Rapid T_1 Measurements in the Very Preterm Neonatal Brain at 1.5T.

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Introduction: Rapid and accurate 3D mapping of T_1 relaxation times is valuable in neonatal imaging as time limitations and motion artifacts may exclude conventional mapping methods. T_1 mapping has the potential to provide quantitative noninvasive monitoring of maturation and pathology in the neonatal brain[1, 2]. Moreover, accurate estimates of T_1 aid in optimizing sequences such as high resolution T_1-weighted imaging and magnetization transfer. A variable flip angle (VFA) spoiled gradient recalled (SPGR) approach with B_1^+ field nonuniformity correction has been recently described for use in adults at 3.0T[3]. Here we apply the VFA-SPGR approach to measure T_1 values of the very preterm brain at 1.5T.

Methods: *Subjects:* The study cohort includes 9 preterm neonates showing a range of pathologies (Table 1) born between 24 to 31 weeks gestational age (GA) (median, 28 $^4/_7$ weeks) and scanned between 26 to 32 weeks corrected GA (median, 29 $^5/_7$ weeks). This cohort is part of a larger longitudinal multimodal study being performed at our institute. Informed written consent was signed by all parents. The infants were imaged according to a research protocol approved by the institutional research ethics board. All but two (B and I) were scanned without sedation. Radiological assessment was done by two neuroradiologists (JPSF, BT) with experience in neonatal imaging. *MR Acquisition*: MR scans were performed at 1.5T on a GE Signa Excite HD scanner (GE, Milwaukee, WI, USA) using an MR-compatible incubator and neonatal head coil (Advanced Imaging Research, Inc. Cleveland, OH, USA). The incubator fits on the scanner table and includes MR-compatible oxygen and air tanks along with monitors for blood pressure, oxygen saturation, respiration, and electrocardiography. High resolution 3D T_1 mapping was achieved by acquiring 20 axial slices centered at the level of the basal ganglia using the following experimental parameters: TR/TE=3.9/1.8ms, flip angles of 2°, 9° and 19°, 1.1x1.1x2 mm voxel size and 140 mm FOV [3]. For accurate flip angle calculation, a rapid B_1^+ mapping sequence was employed using 8 shots SE-EPI (TR/TE=4000/15ms), 60° and 120° excitation angles and 120° and 240° refocusing angles. Total time for T_1 mapping was 3min and 36s. *Analysis*: Pixel-by-pixel T_1 maps were calculated and corrected for B_1^+ field nonuniformity using Matlab (Mathworks,Natick, MA)[3]. Mean and SD values of T_1 were computed for regions of interest (ROIs) drawn within the frontal white matter (FWM), periventricular WM (PVWM), posterior WM (PWM), frontal gray matter (FGM), posterior GM (PGM) and basal ganglia (BG). All ROIs were drawn by one radiologist (JPSF). ROIs for the FWM, PVWM, PWM, FGM and PGM were obtained from a single slice at the level of the centrum semiovale, whereas ROIs for the BG were chosen from a 10 mm inferior slice. Measurements were obtained from both the left and right hemispheres and then averaged to yield a single value. The average area of the ROIs by brain region were: FWM, 17 mm^2; PVWM, 12 mm^2; PWM, 12 mm^2; FGM, 3 mm^2; PGM, 3 mm^2; BG, 10 mm^2. A Wilcoxon signed-rank test was used to test for differences in T_1 values between two ROIs by comparing these values pair-wise across subjects. A Friedman test of rank-ordering was used to assess whether the variation among subjects was consistent across regions and also if the variation among regions was consistent across subjects. Statistical analyses were preformed using the R statistical software (www.r-project.org).

Table 1 – Radiological assessment of premature neonates participating in the study.

Infant	GA (wks)*	CGA (wks)§	Radiological Assessment (Based on conventional spin-echo (T_1-, T_2-weighted) and gradient echo scans)
A	24 $^{5/7}$	26 $^{4/7}$	Grade IV left-sided GMH¥.
B	27 $^{1/7}$	28 $^{0/7}$	Grade II right-sided GMH.
C	28 $^{1/7}$	29 $^{1/7}$	Small ischemic focus in the left medial frontal WM.
D	28 $^{4/7}$	29 $^{3/7}$	Grade II GMH, periventricular leukomalacia, hypoxic-ischemic encephalopathy.
E	28 $^{2/7}$	29 $^{5/7}$	Small focus of ischemic lesion in the centrum semiovale.
F	29 $^{0/7}$	29 $^{5/7}$	Grade II left-sided GMH, bilateral intraventricular bleed.
G	30 $^{0/7}$	31 $^{2/7}$	Grade I GMH, extra-axial hemorrhage.
H	29 $^{3/7}$	31 $^{4/7}$	Grade II GMH, parenchymal foci of hemorrhage in the right frontal WM.
I	31 $^{0/7}$	32 $^{2/7}$	Grade II left-sided GMH, bilateral foci of periventricular hemorrhage, extra-axial hemorrhage.

