QUANTITATION OF CHANGES IN CEREBRAL BLOOD FLOW AND LONGITUDINAL RELAXATION RATE (R_1 =1/T_1) INDUCED BY MILD HYPEROXIA

H. Tamura[1], T. Nagasaka[2], K. Shimada[2], J. Nishikata[1], M. Shidahara[1], S. Mugikura[3], and Y. Machida[4]

[1]Department of Medical Physics, Tohoku University, Graduate School of Medicine, Sendai, Miyagi, Japan, [2]Department of Radiology, Tohoku University Hospital, Sendai, Miyagi, Japan, [3]Department of Diagnostic Radiology, Tohoku University Hospital, Sendai, Miyagi, Japan, [4]Department of Medical Imaging and Applied Radiology, Tohoku University, Graduate School of Medicine, Sendai, Miyagi, Japan

Introduction: Adequate oxygenation and cerebral blood flow (CBF) are crucial to brain metabolism (herein, cerebral metabolic rate of oxygen will be denoted as $CMRO_2$). Increases in tissue oxygenation and decreases in CBF with breathing 100% oxygen (O_2) have been observed by using T_1 relaxometry [1] and arterial-spin-labeling (ASL) methods [2, 3]. Quantitation of those changes induced by hyperoxia is expected to help understand pathophysiology of living tissue. However, those changes are affected by arterial partial pressure of carbon dioxide ($PaCO_2$) as well as that of oxygen (PaO_2). To our knowledge, there has been no quantitative data of those effects of PaO_2 where the effects of $PaCO_2$ are excluded. Our intension was to extract those effects of PaO_2 noninvasively and to examine if the changes in R_1, as a probe of tissue oxygenation, relate to the changes in CBF.

Methods: *Data acquisition*- Seven healthy volunteers (age, 22-24) were scanned on a 3T Siemens Trio a Tim system with a 12-channel head receive coil. A pair of epochs of normoxia and hyperoxia was repeated three times (6 epochs in total). During hyperoxia, nearly 50% O_2, generated by mixture of room air and medical 100% O_2, was supplied with a facemask for routine clinical use. A nasal cannula was used to monitor partial pressures of end-tidal O_2 and CO_2, which were regarded as PaO_2 and $PaCO_2$, respectively. A series of 12 images for R_1 mapping (series R) and a series of 90 images for CBF mapping (series F) were obtained in the following order: the first epoch, F-R; each of the 2nd to 4th epoch, R-F-R; the 5th epoch, R-F; the last epoch, F. To eliminate inflow effect on T_1, the series R was acquired with a non-selective-IR prepared turbo-FLAH sequence at 20 second intervals. A transaxial section of 2-cm thickness through the thalamus was imaged with a field of view, 25 cm; a flip angle, 8°; TR/TE, 3.3/1.41 ms; phase encoding steps, 128. The IR preparation was altered repeatedly in the same serial order: no inversion pulse, TIs of 200, 400, and 1500 ms. A set of the 4 successive images can produce an R_1 map, so that the mapping rate is about 20 s. CBF maps were obtained with Q2TIPS sequence [4] with a slice thickness, 1 cm; TR/TE, 2500/13 ms; TI_1, 700 ms; TI_2, 1800 ms; a field of view, 25.6-cm; an imaging matrix, 64×64. The successive tag and control images were subtracted to produce a raw CBF map and added to produce a BOLD map [5] with a mapping rate of 2.5 s. *Data analysis*- All images were transferred to a personal computer and registered to the first image with rigid-body transformation. After R_1 maps were estimated by fitting a 3-parameter model to the data of R series, the matrix size was reduced to 64×64. According to the R_1 values, white-matter (R_1>0.86 s^{-1}) and gray-matter (0.86>R_1>0.62 s^{-1}) regions were segmented (Fig. 1). Raw CBF maps were multiplied by exp(r PaO_2 TI_2) to compensate for the effect of arterial-blood T_1 on ASL signals, where r (= 1.5×10^{-4} s^{-1} per mmHg PaO_2) is the relaxivity of arterial blood measured on the same 3T system with the above technique applied to the abdominal aorta. We assumed a linear model: $y = p_1 + p_2\,t + p_3\,PaO_2 + p_4\,PaCO_2$ to fit the observed data, where y is R_1, CBF, or BOLD-signal intensity, t is time, and p_{1-4} are parameters to be estimated. Especially p_3 is the coefficient that specifies the change in y per unit PaO_2. Relationship between the estimate of p_3 for R_1 (p_{3R1}) and that for CBF (p_{3CBF}) was analyzed.

