A Comparison Study of Imaging Absolute CBF Change in Rat Brain with SR-T1app method and CASL technique

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Introduction: The quantitative measurement of Cerebral Blood Flow (CBF) change with the Saturation Recovery T_1^{app} (SR-T_1^{app}) method has been proposed and validated using Laser Doppler Flowmetry (relative CBF change) under both hypercapnia and ischemia conditions in the rat brain[1]. The possible inflow and transit delay implication on measuring R_1^{app} ($1/T_1^{app}$) as well as the subsequent CBF change has also been investigated[2]. In the present study, we aim to directly compare the absolute rat brain CBF increase induced by transient mild hypercapnia using the SR-T_1^{app} method with the Continuous Arterial Spin Labeling (CASL) technique.

Theory: Previously described T_1^{app} (or R_1^{app}) images were measured by the combination of global brain saturation preparation and EPI readout following a varied Saturation-Recovery time (T_{SR}). The relationship of CBF and R_1 can be formulated [3-4]: $R_1^{app} = R_1^{int} + CBF/\lambda$ (Eq. 1), where R_1^{app} is the apparent R_1, R_1^{int} stands for intrinsic R_1 which is a constant and insensitive to physiologic change, λ (=0.9ml/g) is the blood-tissue water partition coefficient; thus, $\Delta CBF \approx \lambda \times \Delta R_1^{app}$. For the two-coil system CASL measurement, the absolute CBF image can be created from a pairwise subtraction of the labeled and control image on a pixel-by-pixel basis, according to $CBF=[\lambda \times R_1 \times (S_C - S_L)]/[S_L + (2\times\alpha - 1) \times S_C]$ (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 and it is determined by: $\alpha = \alpha_1 \times TL/TR$. α_1 is the initial degree of spin labeling measured at the labeling plane, which is equal to 1 for inversion and 0.5 for saturation; the duty cycle is defined as TL/TR, where TL is the length of the labeling RF pulse, TR is the repetition time.

Material and MRI method: MRI experiments were carried out in a horizontal 9.4T animal magnet. An 8-shaped surface coil (2.8cm×2cm) was used to acquire rat brain images. A separate 8-shaped coil (1cm diameter for each loop) was used for carotid arterial spin labeling with negligible magnetization effect between tissue water and macromolecules[5]. The distance between the labeling plane and the brain image slice was adjusted to about 2cm to reduce the interaction between the two coils. Twenty experiments of hypercapnia were conducted in nine rats for comparing CBF change measured with the SR-T_1^{app} method and CASL technique. The hypercapnia was induced by switching to an inhalation bag with mixed gases (6% or 3% CO_2, 34% O_2, 58% N_2O and 2% isoflurane). All the R_1^{app} images and CASL measurements were acquired before (i.e., normocapnia or control) and during stable hypercapnia condition when the animal physiology was within a normal range. Gradient echo EPI (TE=21ms; FOV=3×3cm; image matrix=64×64; 2 mm thickness) combined with the saturation-recovery preparation was used for imaging T_1^{app} with nine varied T_{SR} of 0.008, 0.1, 0.2, 0.3, 0.4, 0.5, 1.4, 3 and 10 s. A modified TurboFLASH sequence (TE=30ms; TR=3sec; FOV=3×3cm; image matrix=64×64; 2 mm thickness) was used for the CASL experiment. The duration of the RF labeling pulse was 2.2 sec. The labeling pulse was also applied at a plane equilateral symmetry to the brain image plane to balance the off-resonance effect of the static spins in the image plane. ROI data taken from the rat somatosensory cortex were used to perform the R_1 regression analysis and to determine R_1^{app}, ΔR_1^{app} and subsequently ΔCBF. ΔCBF was also calculated with the CASL technique using the identical ROI as in the SR-T_1^{app} method. MRI data analysis was performed using the Matlab software package. ΔCBF maps with these two methods were generated with two-dimensional median filtering on a pixel by pixel basis and then overlapped on an anatomic image. Correlation coefficient and its associated p-value between the SR-T_1^{app} and CASL measurement results were calculated.

Results: The measured initial spin inversion efficiency α_1 is 0.76±0.02 (n=9), which leads to the effective efficiency of the arterial spin labeling α as 0.56 in Eq.2. This value is consistent with previous reports, ranging from 0.71 to 0.82[6-7]. Figure 1a shows a strong and positive linear correlation between ΔCBF values obtained with the SR-T_1^{app} method and CASL technique in nine rats with twenty occurrences of hypercapnia. Figure 1b shows the linear fitting of R_1^{app} measured with the SR-T_1 method versus absolute CBF measured with the CASL method in nine individual rats. R_1^{int} and λ can be estimated according to Eq.1 through the fitting shown in Fig. 1b. The mean R_1^{int} and λ were 0.463 s^{-1} and 1.02 ml/g, respectively. Figure 2 shows an anatomic brain image and ΔCBF maps induced by four occurrences of hypercapnia with graded CO_2 concentration in a representative rat. Similar amplitude and patterns of ΔCBF maps imaged by the SR-T_1 method and CASL technique are clearly observed. Both techniques are sensitive to the inhaled CO_2 concentration. For example, CBF increased less at 3% CO_2 than at 6% CO_2.

