SR-T_1^{app} Method of Imaging Absolute CBF Change in Rat Brain at 9.4T and 16.4T

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Introduction: Cerebral Blood Flow (CBF) and its dynamic change are closely related to brain function, metabolism, and viability. Saturation-Recovery T_1^{app} (SR-T_1^{app}) measurement provides a simple and effective tool for monitoring rat brain CBF change and other useful information such as Blood-Oxygen-Level Dependence (BOLD), basal CBF and artery transit time simultaneously[1-4]. It is well known that the proton longitudinal relaxation time T_1^{app} is a magnetic field dependent parameter, specifically, T_1^{app} increases when field strength goes up. In contrast, the alteration of CBF corresponding to physiological and/or pathological change should be field independent. In this study we were intrigued by the distinct property difference and field dependence between T_1^{app} and CBF change. The rat brain CBF increase induced by hypercapnia was measured using the SR-T_1^{app} technique at both 9.4T and 16.4T to test whether it is consistent at different magnet field strengths.

Theory: T_1^{app} (or R_1^{app}) images were acquired by the combination of global brain saturation preparation and EPI readout following a varied Saturation-Recovery time (T_{SR}). Due to the small size of the rat brain associated with a considerably short artery transit time, the measured T_1^{app} actually is flow-related and mainly dominated by CBF[2,4]. The relationship of CBF and R_1 can be formulated[1,5]: $R_1^{app} = R_1^{int} + CBF/\lambda$ (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, $\Delta CBF \approx \lambda \times \Delta R_1^{app}$ (Eq. 2). Continuous Arterial Spin Labeling (CASL) technique is an established method to quantify CBF, which is calculated with a pairwise subtraction of the labeled and control image according to $CBF=[\lambda \times R_1 \times (S_C - S_L)]/[S_L + (2\times\alpha - 1) \times S_C]$[6] (Eq. 3), 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.

Material and MRI method: MRI experiments were performed at either a 9.4T/31cm or a 16.4T/26cm bore magnet interfaced with VNMRJ consoles (Varian, CA). Two identically sized 8-shaped surface coils (2.8cm×2cm) with different resonance frequency were used to acquire rat brain images. A separate 8-shaped coil (1cm diameter) was used for carotid arterial spin labeling for the 9.4T experiment[7]. The distance between the labeling plane and the brain image slice was adjusted to about 2cm to reduce the interaction between the tagging and head RF coils. Nine experiments of hypercapnia (6% CO_2, 34% O_2, 58% N_2O and 2% isoflurane) were conducted in 5 rats for comparing CBF change measured with the SR-T_1^{app} method and CASL technique at 9.4T. Another 5 rats with 8 occurrences of the same level of hypercapnia were carried out at 16.4T to compare ΔR_1^{app} and ΔCBF values with those at 9.4T. All the R_1^{app} images and CASL measurements were acquired before (i.e., normocapnia or control) and during hypercapnia condition when the animal physiology was within a normal range. Gradient echo EPI (TE=17ms; FOV=3.2×3.2cm; image matrix=64×64; 2 mm thickness) combined with the saturation-recovery preparation was used for imaging T_1^{app} with 32 varied T_{SR} values range from 0.011 to 12s for both 9.4T and 16.4T experiments. A modified TurboFLASH sequence (TE=30ms; TR=3sec; FOV=3.2×3.2cm; image matrix=64×64; 2 mm thickness) was used for the CASL experiment at 9.4T. The duration of the RF labeling pulse was 2.2 sec. MRI data analysis was performed using the Matlab software package. 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. Absolute CBF and ΔCBF was also calculated with the CASL technique using the identical ROI as in the SR-T_1^{app} method at 9.4T. Finally, ΔCBF maps created with SR-T_1^{app} method (both 9.4T and 16.4T) as well as ΔCBF maps calculated with CASL method (at 9.4T) were generated and then overlapped on the corresponding anatomic images.

Results: The average of absolute R_1^{app} values of the rat brain cortex under the control condition at 9.4T and 16.4T were 0.420 and 0.496 s^{-1} respectively, corresponding to an 18% longer of T_1 at 16.4T than at 9.4T. However, no statistical difference ($p=0.28$) was found between ΔR_1^{app}s and thus ΔCBF obtained at 9.4T and 16.4T despite of the significant R_1^{app} discrepancy ($p<0.01$) between the two field strengths (See Table 1). The effective efficiency of the arterial spin labeling α used in Eq.3 was 0.59±0.01 (n=4), which led to a baseline CBF of 1.2±0.2 ml/g/min and it agrees well with most of previous reports[6] of rat brain cortex under the similar anesthesia condition. The measured cortex ΔCBF increases during hypercapnia measured by the SR-T_1^{app} method and CASL method at 9.4T and 16.4T were also coincidently matched ($p>0.05$, One-way ANOVA). Figure 1 shows a similar pattern and magnitude of CBF increase maps under hypercapnia condition using both techniques at different magnet field strengths.

