# Quantitative Study of Longitudinal Relaxation Rate Change in the Transient MCAO Rat Brain

Xiao Wang[1], Afshin A Divani[2], Xiao-Hong Zhu[1], Jessica Nordberg[2], Julian Tokarev[2], Yi Zhang[1], and Wei Chen[1]

[1]*Center for Magnetic Resonance Research, Department of Radiology, University of Minnesota Medical School, Minneapolis, Minnesota, United States,* [2]*Neurology, University of Minnesota, Minnesota, United States*

**Target Audience:** MRI scientists and Researchers interested in brain physiology, pathology and pre-clinical disease model studies.

**Purpose:** The longitudinal relaxation rate (time) $R_1$ ($T_1$) is a crucial physical property reflecting the spin-lattice decay of the MR signal due to the interactions of the spins with their surroundings. It greatly influences the imaging parameters we choose to improve the desired contrast of the images and its alteration in tissue is also closely related to the underlying pathology of variety of diseases. The purpose of this study is to investigate the $R_1$ change of the rat brain tissue subsequent to the middle cerebral artery occlusion (MCAO) on day 1 and day 7 after a 1-hour occlusion. In order to examine the contribution of perfusion to $R_1$, cerebral blood flow (CBF) was also measured using continuous arterial spin labeling (CASL) technique within the same experimental session.

**Materials and Methods**: Ten MCAO rats (body weight: 384±45g) were scanned on day 1 and six of them were repeated on day 7 after 1-hour occlusion. MRI measurements were performed using a 9.4T/31cm magnet interfaced with VNMRJ consoles (Varian) and a $^1$H surface coil (2.8cm×2cm). The $T_2$-weighted images were acquired with a fast spin echo sequence (TE=10ms; TR=4sec; FOV=3.2×3.2cm; matrix=256×256; thickness=1 mm; 8 echo train length). Gradient echo EPI (TE=17ms; FOV=3.2×3.2cm; image matrix=64×64; 1 mm thickness) combined with the saturation-recovery preparation was used for imaging $T_1$ with 32 varied saturation-recovery time ($T_{SR}$) values range from 0.011 to 12s. The apparent $R_1$ and CBF can be linked with $R_1 = R_1^{int} + CBF/\lambda$ (Eq. 1) [1-2], where $R_1^{int}$ is the intrinsic $R_1$ of tissue water and $\lambda$ (=0.9ml/g) is the blood-tissue water partition coefficient. A modified TurboFLASH sequence (TE=30ms; TR=3sec; FOV=3.2×3.2cm; image matrix=64×64; 1 mm thickness) was used for the CASL experiment. The duration of the RF labeling pulse was 2.2 second. The CBF was computed following $CBF=[\lambda\times R_1\times(S_C-S_L)]/[S_L+(2\times\alpha-1)\times S_C]$ (Eq. 2) [3], where $S_C$ and $S_L$ are signal intensity of the image without and with the RF spin labeling respectively, $\alpha$ is the effective efficiency of the arterial spin labeling.

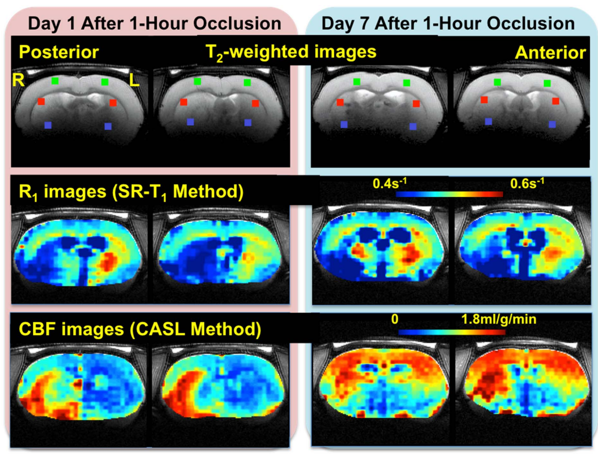


Figure 1 Two continuous coronal brain slices of the $T_2$-weighted images, $R_1$ and CBF images in one representative rat scanned on day 1 and day 7 after 1-hour MCA occlusion. The color squares overlapped on the $T_2$-weighted images are symbolic ROIs at cortex, peripheral lesion area and core lesion area and corresponding ROIs of the contralateral (control) side.

**Results**: Figure 1 shows two continuous coronal images of $T_2$-weighted images, $R_1$ and CBF images in one representative rat scanned on day 1 and day 7 after 1-hour MCA occlusion. The $T_2$-weighted images show hyper-intensity in mostly the sub-cortex area at the lesion side on both day 1 and day 7 post-occlusion. Compared with the $T_2$-weighted images on day 1, the hyper-intensity lesion area on day 7 appears smaller, the intensity is less uniform and the margin of lesion is less clear, which indicates the absorption and improvement of the pathological process. The characteristics (uniformity and margin of the lesion) of the $R_1$ images are similar to $T_2$-weighted images, except for the intensity of lesion area showing hypo-intensity instead of hyper-intensity in the $T_2$-weighted images. Interestingly, the peripheral lesion area of the ipsilateral side shows higher baseline CBF than the contralateral control side in most (6 out of 10) of the MCAO rats on day 1 and remains hyper-perfused on day 7 after the occlusion. Table 1 summarizes the mean and standard deviation of $R_1$ and CBF from ROIs at both lesion and control sides.

