Pituitary	1643.6±90	587±133	0.011
Thalamus	1865±145	1357.5±33	0.0006
Ventricles	1979±362	2322±230	0.18

Materials and Methods: 4 C57BL/6 mice received an intraperitoneal injection at a daily dose of 30mg/kg MnCl₂ (15mMol/l) during 5 days⁴ while 2 mice were injected with the same volume of saline. 24 hours following the last injection, each mouse was anesthetized with isoflurane (4%) in a mixture of air and oxygen and positioned in a dedicated cradle equipped with ears and bite bars. During MRI, both temperature (36±1°C) and respiration were continuously controlled. Isoflurane was decreased to 1% and a T/R quadrature surface coil (14mm diameter) was placed over the mouse's head. All the images were acquired at 14.1T (Varian, Agilent). Prior to the acquisition of 3D MP2RAGE images at high resolution, fast spin echo images were acquired and shimming using FAST(EST)MAP⁵ in a 5.5x6x4mm³ voxel was performed down to a linewidth below 30Hz. MR images were reconstructed offline using Matlab and ImageJ routines. Mean T₁ values were calculated from ROIs drawn on T₁ maps calculated as described by Marques et al.² Mean T₁ values were compared with a one-way ANOVA corrected for Bonferroni test. A pvalue<0.05 was considered significant.

Results and Discussion: MP2RAGE images were acquired based on previous T₁ calibrations⁶ at 14.1T. The following parameters were used: TRseg=6000ms; TR_{GRE}=10.21ms, TE=4.99ms, T₁₁=400ms; T₁₂=3014ms; flip1=2°; flip2=3°; FOV=18x18x25mm³; Matrix=256x256x192; nave=5-6. The total acquisition time was approximately 1hour and 17minutes. Magnitude images of a mouse brain that received 5x 30mg/kg MnCl₂ acquired at the two different inversion times are shown in the axial and coronal planes together with the corresponding T₁ maps (Fig1A). For comparison purposes, T₁ maps in a mouse injected with saline are also shown (Fig1B). Table1 presents mean T₁ values across animals in various brain structures in MnCl₂ and saline injected mice. Strong significant T₁ decreases were found in the cortex, hippocampus, thalamus and pituitary gland (P<<0.05). Compared to previous measurements⁷ at 9.4T, T₁ values and changes following MnCl₂ were of the same magnitude although longer T₁ values would be expected at 14.1T. This may indicate that further improvements in SNR and B1 transmit field may be needed.

Conclusion: MP2RAGE at 14.1T provides a unique opportunity to simultaneously obtain T₁ and highly resolved structural images in the mouse brain that are of interest for further preclinical investigations of neurological disorders.

References: 1. Shah NJ et al. Quantitative T₁ mapping of hepatic encephalopathy using magnetic resonance imaging. *Hepatology*. 2003;38:1219-26. 2. Marques JP, et al. MP2RAGE, a self bias-field corrected sequence. *Neuroimage*. 2010;49:1271-81. 3. Marques JP et al. New developments and applications of the MP2RAGE sequence-focusing the contrast and high spatial resolution R1 mapping. *PLoS One*. 2013;8:e69294. 4. Grunecker et al. Fractionated manganese injections: effects on MRI contrast enhancement and physiological measures in C57BL/6 mice; *NMR in Biomed*. 23:913-921. 5. Gruetter R et al. Magn Reson Med. 2000;43:319-23. 6. MP2RAGE in mice. *Proceedings of the 21st annual ISMRM meeting*, Milan, Italy; 2014. 7. Kuo et al. *JMRI*; 2005;21:334-339.