Assessing the Accuracy of Calculations of the Functional Changes in CMRO2 From Blood Oxygenation Data

A. L. Vazquez[1], M. Fukuda[1], and S-G. Kim[1]
[1]Radiology, University of Pittsburgh, Pittsburgh, PA, United States

Introduction: The brain relies on the consumption of oxygen to sustain its function. BOLD fMRI is sensitive to the amount of deoxygenated blood in the imaging volume and, therefore, also to CMR_{O2} but their relationship is not straightforward and models are used to bridge the gap between blood oxygenation signals and tissue CMR_{O2}. Commonly used models to quantify the changes in CMR_{O2} from blood oxygenation data rely on a number of important assumptions as well as a calibration procedure (1,2,3). The aim of this work is to assess the accuracy of blood oxygenation methods to quantify changes in CMR_{O2} by evaluating the validity and impact of two common model assumptions: (i) arterial blood is fully oxygenated, and (ii) the transport of oxygen from blood to tissue is nearly instantaneous. In addition, the efficacy of hypercapnia data to calibrate the changes in blood oxygenation for the calculation of CMR_{O2} was examined. For this purpose, measurements of the oxygen tension (P_{O2} in arteries, tissue and veins), CBF, and blood oxygenation were obtained using oxygen microelectrodes, a laser Doppler flowmetry (LDF) and deoxyhemoglobin-sensitive optical imaging of intrinsic signal (OIS, a BOLD fMRI surrogate), respectively, from two experimental conditions. In one condition (suppressed-CBF), a pharmacological agent was used to suppress activation-evoked changes in CBF such that the changes in tissue and blood oxygenation are produced solely by CMR_{O2} without affecting neural activity (4,5). The other condition (control) consisted of conventional data where evoked changes in tissue and blood oxygenation were used in combination with like data from a hypercapnia challenge to calculate the evoked changes in CMR_{O2}.

Methods: Nine male Sprague-Dawley rats (330 to 480 g) were used in this work following an experimental protocol approved by the University of Pittsburgh's IACUC. The animals were anesthetized using isoflurane (2% for surgery and 1.4% during experiments) and placed in a stereotaxic frame. The skull was removed over the somato-sensory area and covered with agarose gel. Two needle electrodes were placed in the left forepaw of the animals for electrical stimulation and a preliminary imaging experiment (OIS, 620nm light) was performed to determine the activation area. The changes in P_{O2} were measured within the activation area on the surface of a pial artery, a nearby pial vein and tissue (300µm deep). A circular ROI, 100µm in radius, centered on the tip of the tissue P_{O2} probe, excluding the probes and pial vessels, was used to represent the changes in blood oxygenation from the OIS data. To suppress the CBF response, sodium nitroprusside (sNP) was continually infused intra-venously. The LDF and P_{O2} data were used to calculate the dynamic changes in CMR_{O2} using a dynamic model (5). The LDF, P_{O2} and OIS data from the control condition were used to calculate the changes in CMR_{O2} using an ideal calibration coefficient (obtained by assuming that the change in CMR_{O2} estimated from the suppressed-CBF data is the same as that from the control condition data; the field potential activity between these conditions was not significantly different, p=0.31). The impact of the arterial oxygenation on the CMR_{O2} estimates was assessed by comparing the CMR_{O2} changes obtained using the arterial P_{O2} data vs. a constant arterial P_{O2} of 150mmHg. To determine whether the transport of oxygen from blood to tissue is nearly instantaneous, the temporal differences between the tissue P_{O2} and OIS data were examined. In addition, CMR_{O2} estimates obtained from a dynamic model and its steady-state form were compared. Lastly, the efficacy of a hypercapnia challenge to calibrate the OIS data was examined. The hypercapnia challenge consisted of CO_2 (10%) in air administered for 45 s which increased end-tidal CO_2 to ~7.5%. The hypercapnia LDF and OIS data were then used to calculate a calibration coefficient as done in (1).

