Basal CBF and CBF fMRI of rhesus monkeys on a Siemens Trio 3T using a three-coil continuous arterial-spin-labeling technique

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Introduction Non-invasive cerebral blood flow (CBF) measurement had made critical impact in both research and clinics and is gaining wide acceptance for studying normal and diseased neurophysiology and functions. fMRI based on CBF changes is more spatially specific to the site of neural activity and easier to interpret than the BOLD fMRI signals. Recent evidence suggests that CBF fMRI is capable of resolving cortical columns [1]. Combined blood flow and BOLD measurements offer the means to estimate the stimulus-evoked changes in cerebral metabolic rate of oxygen consumption associated with increased neural activity [2].

CBF measurement using a separate neck coil for continuous arterial spin labeling (ASL) technique is generally more sensitive relative to the single-coil technique, particularly in small animals (such as rodents) where the transit time is short [3]. This technique had also been extended to human study in a few labs [4], although its advantage over the single coil technique is less clear because of the long transit time in human (1-2 s). The implementation of separate neck coil on clinical scanners is difficult because clinical scanner software and hardware are less conducive (such as lacking standard second RF channel and the need to ensure patient safety with hardware addition). The goal of this study was to implement a three-coil arterial spin-labeling technique on a clinical scanner (Siemens 3T Trio) for non-human primate studies. Hardware circuitries were built, interfaced and tested on a Siemens 3T Trio. This technology was demonstrated by obtaining high-resolution basal CBF measurements as well as combined CBF and BOLD fMRI associated with hypercapnic challenges under graded isoflurane concentrations. The short transit time in monkey relative to human and the long T_1 at relatively high field are expected to yield some advantages over the single-coil ASL technique.

Methods Rhesus monkeys were imaged under 0.8 to 1.2% isoflurane to gauge the effect of isoflurane on CBF changes associated with hypercapnia (5% CO_2, 21% O_2 and balance N_2). End-tidal CO2, O_2 saturation, heart rate, respiration rate, and rectal temperature was monitored continuously and regulated.

CBF MRI was implemented on a 3.0T Siemens Trio using Siemens whole-body RF transmit coil, a custom-made single-loop receive-only coil (9 cm diameter) and a custom-made butterfly neck coil (each loop ~ 3 cm diameter) at the level of the carotid arteries for arterial spin labeling. The hardware circuitry to drive the butterfly neck coil for arterial spin labeling was an independent unit triggered via an optical TTL pulse and synchronized via the 10MHz signal from the Siemens console. This unit included an RF synthesizer, RF amplifier, Watt meter, optical-electrical signal relays, and a detuning circuit to decouple coils. The neck coil was positioned ~4.5 cm posterior and ~5 cm ventral of the brain surface coil center.

CBF images were acquired with 1.5 isotropic resolution using single-shot gradient-echo EPI. Other imaging parameters were: TR = 3.5 s, labeling duration = 2.1 s, 10 imaging slices, TE = 29 ms, matrix = 64 × 64, FOV = 9.6 × 9.6 cm, and labeling gradient of 0.3 G/cm. The non-labeled images were acquired without RF excitation to the neck coil. Power levels from 0 to 4 Watts were used to determine the optimal power for arterial spin labeling and to determine labeling efficiency. Post-labeling delays of 0 to 1.5 s were studied to optimize tissue contrasts avoiding large vessel contributions. CBF fMRI was obtained over 4 mins, where hypercapnia was initiated after 2 mins of baseline (air). Data analysis was performed using Matlab codes to obtain ΔS signal changes and quantitative CBF as described elsewhere [5]. The non-labeled images were taken as BOLD signals. Cross-correlation analysis was performed to obtain hypercapnia-induced BOLD and CBF percent changes.