Discussion and conclusion: Our measured rat brain cortex T_1^{app} (2.38±0.01s) at 16.4T is consistent with previously reported[8] 2.27s in the similar region of the rat brain at 16.4T, which is about 18% longer than the T_1^{app} (2.02±0.01s) measured at 9.4T under normocapnia condition. The R_1^{app} at 16.4T under hypercapnia condition is also significantly smaller than that at 9.4T ($p<0.01$). Interestingly, ΔR_1^{app}, however, shows no statistical difference between at 9.4T and at 16.4T. Consequently, the ΔCBF values calculated from ΔR_1^{app} using Eq.2 should be the same regardless of the different field strength of magnet being used to obtain R_1^{app}. The field strength independence of ΔR_1^{app}, and thus ΔCBF at 9.4T and 16.4T provides another piece of evidence of the validity of SR-T_1^{app} method for quantifying CBF changes in the rat brain. In addition, the agreement of the rat brain cortex ΔCBF during hypercapnia measured with the SR-T_1^{app} method and with the CASL technique further proves that the SR-T_1^{app} method truly reflects the CBF change. Moreover, the similarity of spatial patterns and magnitude of ΔCBF maps generated with the SR-T_1^{app} method and the CASL technique indicates its effectiveness, sensitivity and accuracy, 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. 1). We compared ΔR_1^{app} at the relatively high field strength in this study, however, there should be no hurdle to apply the SR-T_1^{app} method at lower field strength since the concept is the same. In addition, the absolute CBF could also be obtained[3] once the R_1^{int} is known (according to Eq.1). It is worth pointing out that R_1^{int}, like R_1^{app}, is a field dependent value, which needs to be determined at a given field strength (by extrapolation R_1^{app} when CBF approaches zero)[3]. In conclusion, the SR-T_1^{app} method for quantifying absolute CBF change in the rat brain has been further verified at 16.4T. 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.

Table 1. Summary of rat brain cortex absolute R_1 under both normocapnia ($R_{1\text{-norm}}$) and hypercapnia ($R_{1\text{-hyper}}$) conditions as well as ΔR_1 ($R_{1\text{-hyper}} - R_{1\text{-norm}}$) calculated with the SR-T_1 method (at both 9.4T and 16.4T); absolute CBF under normocapnia (CBF_{norm}) and hypercapnia (CBF_{hyper}) conditions obtained with CASL method at 9.4T; and the CBF increase during hypercapnia ΔCBF computed with the SR-T_1 method (at both 9.4T and 16.4T) and the CASL method (at 9.4T). (Mean±SEM)

SR-T_1 Method	16.4T (n=8)	9.4T (n=9)	CASL Method	9.4T (n=9)
$R_{1\text{-norm}}$ (s^{-1})	0.420±0.002	0.496±0.004	CBF_{norm}(ml/g/min)	1.200±0.198
$R_{1\text{-hyper}}$(s^{-1})	0.440±0.002	0.514±0.004	CBF_{hyper}(ml/g/min)	1.990±0.228
ΔR_1(s^{-1})	0.020±0.001	0.018±0.002	----	----
ΔCBF(ml/g/min)	1.080±0.078	0.950±0.090	ΔCBF(ml/g/min)	0.790±0.084

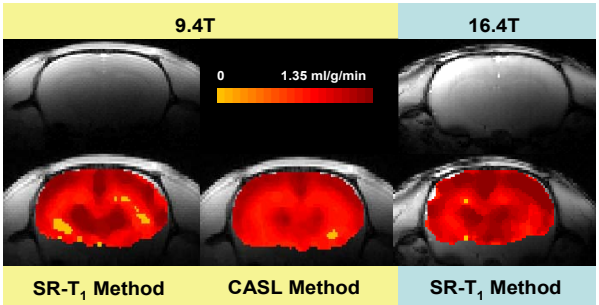

Figure 1. Coronal anatomic images and the increased CBF during hypercapnia ΔCBF maps of the rat brain created with the SR-T_1 method (at both 9.4T and 16.4T) and the CASL method (at 9.4T).

Acknowledgments: NIH grants: NS41262, NS57560, P41 RR08079 and P30NS057091; and WM Keck foundation.

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