Novel Cardiac Spin Labeling (CSL) for CBF MRI in Mice

E. R. Muir[1], Q. Shen[1], and T. Q. Duong[1]
[1]Yerkes Imaging Center, Emory University, Atlanta, GA, United States

INTRODUCTION Cerebral blood flow (CBF) measured by the continuous arterial spin labeling (cASL) technique with a separate labeling neck coil is generally more sensitive compared to single-coil ASL. Unlike dynamic susceptibility contrast MRI, cASL can achieve very high spatial resolution by signal averaging since it is not constrained by the high temporal resolution required to image the passing bolus. While cASL is commonly used to image CBF in rats (*1, 2*), monkeys (*3*) and humans (*4*), its extension to mouse is limited (*5, 6*) by the short distance (< 1 cm) between the neck and the brain coil, which causes the neck coil to saturate the brain signals. This occurs even when the coils are actively decoupled, label coil size is minimized, and the inter-coil distance is maximized. We report a new approach to overcome this limitation by placing the labeling coil at the heart position, which we referred to as the **Cardiac Spin Labeling (CSL)** technique. We applied this approach to image high-resolution quantitative CBF and physiologically evoked CBF changes in normal mice. Other potential unique applications are discussed.

METHODS Four mice (25-30 g) were imaged under ~1% isoflurane and spontaneous breathing conditions. Respiration rate and rectal temperature were monitored and maintained within normal physiological ranges. MRI was performed on a 7T/30cm scanner with a 150 G/cm gradient (6 cm ID) using a small surface brain coil with active decoupling (ID = 1.1 cm) and a small circular heart coil (ID = 0.9 cm) for spin labeling placed in the heart position. cASL CBF (*7*) was acquired using EPI with a 1.28x1.28 cm FOV, 128x128 matrix (4 shots) or 64x64 (single shot), seven 1-mm slices, 2.1 s labeling pulse, 2.5 s TR per shot, and 10 ms TE.

Hypercapnic challenges involved 3 mins air and 3 mins of 5% CO_2 in air. CBF images (ml/g/min) were calculated by, $S_{BF} = \lambda/T_1 \bullet (S_c - S_L)/(S_L + (2\alpha - 1)\, S_c)$, where S_C and S_L are signal intensities of the non-labeled and labeled images, respectively, T_1 is 1.8 s at 7T, λ is the water brain-blood partition coefficient (0.9). α, the labeling efficiency, was measured to be 0.76 (n = 3), consistent with neck cASL labeling in rats. Basal CBF values were obtained from images acquired during "non-stimulation" periods. BOLD images were taken from the non-labeled images.

RESULTS Quantitative blood-flow images at 200x200x1000 µm (**Figure A**) and 100x100x1000 µm (**Figure B**) show excellent and heterogeneous blood-flow contrast. Blood flow in the corpus callosum (white matter) is low compared to the gray matter as expected. The group-average whole-brain CBF was 0.77 ± 0.16 ml/g/min (n = 4), consistent with CBF values reported in isoflurane-anesthetized rats under similar experimental conditions (*7*) and in mice measured using autoradiography (8, 9). **Figure C** shows time courses of CBF and BOLD fMRI responses to hypercapnia. The CBF and BOLD % changes were 108 ± 13 % and 2.40 ± 0.08 % (n = 3), respectively, within the ranges reported in rats under similar experimental conditions (*7*).

DISCUSSION The CSL technique offers the following advantages for mouse CBF imaging, namely: 1) The distance between the heart and the brain (~2 cm) in mouse is sufficiently large to avoid saturation of the brain signals by the neck coil. 2) At this separation with the coil sizes for mouse imaging, active decoupling is unnecessary if the two surface coils are placed as parallel as possible, which simplifies experimental setup, so this approach could result in broader utility for mouse CBF imaging. This concept should also apply to rats and other similar size species. 3) Finally, this approach also offers whole body blood-flow imaging for organs that are within reasonable transit time. These organs include kidney, brain stem and cerebellum, where the latter two are often not studied by the conventional neck labeling approach because these structures are susceptible to saturation effect due to their close proximity to the neck labeling coil and/or the vertebral arteries supplying these structures are generally not effectively labeled by the neck coil.

CONCLUSIONS This study demonstrates a proof of principle that CBF in mice can be imaged using a separate labeling coil positioned at the heart, overcoming current limitations. This approach should provide an important tool to study widely available mouse disease models, including models of ischemic stroke and Alzheimer's disease.

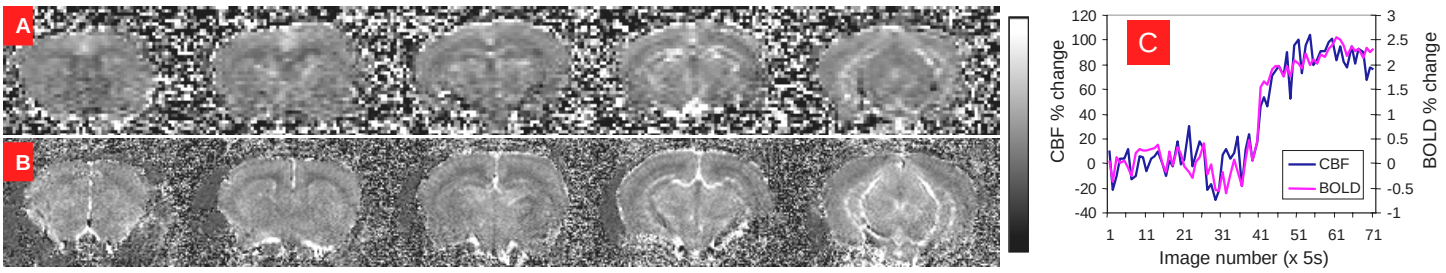

Figure. Blood-flow image at (**A**) 200x200x1000 and (**B**) 100x100x1000 µm. Scale bar indicates -1 to 3 ml/g/min. (**C**) CBF and BOLD % changes responding to 5% CO_2 from one representative animal.

REFERENCES 1) Silva et al, JCBFM 1999, 19:871. 2) Duong et al, MRM 2000, 43:383. 3) Zhang et al, NeuroImage 2007, 34:1074. 4) Talgala et al, MRM 2004, 52:131. 5) Foley et al, MRM 54, 798. 6) van Dorsten et al, NMR Biomed 1999, 12:525. 7) Sicard & Duong, NI 2005, 25:850. 8) Maeda et al, JCBFM 2000, 20:10. 9) Vasconcelos et at, Neurobiol Disease 2005, 18:270. Support in part by a Venture Grant via P50 AG025688.