Quantification of Cerebral Arterial Blood Volume and Cerebral Blood Flow using MOTIVE approach

T. Kim[1,2], S-G. Kim[2]

[1]CMRR, Radiology, University of Minnesota, Minneapolis, MN, United States, [2]Brain Imaging Research Center, Neurobiology, University of Pittsburgh, Pittsburgh, PA, United States

Introduction

Cerebral blood volume (CBV) and cerebral blood flow (CBF) have been measured for the understanding of brain function and physiology. Both CBV and CBF are tightly regulated by arterial vessels, which have rigorous control mechanisms consisting of endothelial cells and smooth muscles. Thus, it is important to quantitatively measure cerebral arterial blood volume (CaBV). We propose to measure CaBV and CBF quantitatively using MRI techniques which rely on independent *mo*dulations of *ti*ssue and *ve*ssel signals (MOTIVE). Signal intensity from the vessel pool can be changed by arterial spin labeling (1), while tissue signal can be selectively reduced by magnetization transfer (MT) effects (2.3). With modulation of applied MT levels in conjunction with arterial spin labeling, signals originated from tissue and vessel can be separated. This approach was applied to measure CaBV and CBF in rat.

Theory

It is assumed that MRI signals originate from three, non-exchangeable compartments; tissue, arterial blood, and venous blood. Since water in capillary exchange with tissue water, the tissue pool contains capillary. At 9.4T, T_2 of tissue and arterial blood is 40 ms, while T_2 of venous blood is 5-7 ms (4). When the echo time is >3 times the T_2 value of venous blood, signal intensity from the venous blood pool will be negligible, thus remaining signals represent tissue and arterial blood. At a steady state condition with the MT effect, the signal intensity at an appropriate spin echo time TE, S_{sat} can be written as $S_{sat} \equiv (1-v_a)M_{sat}\cdot e^{-R_{2(tissue)}\cdot TE} + v_a \cdot M_0 \cdot e^{-R_{2(artery)}\cdot TE}$. Where, v_a is the volume fraction of arterial pool, R_2 is the transverse relaxation rate at the corresponding compartment (tissue and artery), M_{sat} is the saturated tissue magnetization at each MT level, and M_0 is the fully relaxed magnetization. Control and arterial spin labeled images with different MT levels are obtained without changing arterial spin labeling efficiency. Difference signal between the two images (referred to as "ASL" signal) originates from MT-dependent tissue and MT-independent arterial blood. The normalized ASL signal, $\Delta S_{sat}/S_o$ can be written as $\Delta S_{sat}/S_0 = C\cdot(S_{sat}/S_o) + v_a\cdot(2\alpha - C)$ where C is a constant related to tissue perfusion, and α is the spin labeling efficiency. By fitting a linear function to $\Delta S_{sat}/S_0$ vs. S_{sat}/S_0, the slope and intercept can be calculated. Since the intercept = $v_a\cdot(2\alpha$ – slope), the CaBV (v_a) can be calculated. The slope C is directly related to CBF as CBF = $(\lambda/T_1)\cdot[C/(2\alpha\text{-}C)]$, where λ is the blood-to-tissue partition coefficient (0.9 ml/g) (5), and T_1 is T_1 of tissue without MT effects. The calculated CBF value here has no contributions of the arterial blood pool.

Methods

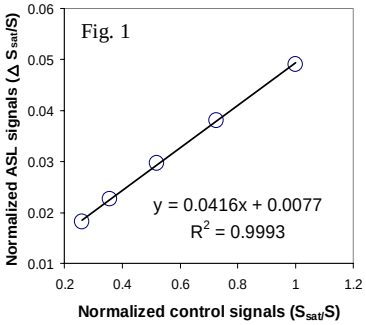
Ten male Sprague-Dawley rats (300-350 g weight) were initially anesthetized with 5% isoflurane, orally intubated, and then maintained with 1.5% isoflurane in 1:2 O_2:N_2 gas mixture. Rectal temperature, blood pressure and blood gases were maintained within normal physiological ranges.

