Cerebral Vascular Reactivity Assessment Using the SR-T$_1$ Method in Normal and MCAO Rat Brain

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Target Audience: MRI scientists and Researchers interested in perfusion imaging, brain physiology and pathology and pre-clinical stroke studies.

Purpose: Cerebral vascular reactivity (CVR) is a valuable physiologic property of assessing brain arteries response to vasoactive challenge. It could be evaluated by positron emission tomography (PET), single-photon emission computed tomography (SPECT) and transcranail Doppler (TCD) ultrasonography. More recently, it has also been assessed by functional magnetic resonance imaging (fMRI) blood-oxygen-level dependent (BOLD) signal response and arterial spin labeling (ASL) cerebral blood flow (CBF) calculation (Review paper and reference cited therein[1]). The innovation of this study comes from the ASL-CBF based CVR calculation in response to hypercapnia, denoting the extent of CBF change subsequent to the vessel incitement could reflect vascular reactivity. The saturation-recover T$_1$ (SR-T$_1$) method of imaging CBF change has previously validated with the Laser Doppler flowmetry measurement[2], the continuous arterial spin labeling (CASL) technique[3] and at different field strength[4]. Therefore, it would be interesting to examine whether the SR-T$_1$ method could be used to evaluate the CVR.

Materials and Methods: Nine normal rats and ten MCAO rats[5] under 1.8% isoflurane anesthesia were scanned on day 1 after 1 hour MCA 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). T$_1$-weighted image of normal rat brain was acquired using TurboFLASH imaging sequence with the following imaging acquisition parameters: TR = 10 ms, TE = 3.1 ms, image slice thickness = 2 mm, field of view (FOV) = 3.0 cm×3.0 cm; image matrix size = 128×128. 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 CBF change (ΔCBF) can be calculated with $\lambda \times \Delta R_1$ (Eq. 1)[2], where λ (=0.9ml/g) is the blood-tissue water partition coefficient; ΔR_1 is the longitudinal relaxation rate difference between the R$_1$ measured under hypercapnia and normocapnia conditions. 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), where S$_C$ and S$_L$ are signal intensity of the image without and with the RF spin labeling respectively, α is the effective efficiency of the arterial spin labeling. The ASL and SR-T$_1$ based CVR calculation follows Eq.3 and 4, where CBF$_{normo}$, R$_{1-normo}$ and PetCO$_{2-normo}$ are the CBF, R$_1$ and end-tidal CO$_2$ concentration under normocapnia condition respectively, and CBF$_{hyper}$, R$_{1-hyper}$ and PetCO$_{2-hyper}$ are those values under hypercapnia condition. Mild hypercapnia was induced with 6% CO$_2$ inhalation.

$$CVR_{ASL} = \frac{100}{CBF_{normo}} \cdot \frac{CBF_{hyper} - CBF_{normo}}{PetCO_{2-hyper} - PetCO_{2-normo}} \quad (Eq.3)$$

$$CVR_{R_1} = \frac{100}{R_{1-normo}} \cdot \frac{R_{1-hyper} - R_{1-normo}}{PetCO_{2-hyper} - PetCO_{2-normo}} \quad (Eq.4)$$

Results: Figure 1 shows the anatomic coronal images and the CVR images created with the CASL method and with the SR-T$_1$ technique in a representative of normal rat as well as an MCAO rat scanned on day 1 after a 1-hour MCA occlusion. The lesion areas in the right side of the MCAO rat brain show hyper-intensity in T$_2$-weighted images involving both the cortex and sub-cortex of the brain. The CVR image of the normal rat shows symmetric response in the cortex and thalamus cross two hemispheres, while the MCAO rat reveals the extensively impaired vascular response to CO$_2$ nearly covers one hemisphere at the lesion side. In addition, the pattern of CVR images generated with the CASL method and those created with the SR-T$_1$ technique is similar in both normal rat brain and the MCAO rat brain. Table 1 summarizes the mean and standard deviation of the mean of CVR in different ROIs calculated with the SR-T$_1$ method and the CASL technique in 10 MCAO rats. The CVR values of the normal side of the MCAO rat brain calculated with the CASL technique are consistent with the literature report under similar anesthesia level and CO$_2$ concentration[6]. In addition, there is an excellent agreement between the normalized CVR values in the varied lesion ROIs to the cortex CVR at the control side calculated with these two techniques although their absolute scales are different (Fig. 2).

