Correlation of CBV changes with fMRI and laser-Doppler measurements: Implications on CMR_{O2} calculation

P. Herman[1,2], B. G. Sanganahalli[1,2], and F. Hyder[1,2]

[1]MRRC, Yale University, New Haven, CT, United States, [2]Diagnostic Radiology, Yale University, New Haven, CT, United States

INTRODUCTION

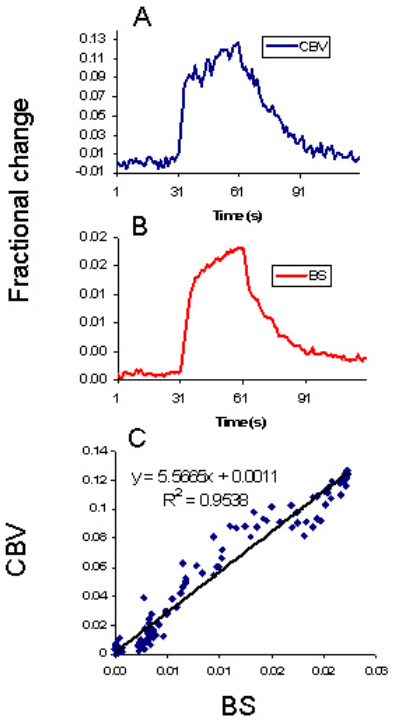
Quantitative mapping of changes in CMR_{O2} with BOLD calibration has become a popular modality for studying functional brain activity [1] because it is proportional to changes in energy consumption associated with alterations in neuronal activity induced by the stimulation [2]. Typical BOLD calibration experiments require multi-modal measurements of CBF, CBV, and BOLD signal to predict CMR_{O2} changes. CBF measurements with MRI techniques are frequently substituted by laser-Doppler measurements. Injection of long-lasting MRI contrast agent is necessary to obtain an MRI signal that was highly weighted by CBV. Instead of measuring CBV it can be calculated using vascular physiology based models such as the "delayed compliance model" [3] or the "balloon model" [4]. The aim of this study was to find an alternative method to estimate the CBV changes during stimulation, which can be used with larger temporal resolution what the MRI methods can provide.

METHODS

Animal preparation**:* Sprague-Dawley rats were tracheotomized and artificially ventilated (70% N_2O, 30% O_2). The anesthesia was switched to i.p. α-chloralose (80mg initial dose, then 40 mg/kg/hr) from Halothane (1-2%) after the surgery. Femoral arterial line was used for monitoring blood pressure, acid-base balance and blood gases throughout the experiment. ***Forepaw stimulation: Copper wires were inserted below the skin of the forepaw. Each stimulus train lasted 30s with 3Hz frequency, 2 mA in amplitude and 0.3 ms in duration. ***CBV measurement** (n=6):* All fMRI data were obtained on a modified 11.74T Bruker horizontal-bore spectrometer (Billerica, MA) using a ^1H resonator/surface coil RF probe. All images were acquired with gradient echo EPI (TR/TE=1000/12.53 ms). The focal CBV response was measured by injection of iron oxide nanocolloid (Combidex 15 mg/ml, Advanced Magnetics Inc, Cambridge, MA). The details of measurements are in ref. [2]. ***LDF and backscatter measurement** (n=12):* The rat was placed in a stereotaxic holder (Kopf Instruments, Tujunga, CA) on a vibration-free table inside a Faraday cage. Tiny burr holes above the somatosensory region [4.4 mm lateral and 1.0 mm anterior to bregma] were drilled and fiber optodes (interoptode distance: 200 μm) were inserted into the three different depth of the cortex with stereotaxic manipulators to measure the laser-Doppler flux and backscattered light intensity (Oxford Optronix, Oxford, UK). The signal was then digitized with a μ-1401 interface using SPIKE-2 software [4]

RESULTS AND DISCUSSION

The stimulus activated voxels of the MRI images covered the entire somatosensory cortex and the averaged values of their time series were used in the calculation (**Fig A**). The backscattered light intensity signals (BS) from the upper, middle and lower part of the cortex didn't show significant differences; therefore their average values represented BS of the entire cortex (**Fig B**). We found a strong (R^2=0.95) correlation between the MRI measured CBV and the optically measured back scattered light intensity (**Fig C**). The mean square error of the deviation was $1.3*10^{-4}$ after the scaling correction (scaling factor = 5.6). The contrast agent used in the MRI CBV measurement is diluted in plasma volume which follows CBV changes after hematocrit correction. The BS signal intensity depends on the scattering property of the brain tissue and the concentration of absorbers (i.e. oxidized and reduced hemoglobins). Higher signal intensity means lower concentration of absorbers. The wavelength of the applied laser light was 805nm which is an isosbestic point of the hemoglobin absorption curves, therefore only the number of the hemoglobin molecules can affect the BS intensity. Since oxygenation change doesn't influence the BS signal, it refers to the RBC volume which follows the change of the CBV. However, because of the Fahraeus-effect, the instantaneous hematocrit (tube hematocrit) is varying in the small vessels, the discharge hematocrit remains constant therefore the RBC volume can be used to follow the CBV changes. We showed that the backscattered signal from the laser-Doppler measurement can substitute the CBV measurement without any modeling effort to calculate the CMR_{O2}.



A, B Time courses of fractional change of CBV and BS (Backscattered light intensity). The stimulus is from 30 to 60s. **C**: Linear fit of CBV against BS. R^2=0.95 proves high correlation between BS and CBV.

REFERENCES

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