All MRI measurements were performed on a 9.4T/31 cm Varian system. To measure CaBV and CBF values simultaneously, we developed a pulse sequence to induce various MT levels using the two-coil system without changing spin tagging (see Fig. 1 in ref. 6). To modulate a level of MT effects, a pair of RF pulses, a 100ms-long spin tagging pulse in the neck coil followed by a 100ms MT-inducing pulse in the head coil, was repeated during 8 sec. In order to generate different MT effects, five RF power levels were used in a randomized order, achieving steady-state magnetization levels of M_0, ~0.73M_0, ~0.52 M_0, ~0.36M_0 and ~0.26M_0. Since active decoupled switching coils were used, there are no asymmetric MT effects between the two images (confirmed experimentally). After spin preparation, single 2mm-thick coronal images were acquired using an adiabatic-version double-spin echo EPI technique with TE of 25 ms, TR = 10 s, matrix size of 64 x 32, and FOV of 3.0 x 1.5 cm^2. The labeling frequency was ~-8500 Hz (with a field gradient strength of 1 gauss/cm). Arterial spin labeling efficiency at the carotid arteries α_o was measured

Results and Discussion

The measured tagging efficiency at carotid arteries with an 8-s long RF pulse was 0.82 ± 0.01. In our studies, the tagging efficiency $\alpha=\alpha_0*\exp(-\tau/T_{1a})=0.37$ (50% of tagging efficiency) was used (confirmed experimentally), where τ is the transit time from the labeling plane to the imaging slice (0.2s) and T_{1a} is the T_1 of arterial blood (2.3s). Normalized ASL signals ($\Delta S_{sat}/S_0$) were fitted against normalized control signals (S_{sat}/S_0) with same MT levels (Fig.1). In the cortex area, the arterial volume fraction was found to be intercept/(2α – slope) = 1.1%. Similarly, the arterial blood volume fraction map of a representative animal is shown in Fig. 2. The highest CaBV values are located at large arteries; which are at the anterior cerebral artery (red arrow) in the medial side of the cortex, and at the middle cerebral artery (yellow arrow) in the ventral edge of the brain. This is consistent with known arterial vascular structures. The average CaBV was 1.1 ± 0.3, and 1.1 ± 0.3 % (n = 10) in the cortex and caudate putamen, respectively. Arterial blood volume (1.1%) in our studies agrees extremely well with 1.1 ± 0.4 % in humans reported by Ito et al. (7), in which a dynamic blood and tissue compartment model was used in conjunction with $C^{15}O$ and time-dependent $H_2{}^{15}O$ PET studies. When tissue signal was separated from blood signal, the perfusion map without arterial blood contamination can be obtained from the slope of linear fitting (Fig. 3). The CBF value of the cortex is 1.94 ± 0.34 ml/g/min (n = 10).

The CaBV measurement with the MOTIVE method can be repeated in the same subject, and can increase SNR by averaging. The MOTIVE approach can be applicable to pulse arterial spin labeling, and to quantification of arterial blood volumes in humans.



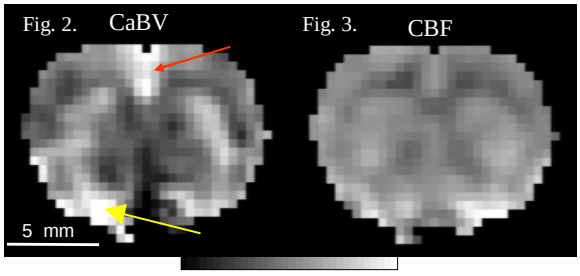


Fig.1: ASL signals vs. baseline signals. Data was obtained from the cortex ROI. Each data point has a different MT level. **Fig. 2 and 3:** CaBV and CBF maps of one rat. From ASL data with five MT levels, CBF and CaBV were determined on a pixel-by-pixel basis. Gray scale in the bottom of images: 0 – 3.5% for the arterial volume map, and 0-3 ml/g tissue/min for the CBF map. Arrows indicates large arterial vessels.

References

1. Detre et al., MRM 23: 37-45 (1992) 2. Balaban et al., Radiology 180:671-675 (1991). 3. Wolff et al., MRM 10: 135-144 (1989). 4. Lee et al., MRM 42:919-928 (1999). 5. Herscovitch et al., JCBFM 5: 65-69 (1985). 6. Kim and Kim, ISMRM abstract 1372 (2004). 7. Ito et al., Ann Nucl Med 15:111-116 (2001)

Acknowledgement : This study was supported by NIH grant (EB001977, EB003375, NS44589)