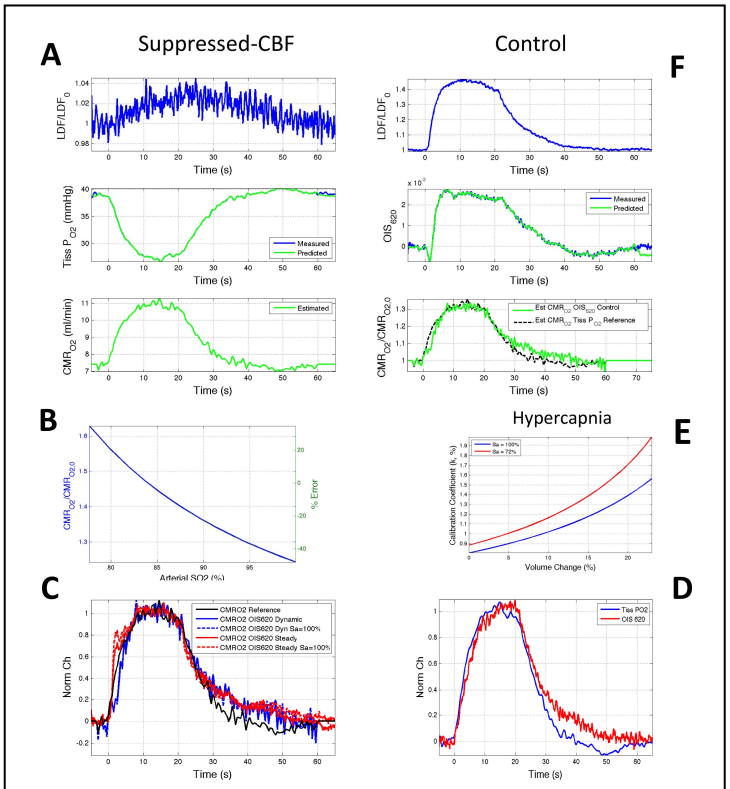

Fig. 1: (A,F) CMR_{O2} estimates; (B,C) Arterial oxygenation impact; (C,D) Steady-state oxygen transport impact; (E) Calibration coefficient vs. CBV.

Results and Discussion: Under suppressed CBF conditions, CBF increased by 2.7% while tissue P_{O2} and OIS decreased by 29% and 0.32% due to forelimb stimulation. CMR_{O2} was calculated to increase by 3.5 ml/min (Fig 1A). Under control conditions, CBF, tissue P_{O2} and OIS increased by 43.9%, 27% and 0.24% due to forelimb stimulation. A systematic error is introduced in CMR_{O2} calculations when a fully oxygenated arterial input is assumed (Fig 1B); however, this error was not observed to affect the temporal estimates of CMR_{O2} (Fig 1C). The changes in tissue P_{O2} and blood oxygenation were observed to be in near equilibrium over a time-scale of 1 to 2 s (Fig. 1D). This difference was evident in the dynamic vs. steady-state CMR_{O2} estimates (Fig 1C). Considering that most fMRI measurements are made over this temporal scale, steady-state models are appropriate in these studies for the calculation of CMR_{O2}. The hypercapnia challenge increased CBF, tissue P_{O2} and OIS by 47.4%, 56% and 0.26%. The calibration coefficient calculated from the hypercapnia data was not similar to the ideal calibration coefficient calculated assuming CMR_{O2} increased by 3.5ml/min (31.9%). Some of this difference can be attributed to changes in CBV (Fig. 1E), indicating that this is an important parameter to measure in calibrated fMRI experiments. Interestingly, the dynamic CMR_{O2} estimates obtained from the control condition data using the ideal calibration coefficient closely resembled that obtained using the tissue P_{O2} suppressed-CBF condition data (Fig. 1F).

References: (1) Davis TL, et al., PNAS 95:1834 (1998); (2) Kim SG, et al., MRM 41:1152 (1999); (3) Hyder F, et al., NMR Biomed 14:413 (2001); (4) Nagaoka T, et al., JCBFM 26:1043 (2006); (5) Masamoto K, et al., Neuroimage 40:442 (2008); Vazquez A, et al., Neuroimage 42:49 (2008). This work was supported by NIH grant F32-NS056682, K01-NS066131, R01-NS048599 and R01-EB003375.