Continuous Arterial Spin Labeling (CASL) of Cerebral Blood Flow of Mouse at 9.4T

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INTRODUCTION Perfusion MR imaging is a powerful tool for studying metabolic function in brain, such as stroke, tumor and neurodegeneration. Recently, increased number of animal models allowed us understanding brain normal functions and its dysfunctions (1,2,3). However, no-invasive studies of cerebral blood flow (CBF) in mouse using continuous arterial spin labeling (CASL) remains challenging probably due to limiting factors, i.e. reduced sensitivities because of small volume of interest, and increased magnetic susceptibility etc. On top of that, the distance between heart and brain is shorter than in rats and thus limiting CASL on carotid artery for CBF of mouse brain (1). We noticed that the innominate artery located in front of the heart towards brain (Figure 1) and such distance to brain could be sufficient to deliver satisfactory labeling efficiency with minimal saturation effects for applying CASL on mouse. Thus, we implemented an actively-detuned two-coil system including one butterfly coil for labeling and further evaluate feasibility of performing CASL on the innominate artery for mapping CBF of mouse at 9.4T.

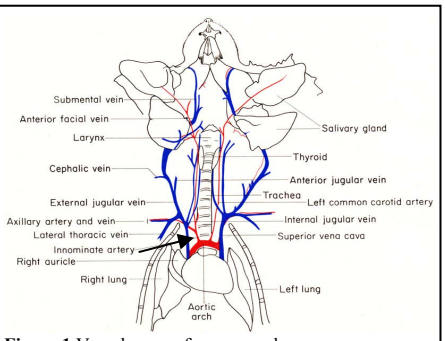

Figure 1 Vessel maps of mouse neck (*http://www.informatics.jax.org/cookbook/subjectindex.shtml*). The black arrow indicates a possible labeling plane at the level of the innominate artery when applying a z-gradient.

METHODS

MR Instruments: All MR experiments were carried out in a horizontal, 9.4T/26cm magnet (Magnex Scientific, UK), with a 12-cm-diameter gradient (400mT/m in 200μs), interfaced to a DirectDrive console (Varian Inc., USA). A quadrature coil with two geometrically decoupled 12mm-inner-diameter loops at 400MHz was used an RF transceiver for imaging. An 8-mm-inner-diameter butterfly resonating at 400MHz was used for labeling. Both coils were with built-in active detuning components and connected to a home-built actively detuned system.

Animals: Six male C57/BL mice (25-32g) were used for this study according to the local ethics committee. Immediately after induced anesthesia using isoflurane, animals were well-maintained at >100bpm for breathing by adjusting the rates of isoflurane in the range of 0.8-1.5% and temperature ~36ºC through circulating warm water. Two animals were sacrificed at the end of studies for assessing magnetization transfer effect, as described below.

MR Methods: CASL components were implemented in a semi-adiabatic SE-EPI sequence with negative and position reference scans (4), including one 2.1-sec labeling hard pulse, a z-gradient (1.4G/cm) and 1 second delay. Immediately after improved field homogeneities using FASTMAP (5), 16 pairs of 4-segmented SE-EPI images with the following parameters, i.e. TE=40ms, FOV=23×15mm^2, RO×PE=128×64, SW=200kHz, were acquired for mapping blood flow. The blood flow maps were calculated as previously described assuming the labeling efficiency at 0.8 (2). Region of interests was obtained in the same fashion as in Muir ER et al. 2008 (1).

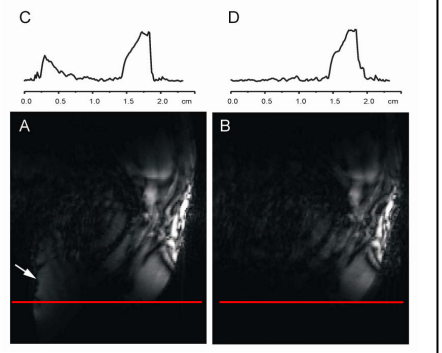

Figure 2. Comparison of sagittal GRE images without/with active detuning. A and B are GRE images acquired using the neck coil as transceiver without and with active detuning image coil on top of the tagging coil. The arrow in A indicated the apparent signal intensity difference when comparing with B. The corresponding project profiles indicated by red lines in A and B were displayed in C and D respectively.