Results: A typical result of the model fitting is shown in Fig. 2. The p_3 values are listed in Table 1. Because an artifact due to susceptibility of O_2 in the paranasal sinuses were noted on the BOLD maps, the regions of interest were confined to the posterior half of the segmented white and gray matter. The p_{3R1} for white matter was plotted against the p_{3CBF} in Fig. 3. No significant correlation was observed (P = 0.18).

Discussion: Changes in R_1 induced by hyperoxia may reflect changes in tissue pressure of O_2 (PtO_2). O_2 solubility in gray matter is 0.0013 mM per mmHg O_2 [6]. Relaxivity of dissolved O_2 in body tissue would be nearly equal to that in saline (0.13 s^{-1} per mM dissolved O_2 at body temperature for 3 T, measured in our laboratory). Therefore, the relaxivity due to dissolved O_2 in the brain would be 1.7×10^{-4} s^{-1} per mmHg PtO_2. Meanwhile, venous O_2 (PvO_2) changes due to increases in PaO_2, which is a function of $CBF/CMRO_2$ ratio and blood hemoglobin concentration, is approximately 0.02 mmHg/mmHg PaO_2 as shown in Fig. 4. If the increase in PvO_2 is equal to that in PtO_2, brain tissue relaxivity would be 3.4×10^{-6} s^{-1} per mmHg PaO_2, which is 2-3 times smaller than the p_{3R1} in Table 1. Thus, changes in PtO_2 with hyperoxia might be 2-3 times larger than those in PvO_2. Moreover, no correlation between the p_{3R1} and p_{3CBF} (Fig. 3) might substantiate the report that $CBF/CMRO_2$ does not change during hyperoxia [7].

References: [1] Mills SJ, et al. *Proc ISMRM, Honolulu* 2009; p2746. [2] Bulte DP, et al. *JCBFM* 2007; 27:69-75. [3] Zaharchuk G, et al. *AJNR* 2008; 29:663-67. [4] Luh W-M, et al. *MRM* 1999; 41:1246-54. [5] Wong EC, et al. *NMR Biomed* 1997; 10:237-49. [6] Thews G. Pfluegers Arch Gesamte Physiol Menschen Tiere 1960; 271:197-226. [7] Xu F, et al. *Proc ISMRM, Stockholm* 2010; p1137.

Fig. 1: Segmented (a) white and (b) gray matter regions overlaid on a raw ASL image. The color scale indicates R_1 values.

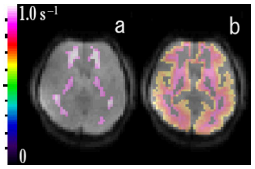


Fig. 2: Model fitting to time-series R_1. The red points are observed data; solid line, estimated model; dotted lines, estimated changes caused by O_2 and CO_2.

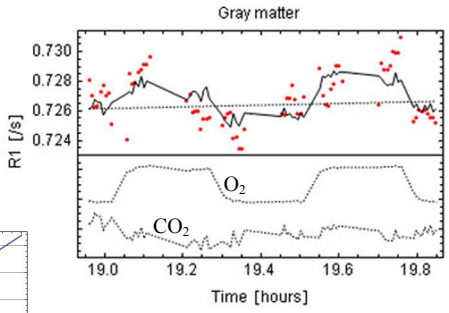
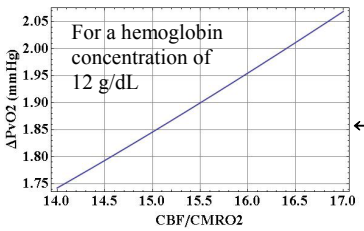


Table 1: Estimated p_3 values (± interindividual sd, n = 7)

	White matter	Gray matter
BOLD (10^{-3}% per mmHg PaO_2)	1.6±0.4	2.3±0.4
CBF (10^{-2}% per mmHg PaO_2)	−4.7±3.4	−2.8±2.1
R_1 (10^{-5} s^{-1} per mmHg PaO_2)	1.1±0.4	1.2±0.4



←**Fig. 4: Changes in PvO_2 when PaO_2 increases from 100 to 200 mmHg. The figure is obtained based on the equation of (arterial blood O_2 content) − (venous blood O_2 content) = $CMRO_2$/CBF.**

Fig. 3: R_1 versus CBF response to hyperoxia.