Characterizing Brain Oxygen Metabolism in Patients with Multiple Sclerosis with T2-Relaxation-Under-Spin-Tagging (TRUST) MRI

Y. Ge[1], Z. Zhang[1], H. Lu[2], L. Tang[1], H. Jaggi[1], J. Babb[1], J. Herbert[3], and R. I. Grossman[1]

[1]Department of Radiology, New York University Langone Medical Center, New York City, NY, United States, [2]Advanced Imaging Research Center, University of Texas Southwestern Medical Center, [3]Department of Neurology, New York University Langone Medical Center, New York City, NY, United States

Introduction

In multiple sclerosis (MS), there has been growing evidence that neurodegeneration including axonal loss occurs progressively and is the most significant mechanism of clinical disability and cognitive impairment. Several PET studies have shown cerebral hypometabolism with significantly decreased oxygen metabolic rate in both gray matter and white matter in MS (1). The current study was to determine whether oxygen metabolic abnormalities can be detected using a newly developed T2-relaxation-under-spin-tagging (TRUST) MRI (2), which is a simple and noninvasive technique measuring the venous sinus blood oxygenation (Yv). We hypothesized that Yv, a global index of oxygen consumption, is increased in patients with MS secondary to underutilization of oxygen associated with diffuse and chronic disease neurodegenerative processes.

Methods: 23 patients with clinically definite relapsing-remitting MS (24) (8 males and 15 females; mean age, 38.3 years; range, 22 to 53 years) and 16 healthy volunteers (7 males and 9 females; mean age, 35.2 years; range, 20 to 59 years) were recruited in this study. The mean disease duration for the patient group was 68.4 ± 59.6 months (range 4-256 months) and the mean EDSS score was 1.7 (range 0 - 5.0). MR imaging was performed on a 3.0T whole body MR scanner with an eight-channel array head coil. Since the venous oxygenation may change during sleep, all the subjects were instructed not to fall asleep during the experiments (verified after each session). A complete sequence for TRUST MRI includes labeled and control scans acquired at different eTEs for different T2-weightings (Figure 1). The specific imaging parameters of TRUST were as follows: TR/TE/TI = 8000/19/1200ms, repetition = 4, field-of-view = 230mm×230mm, matrix = 64×64, single-shot EPI, slice thickness = 5 mm, four eTEs: 0 ms, 40 ms, 80 ms, and 160 ms, corresponding to 0, 4, 8 and 16 refocusing pulses with an interval (τ_{CPMG}) of 10 ms in the T2-preparation. The T2 relaxation time of the blood is estimated by repeating the label/control pairs but with increasing T2 weighting. The total acquisition time for TRUST is 4 minutes and 16 seconds. The preprocessing includes pair-wise subtraction to ensure that only blood signal draining into the superior sagittal sinus is shown and quantified. The data post-processing procedures for calculating T2 and Yv from TRUST MRI were described in detail elsewhere [2]. Briefly, the signals from different eTEs were fitted to obtain Carr-Purcell-Meiboom-Gill (CPMG) T2 of the venous blood based on the relationship between blood T2 relaxation time and blood oxygen saturation (Y) (4, 5).

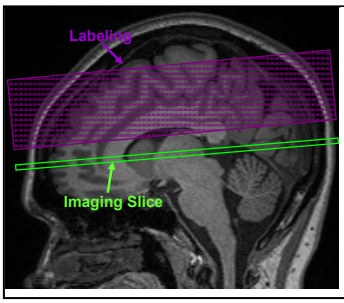
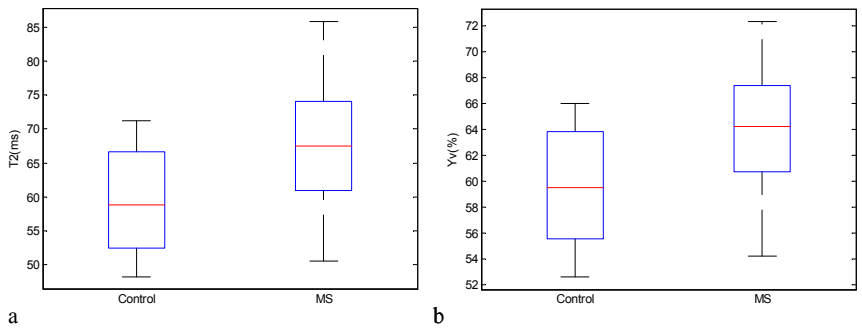


Figure 1. The TRUST sequence includes labeled and control scans acquired at different eTEs for different T2-weightings. The labeled scan.is similar to PICORE arterial spin labeling (ASL) sequence [3], except that the labeling slab is on the venous side and placed above to the imaging slice (area of interest) and the venous draining spins are inverted (instead of arterial blood) in order to obtain, in this case, superior saggittal sinus blood. Labeling slab thickness 50 mm, and gap 25mm

Results: Figure 2 showed the plot box for the comparison of T2 and Yv values in MS and control group. The T2 of the superior sagittal sinus blood was found to be significantly higher in patient group (mean/SD: 68.2/10.1ms) as compared to control group (mean/SD: 59.5/8.2ms) (P = 0.005). Correspondingly, Yv, which is converted from venous blood T2, was also significantly higher in patient than control group (mean/SD: 64.2/5.1% vs 59.6/4.8%, respectively) (P = 0.007), suggesting significantly higher oxygenation level in the venous blood in MS as a result reflecting decreased oxygen consumption.



a b

Figure 2. Box-plot (box-and-whisker representation) of T2 (a) and Yv (b) in 2 clusters in MS patients and controls, demonstrating significantly higher T2 (ms) versus and Yv (%) in patients than controls, respectively.

We found significant positive correlation between Yv and lesion load/volume (r = 0.44, P = 0.03), indicating that patient with more lesions has higher Yv and lower oxygen consumption. There was a significant difference of brain parenchyma fraction (BPF) between patients and controls (P = 0.04), suggesting there is general brain atrophy in MS patients. However, we did not find any correlation between Yv and atrophic measures including BPF. There was no statistical significant correlation between Yv and disease duration in patients with MS.

Discussion: Using TRUST MRI, this study defines for the first time the significantly higher oxygenation level of the venous sinus blood (Yv) in MS, most likely as a result of considerably reduced oxygen consumption or utilization. Our results are consistent with the findings of the prior PET study (1), suggesting that significant underutilization of oxygen in MS might reflect the diffuse neuronal cells inactive state due to diffuse nature of the disease rather than neuronal tissue loss. The study may raise important questions regarding oxygen metabolism in MS as a component of neurodegeneration that leads to progressive and global neuronal cells dysfunction.

References: 1. Sun X et al. Ann Nucl Med 1998; 12:89-94. 2. Lu H and Ge, Y, Magn Reson Med 2008; 60:357-363. 3. Wong EC, et al. NMR Biomed 1997;10:237-249. 4. Wright GA, et al. J Magn Reson Imaging 1991; 1:275-283. 5. Golay X. et al. Magn Reson Med 2001; 46:282-291.