Discussion and conclusion: There is an excellent agreement in the absolute CBF increases measured by the SR-T_1^{app} method and the CASL technique (Fig.1a and Fig. 2). The spatial patterns of the brain ΔCBF maps created with the SR-T_1 method and with the CASL approach are similar for the varied degree of hypercapnia although the ΔCBF maps created with the SR-T_1^{app} method shows more variation in the deep brain region with relatively poor EPI quality due to inhomogeneous B_0 and B_1 fields (see Fig. 2). The amount of CBF increase is consistent with the concentration of CO_2 used in mild hypercapnia, indicating great sensitivity of these two techniques. The calculated R_1^{int} and λ are also coincident with the literature report[8-9]. More importantly, the absolute CBF could be calculated using Eq. 1 and a single T_1^{app} measurement with a given R_1^{int}. Therefore, the SR-T_1^{app} method offers a simple and noninvasive tool to image both absolute CBF and CBF changes in the rat brain when R_1^{int} is determined. Caution needs to be exercised as R_1^{int} is field dependent and the reported R_1^{int} value in the present study is only valid at 9.4T. In conclusion, the SR-T_1^{app} method for quantifying absolute CBF change in the rat brain has been further verified with a two-coil system CASL technique. It should provide a valid, simple and efficient way to image CBF change and potentially absolute CBF in the rat brain under both physiological and pathological perturbations. Finally, this study demonstrates the feasibility to obtain the blood-tissue water partition coefficient of λ *in vivo* using the SR-T_1^{app} imaging approach.

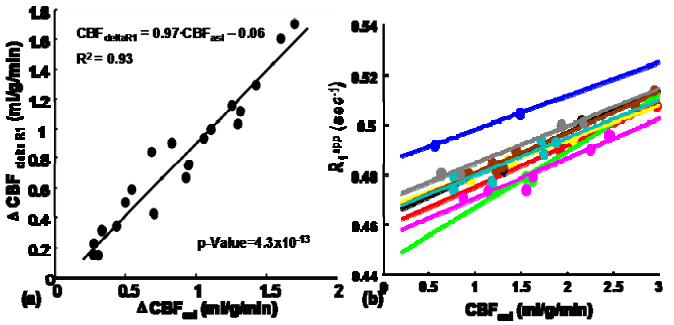

Figure 1 (a) Linear fitting results of brain sensory cortex ΔCBF calculated with SR-T_1 measurement versus with CASL method in 9 rats with 20 occurrences of hypercapnia. (b) Linear fitting results of R_1^{app} measured with SR-T_1 method versus absolute CBF obtained with CASL technique under both normocapnia and hypercapnia conditions. Different colors indicate different individual rats.

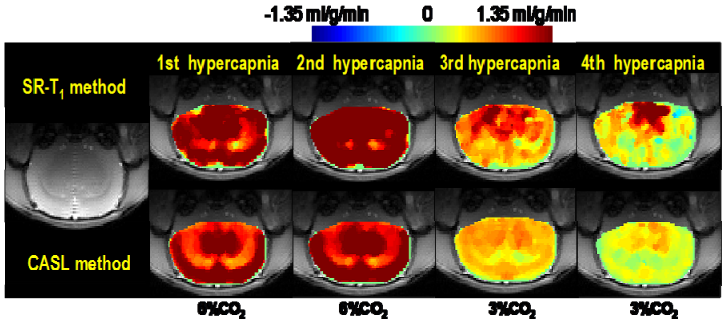

Figure 2 Anatomic image (first column) as well as ΔCBF maps created with SR-T_1 measurement (the upper row) and with CASL method (the lower row) in a representative rat for four occurrences of hypercapnia. 6% CO_2 was used in the 1st and 2nd occurrences of hypercapnia: 3% CO2 was used in the 3rd and 4th occurrences of hypercapnia.

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References: 1. Wang et.al *ISMRM proceedings*, 1481, 2009. 2. Wang et.al *ISMRM proceedings*, 1213, 2010; 3.Kwong et al. *MRM*, 1995; 4. Kim, *MRM*, 1995; 5. Zhang et al. *MRM* 1995; 6. Calamante et al. *MRM*, 1999; 7. Silva et al. *MRM*, 1999; 8. Tsekos et al. *MRM* 1998; 9. Roberts et al. *MRI,* 1996.