**Discussion:** The $R_1$ ($1/T_1$) value of both the lesion side and the control side measured in the MCAO rat brain is consistent with that reported in a previous transient MCAO mice study at 9.4T[4], although the literature report did not evaluate it in the varied extent of injury area separately. The apparent $R_1$ value decrease in the peripheral lesion area and core area due to the pathological alteration (including CBF deficit) induced by the transient ischemia accounts for 13% and 25% on day 1, and 6% and 21% on day 7 of the apparent $R_1$ on the control side. If the CBF related $R_1$ contribution is excluded (using Eq.1), $R_1^{int}$ can be calculated and its alteration would be solely attributed by pathological evolution other than CBF changes. The $R_1^{int}$ decreases to 14% and 25% of its control values on day 1 (8% and 22% on day 7) post-occlusion in the peripheral lesion area and the core area respectively. These results suggest that the $R_1$ decrease at a relatively late perfusion stage (day 1 and day 7) after the occlusion is mainly dominated by the alteration of the brain tissue property instead of CBF deficit, which is different from the $R_1$ decrease in the early stage (in the very beginning few minutes) [5-6] after the occlusion. In addition, $R_1$ shows statistic difference among varied lesion region while no statistic significant difference is found among the baseline CBF on both day 1 and day 7 post-occlusion, indicating that the $R_1$ images are potentially more sensitive to the extent of lesion than CBF images. This is because the baseline CBF after the ischemic attack can be either higher or lower than the homologous control side depending on the severity of the lesion as well as stages of the ischemic progression etc. Conventional $T_1$-weighted images are generally considered less useful for detecting acute ischemic stroke due to their poor sensitivity and specificity. This is not surprising because the $R_1$ change is about 25% of its normal value even at the extreme case and this discrepancy will become less susceptible in the $T_1$/$R_1$-weighted images. However, quantified $T_1$ (or $R_1$) images provide a better contrast and should be a sensitive and reliable imaging modality to monitor the tissue property change for variety of diseases. How $R_1$ or $T_1$ is quantitatively related to the fate of the injured tissue is under investigation.

Table 1 Summary of mean and standard deviation of $R_1$ and CBF in different ROIs on day 1 (n=10) and day 7 (n=6) after 1-hour MCA occlusion. (Mean ± SD)
* means statistic significant difference between the lesion side and the control side (p<0.05)

| Acquisition Time Window | ROI (Pixels) | $R_1$ ($s^{-1}$) (SR-$R_1$ Method) | | CBF (ml/g/min) (CASL Method) | |
|---|---|---|---|---|---|
| | | lesion side | control side | lesion side | control side |
| Day 1 (n=10) | Cortex (17) | 0.49±0.02 | 0.50±0.01 | 0.95±0.43 | 1.05±0.35 |
| | Peripheral(12) | 0.45±0.04 * | 0.52±0.01 | 0.90±0.43 | 1.00 ±0.30 |
| | Core (8) | 0.38±0.04 * | 0.51±0.02 | 0.46±0.38 * | 0.81±0.30 |
| Day 7 (n=6) | Cortex (19) | 0.49±0.01 | 0.49±0.01 | 1.17±0.31 | 1.18±0.28 |
| | Peripheral(13) | 0.49±0.03 | 0.52±0.02 | 1.48±0.36 | 0.98±0.29 |
| | Core (8) | 0.42±0.05 * | 0.53±0.05 | 0.94±0.24 | 0.85±0.51 |

**Conclusion:** In summary, this study demonstrates that $R_1$ in the varied lesion area decreases about 6-25% of its contralateral control at a relatively late stage (day 1 and day 7) after 1-hour MCA occlusion and the $R_1$ decrease is mainly dominated by the brain tissue property alteration. The quantified $T_1$ (or $R_1$) image is an important imaging modality and should provide a noninvasive, sensitive and reliable way to help determining the tissue damage caused by ischemic cerebrovascular disease.

**Acknowledgments:** NIH grants NS057560, NS041262, NS070839, P41 RR08079 & EB015894, P30 NS057091 & NS076408 and WM Keck Foundation.

**References**: 1. Detre et. al., *MRM* 1992; 2**.** Kwong et al. *MRM*, 1995; 3. Silva et al. *MRM*, 1999; 4**.** Barber et al. *Neuroscience Letter*, 2005; 5. Calamante et al. *MRM,* 1999; 6. Wang et al. *Proceedings ISMRM*, 2009.