Validation of Optical Measurements of Cerebral Blood Flow and Volume with SPION and ASL fMRI: Implications for CMRO2 changes during hypercapnia

S. A. Carp[1], D. A. Boas[1], M. A. Franceschini[1], B. R. Rosen[1], and Y. R. Kim[1]

[1]Athinoula Martinos Center for Biomedical Imaging/ Massachusetts General Hospital, Charlestown, MA, United States

ABSTRACT The cerebral metabolic rate of oxygen ($CMRO_2$) is a physiological parameter closely linked to neural activation as well as to various disease states. Simultaneous measurements of cerebral blood volume (CBV), hemoglobin oxygen saturation (SO_2) and blood flow (CBF) are necessary to calculate $CMRO_2$ changes. Such measurements can be obtained non-invasively using near infrared optical spectroscopy though this technique suffers from partial volume effects that lead to an underestimation of the absolute magnitude of hemodynamic variations. In this study, we used simultaneous MR and optical acquisitions to calibrate CBF and CBV optical measures and to obtain estimates of $CMRO_2$ variation during hypercapnic challenges in rodents.

MATERIALS AND METHODS Four normal healthy Sprague-Dawley rats (~300g) were used to record hemodynamic parameters during stepped CO_2 breathing gas changes. A combined optical/MR probe assembly (Figure 1) was fabricated to fit in the animal holder of a small-bore 9.4T MRI system (Bruker). In turn, a cASL sequence with 3000-ms continuous labeling at the carotid arteries, 500-ms delay and EPI read-out was used to acquire CBF with 7.4 temporal resolution [1]; then after bolus injection of MION (36 mg/ml) T_2 weighted EPI images were acquired continuously and CBV maps were calculated from the diffusion and T_2 weighted images with 3.7 seconds temporal resolution [2]. The optical system consisted of a frequency domain spectrometer that provided absolute optical properties at 7 near-infrared wavelengths between 670 and 830 nm at 12.5 Hz and a diffuse correlation spectrometer that provided the time-resolved temporal auto-correlation of the diffusely reflected light at ~1 Hz [3,4]. Hemoglobin concentration and oxygenation were calculated by fitting the optical absorption coefficient at the 7 wavelengths to the known oxy and deoxy-hemoglobin spectra and a correlation diffusion model was used to extract a blood flow index from the temporal auto-correlation functions. Both optical measures were obtained at 4 probing depths, determined by the distance between the source and detection optical fibers. Pairwise comparisons were made between the optical and MR CBF and CBV data (obtained by region of interest averaging as shown in Fig. 2), both to validate the relative time-courses of these parameters, as well as to calculate the partial volume correction coefficients needed to match the magnitude of the relative parameter changes between optical and MR measurements. Finally, the relative $CMRO_2$ during gas changes compared to baseline was calculated as $rCMRO_2=rCBF.rCBV.rOEF$, where $OEF=\gamma(S_{a,O2}-SO_2)$, with $S_{a,O2}$ the arterial hemoglobin oxygen saturation, SO_2 the tissue averaged saturation and γ a scaling factor dependent on the relative weight of the different vascular compartments in the optical measurement.

RESULTS AND DISCUSSION Figures 3 shows sample time-traces of optical total hemoglobin (HbT) and MR cerebral blood volume (CBV) and Figure 4 shows the optical flow index (BFI) and corresponding MR cerebral blood flow (CBF) measurement during stepped increase from 0 to 2.5, 5 and 7.5% CO_2 in the breathing gases. Progressive increases in both CBV and CBF are noted, and the optically measured parameters track the MR ones very well. However, relative increases in optical total hemoglobin and blood flow index represent only a fraction of the corresponding MR measured increases. Additionally, the variation in magnitude of the CO_2 induced changes with depth from the two measurement modalities has a full one to one correspondence for CBV, and in three out of four traces for CBF.

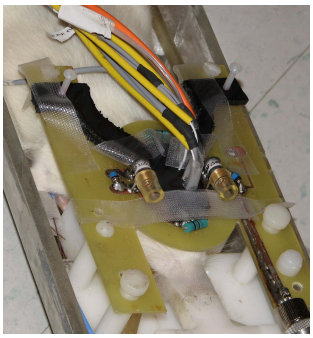

Fig. 1. Optical-MR probe

Fig.2 ASL ROIs

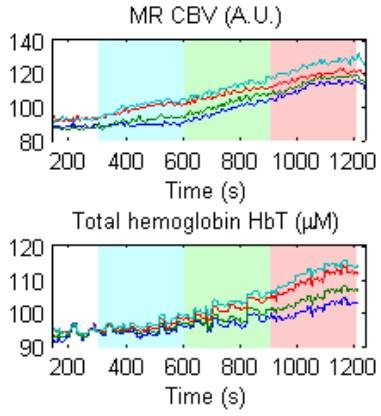

Fig. 3 Optical and MR CBV

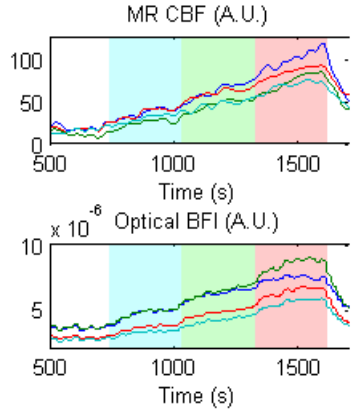

Fig. 4 Optical and MR CBF

Encouraged by these results we attempted to calculate the $CMRO_2$ variation during gas exchanges after calculating scaling coefficients for the optical measurements to match the relative changes in MR derived CBV and CBF. Initial results appear to indicate increased $CMRO_2$ during the hypercapnic episodes. However, this controversial finding may be affected by an overestimation of the flow changes, resulting from uncertain baseline flow in the MR ASL measurement. Further investigation is warranted.

References.

1. Detre, J.A. and D.C. Alsop,. Eur J Radiol, 1999. 30(2): p. 115-24
2. Hamberg, L.M., et al., Magn Reson Med., 1996. 35: p. 168-173
3. Boas, D.A., L.E. Campbell, and A.G. Yodh,. Phys. Rev. Lett., 1995. 75: p. 1855-1858.
4. Culver, J.P., et al.,. J Cereb Blood Flow Metab, 2003. 23(8): p. 911-24.