Results Experiments were performed to ensure the neck coil was properly decoupled and magnetization transfer effect was absent on phantoms and dead monkey brains where blood flow contrast is absent. The decoupling between imaging coils and neck labeling coil was better than 40 dB. In the live rhesus monkeys under 1% isoflurane, we found that the optimal labeling RF power was 1.5-2.0 Watts (at the neck coil) for arterial spin labeling. No visible burn marks in the neck area nor changes in measured physiological parameters were observed during basal conditions. The optimal post-labeling delay was determined to be 0.8-1.0 s for best visual gray matter contrast, which was chosen visually as a compromise between minimizing large vessel contamination and minimizing loss of CBF signal-to-noise ratio.

We targeted a 7-s temporal resolution (one pair images) for fMRI. Figure 1 shows the basal CBF images obtained with the above optimal parameters at 1.5 mm isotropic resolution (4 mins). Figure 2 shows the raw time course data of the CBF and BOLD fMRI measurements and the percent-change maps associated with hypercapnic challenge. The up and down (ΔS) signals are indicative of CBF contrast, which increased during hypercapnia as expected. The BOLD signal (up only) also increased during hypercapnia as expected. Hypercapnia induced large and heterogeneous CBF and BOLD changes over the entire brain as expected. The average CBF percent change was 47±13% and 56±17% and the BOLD percent change was 1.9±0.6% and 2.2±0.8% under 1.2% and 0.8% isoflurane respectively.

Discussion and Conclusion We implemented a three-coil continuous arterial spin labeling technique using a separate neck coil on the Siemens 3T Trio for measuring CBF MRI and fMRI with high spatial and temporal resolution. High quality basal CBF images could be obtained within 4 mins at 1.5 mm isotropic resolution. CBF images showed excellent contrast among white matter, gray matter and CSF, consistent with basal monkey CBF images reported by Zappe et al [6] on a Bruker system. We further demonstrated that combined BOLD and CBF fMRI measurements could be made associated with hypercapnic challenge with a 7 second temporal resolution at 1.5 mm isotropic resolution. The ratio of ΔCBF:BOLD is consistent with those reported previously.

This technique is expected to provide a non-invasive means to study physiology, function, neurovascular coupling, and metabolism (i.e., $CMRO_2$) in non-human primates. Further improvement in both temporal and/or spatial resolution is expected. CBF MRI and CBF fMRI on awake/behaving monkeys is being implemented.

References: [1] Duong et al, PNAS 2001. [2] Davis et al, PNAS 1999. [3] Silva et al, MRM 1997. [4] Zaharchuk et al, MRM 1999. Talagala et al, MRM 2004. [5] Duong et al, MRM 1999. [6] Zappe et al, ISMRM 2005.

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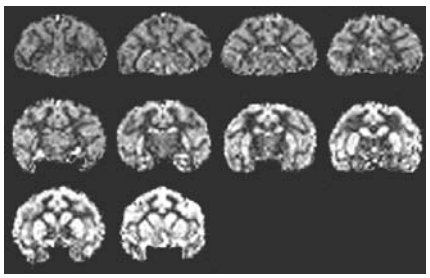

Fig. 1. Basal CBF images at 1.5 mm isotropic resolution.

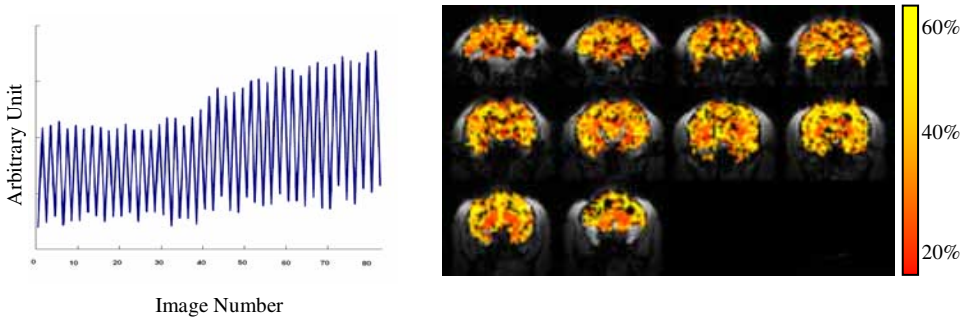

Fig. 2. Raw time course data of CBF measurements and CBF percent change maps (1.2% isoflurane).