RESULTS AND DISCUSSION

The home-built actively-detuned system was initially evaluated on the bench using a network analyzer (Agilent Technologies Inc., USA) and resulting in coupling between these two coils was -50dB. This was further confirmed by *in vivo* neck imaging experiments (Figure 2), in which no signal was observed when the imaging coil was detuned (Figure 2B and 2D). In addition, there was no magnetization transfer signals observed on postmortem brain (data not shown).

Neck images were obtained to ensure that the distance from the heart to the center of brain (Bregma 0) was ~2cm and however, the innominate artery located 1.5-1.7cm away from the center of brain. When we applied the labeling pulse (<1W) and the z-gradient at the targeting level (Figure 1), labeling efficiency was 82±3%. This is very close to other studies in rat brains at 9.4T (2) but slightly higher than previous mouse studies using cardiac spin labeling technique (1). This suggested that applying CASL at the level of the innominate artery of mouse in this study could deliver sufficient labeled spins to imaging planes. When we quantified the SE-EPI images obtained with minimal artifacts and full brain coverage (Figure 3A), blood flow maps were obtained (Figure 3B). The blood flow values (Table 1) are in consistent with previous cardiac ASL studies (1) and [^{14}C]-Iodoantipyrine results (6). Therefore, we conclude that given such quality images could be obtained at high magnetic fields (7), the CASL technique can be implemented at magnet field strengths, i.e. 9.4T and above. This offers possibility of studying various transgenic mouse models with increased sensitivities by means of multi-MR techniques.

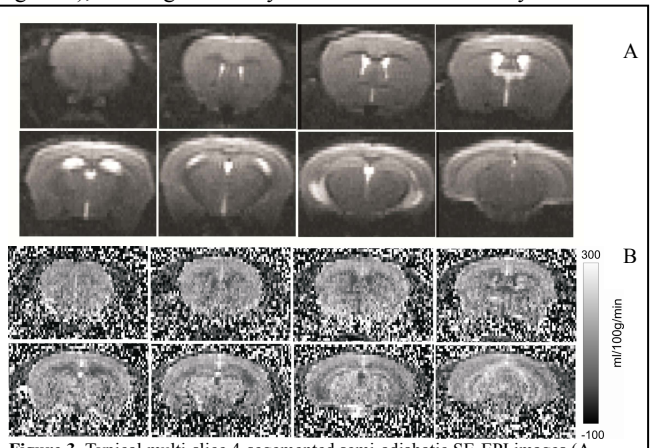

Figure 3. Typical multi-slice 4-segemented semi-adiabatic SE-EPI images (A, TE/TR=40/2000ms) and CBF maps (B) of one mouse brain at 9.4T.

Table1 Summary of regional blood flow of mouse brain under 0.8-1.5% isoflurane (n=6).

Region of interest (ROI)	CBF (ml/100g/min)
Frontal cortex	108.8 ± 4.5
Sensory-Motor Cortex	118.7 ± 7.8
Caudate Putamen	99.3 ± 7.8
Thalamus	125.6 ± 20.8
Corpus Callosum	53.2 ± 2.3
Hypothalamus	88.4 ± 13.6

References: 1.Muir ER et al. *Magn Res Med* 2008; 60:744-748; 2. Choi IY et al. *J Cereb Blood Flow Metab* 2001; 21:653-663; 3. Zhang XD et al. *NeuroImage* 2007; 34:1074-1083; 4. van de Looij Y et al. *Magn Res Med* 2010 (In Press); 5. Gruetter R *Magn Res Med* 1993; 29(6):804-811; 6. Jay TM et al. . *J Cereb Blood Flow Metab* 1988; 8:121-129; 7. Lei H et al. *ISMRM* 2010 #2234

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