Discussion: CVR is an important arterial property reflecting the vascular response to a vasoactive challenge and it is considered related to many diseases, such as arterial stenosis, ischemic stroke and hypertension. The SR-T$_1$ method was designed to measure CBF change originally and had demonstrated to be sensitive and reliable [2-4]. In the present study, it is shown that the CVR images generated with the SR-T$_1$ technique share the similar spatial pattern of that created with ASL based CBF CVR measurement in both normal and MCAO rat brain (Fig. 1), demonstrating its efficacy for vascular reactivity evaluation although the absolute scale of the CVR images computed with these two techniques are different. Compared to other CVR calculation approaches, the SR-T$_1$ method has the advantages of easy to setup and being able to provide other critical information simultaneously, such as parametric T$_1$/R$_1$ of the tissue, BOLD and even baseline CBF if the intrinsic T$_1$ is known.

Conclusion: In conclusion, CVR evaluation with the SR-T$_1$ method was validated with CASL CBF based CVR measurement. Besides the CVR assessment, the SR-T$_1$ method could also be used to monitor CBF change, BOLD and possibly baseline CBF. Therefore, it should be a useful dynamic neuroimaging tool to study rat brain CBF and hemodynamic response under physiological and pathological conditions associated with many cerebrovascular diseases.

Figure 1 Anatomic images and CVR images generated with the CASL method and with the SR-T$_1$ technique in a representative of normal rat brain as well as an MCAO rat scanned on day 1 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 at the lesion side and corresponding ROIs of the contralateral control side.

Table 1 Summary of mean and standard deviation of CVR induced by hypercapnia in different ROIs calculated with the SR-T$_1$ method and the CASL technique. The number in the parenthesis indicates the normalized value by the CVR in cortex region at the control side. (n=10, mean ± SEM)

ROI (pixels)	CVR (%/mmHg) (SR-T$_1$ Method)(n=10)		CVR(%mmHg) (CASL Method) (n=10)	
	lesion side	control side	lesion side	control side
Cortex(17)	0.070±0.012 (0.65)	0.107±0.016 (1)	1.828±0.370 (0.69)	2.659±0.460 (1)
Peripheral(12)	0.004±0.016 (0.03)	0.081±0.012 (0.76)	0.216±0.106 (0.08)	2.413±0.571 (0.91)
Core(8)	0.000±0.013 (0.00)	0.084±0.016 (0.78)	0.000±0.223 (0.00)	2.220±0.431 (0.83)
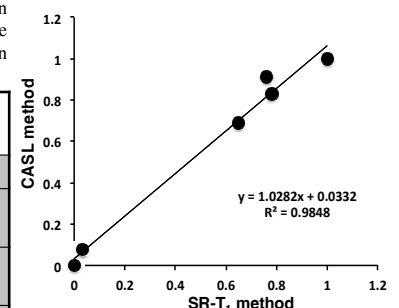
Figure 2 Linear regression of normalized CVR at different ROIs calculated with the SR-T$_1$ method and with the CASL technique in 10 MCAO rats scanned on day 1 after 1-hour MCA occlusion.

y = 1.0282x + 0.0332
R^2 = 0.9848

References: 1. Leoni et. al., *Radiology Research and Practice*, 2012; 2. Wang et. al., *ISMRM Proceedings*, 1481, 2009; 3. Wang et. al., *ISMRM Proceedings*, 4008, 2011; 4. Wang et.al *ISMRM Proceedings*, 2038, 2012; 5. Divani et.al *XXVIth ISCBFM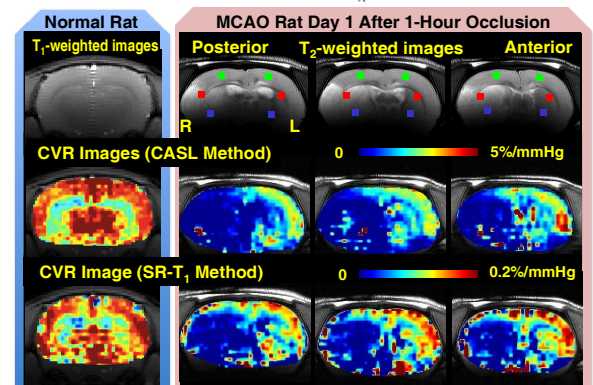*, 2013; 6. Leoni et al. *Neuroimage*, 2011