* GA = gestational age in weeks; § CGA = Corrected GA, GA at birth plus the postnatal age; ¥ GMH = germinal matrix hemorrhage.

Results and Discussion: Fig. 1 shows representative T_1 maps and the drawn ROIs at the level of the centrum semiovale (A) and BG (B) for infant E. The regional variability of T_1 values is depicted in Fig 2a. According to Friedman test for T_1 variation among infants T_1(D,H,I) > T_1(A,B,C,E,F) > T_1(G). Referring to Table 1, it seems that the ordering of T_1 values and the change across subjects relates more to clinical status of the infants than to age. All three infants with severe/multiple parenchymal injury consistently expressed the highest T_1 values among ROIs, while infant G, having a grade I germinal matrix bleed, consistently showed the shortest T_1 values. This result is consistent with a 1.5T study on term infants born preterm that showed a significant decrease in FWM T_1 values in infants with periventricular leukomalacia[1]. Fig. 2b shows mean T_1 values across subjects for the different ROIs. Wilcoxon signed-rank tests showed significant differences (p<0.05) between WM and cortical GM regions. Except for PVWM, these regions also differed significantly (p<0.05) from the BG. The nonparametric ranking Friedman test showed the following significant ordering in T_1 values among the ROIs: T_1(PWM) > T_1(FWM, PVWM) > T_1(BG) > T_1(FGM, PGM). Since we found no reports on T_1 measurements for a similar age group at 1.5T, we compared our results to a recent 3.0T study[2] by calculating the relative difference in T_1 values between WM and GM, $(T_{1FWM}-T_{1FGM})/ T_{1FGM} = 0.35$. A similar expression yielded a relative difference of 0.3 at 3.0T[2]. These results support our preliminary aim and show that the VFA-SPGR approach for T_1 mapping can be used as a rapid quantitative tool for investigating pathology in neonatal brain. Using this method, full brain coverage can be obtained in 5min and 47s.

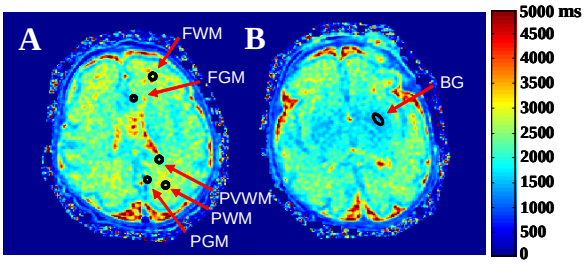

Fig. 1: T_1 maps acquired for infant E and an illustration of the ROIs used at the level of the centrum semiovale (A) and BG (B).

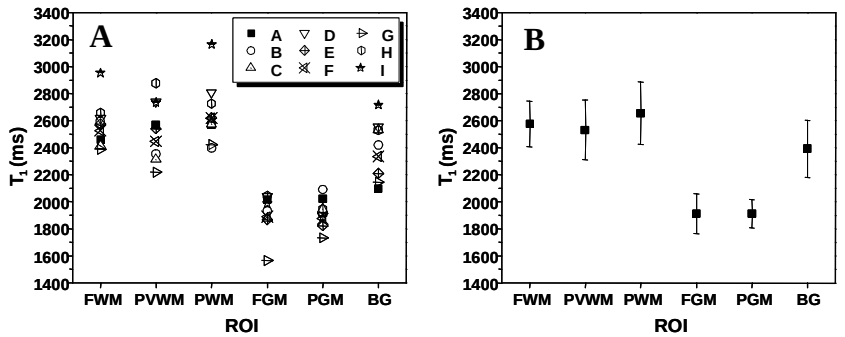

Fig. 2: Regional variability of neonatal brain T_1 values (A) and the mean value across subjects (B).

References: **1.** Counsell SJ et al., *ISMRM Proceedings, 2000; 1933.* **2.** Williams LA et al., *Radiology, 2005, 235:595-603.* **3.** Cheng HL, Wright GA. *Magn Reson Med, 2006, 55: 566-74.*