

Validation of Optical Measurements of Cerebral Blood Flow and Volume with MION and ASL fMRI

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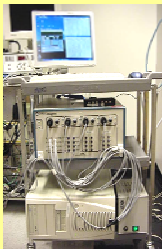
Introduction

The cerebral metabolic rate of oxygen (CMRO₂) is a physiological parameter closely linked to neural activation as well as to various disease states. Optical imaging can offer a noninvasive and inexpensive way to monitor CMRO₂ variations. Estimates of cerebral blood volume (CBV), hemoglobin oxygen saturation (SO₂) and blood flow (CBF) are necessary to estimate CMRO₂ changes. Frequency-domain near-infrared spectroscopy (FD-NIRS) offers a quantitative method to measure the tissue total hemoglobin concentration (and hence CBV) as well as SO₂. On the other hand, diffuse correlation spectroscopy (DCS) is a relatively new technique that can provide an index to cerebral blood flow by measuring the temporal fluctuations in the diffusely reflected optical signal. DCS was introduced in the early 1990's [1] and has been validated in a number of animal and human studies [2-5] for measuring regional and temporal variations in blood flow.

In this work, we attempt to further validate the FD-NIRS and DCS measures of CBV and CBF using functional MRI techniques during a hypercapnic challenge in rats. Specifically, we use Super-paramagnetic Iron Oxide Nanoparticles (SPION) (Martinos Center, Charlestown, MA, USA) as an intravascular MR contrast agent to monitor changes in blood volume, and a continuous ASL sequence to quantify variations in blood flow.

Methods

FD-NIRS (ISS Imagent)



- Frequency-domain (FD) device
- Parallel acquisition of 4 detector channels at 1.0, 1.5, 2.0, 2.5cm
- Sampling rate 12.5 Hz
- 8 wavelengths: 635, 670, 691, 752, 758, 782, 811, 831 nm
- Optical power <3 mW
- Modulation frequency: 110 MHz
- On every 5 sec of 15, interleaved with DCS

DCS



Diffuse Correlation Spectroscopy system (as developed by Yodh and Durduran)

- 1 long coherence length solid state laser (785 nm)
- 4 photon-counting APDs.
- 8 channel multi-τ auto-correlator
- Sampling rate of 1 Hz

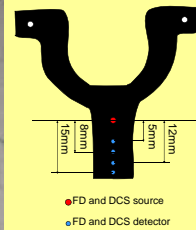
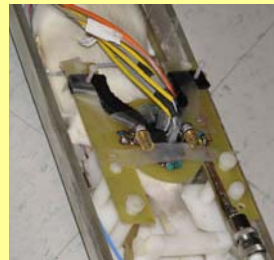
MRI



Bruker Biospin
9.4T MR Scanner
In house ASL coil

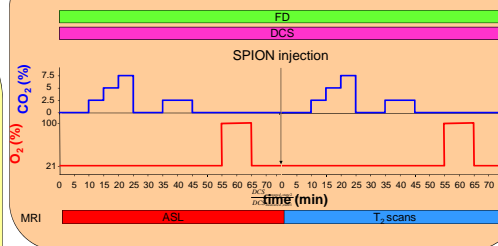
- CBV: SPION, T₂* contrast agent
EPI T₂ weighted imaging, T_R=3.7s
CBV calculated from diffusion and T₂ weighted images
- CBF: cASL sequence
3000 ms carotid labeling
500 ms delay + EPI read-out

Combined optical probe + ASL coil

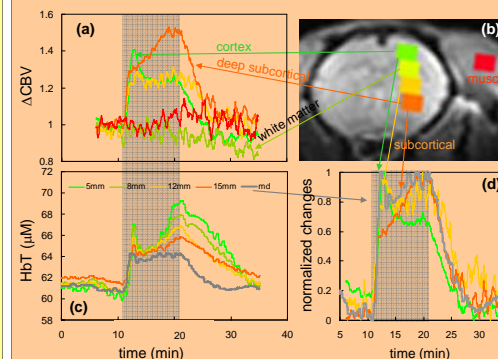


- FD and DCS source
- FD and DCS detector

Protocol



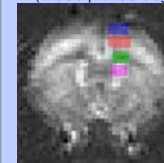
CBV Validation



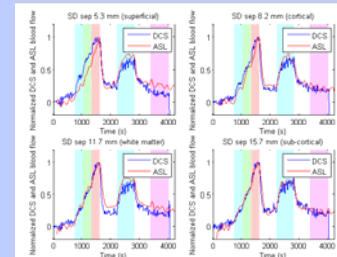
- 7.5 CO₂ 10 minute hypercapnia cycle
- Inhomogeneity of CBV changes in the rat brain makes comparison difficult
- FD-NIRS is most sensitive to subcortical areas due to probe size
- FD-NIRS changes smaller than MR CBV due to partial volume effects
- Multi-distance HbT returns to baseline matching MR CBV
- Good temporal agreement between FD-NIRS and MR

CBF Validation

ASL slice positioned near second optical detector (whole exp. time average)



ROI colors correspond to ASL curves on the right



- 2.5%, 5%, 7.5% CO₂ steps, followed by another 2.5% CO₂ period, and 100% O₂
- Very good correlation between optical and MR CBF measures at all depths

DCS partial volume correction

$$DCS_{meas} = f DCS_{cerebral} + (1-f) DCS_{extracerebral} \rightarrow DCS_{cerebral} = \frac{DCS_{meas} - (1-f) DCS_{extracerebral}}{f}$$

$$r_{CBF} = r_{ASL} = r_{DCS_{corrected}} = \frac{DCS_{meas, state2} - (1-f) DCS_{extracerebral}}{DCS_{meas, state1} - (1-f) DCS_{extracerebral}}$$

The DCS measure of cerebral blood flow can be calibrated using one of the CO₂ level transitions (e.g. 2.5-5%) by assuming no change in extra cerebral blood flow, and using MR ASL relative flow as ground truth. We obtain a value for the compound parameter (1-f)DCS_{extracerebral} and using it to compute optical r_{CBF} for other gas transitions we obtain better than 10% agreement between optical and MR measures in all cases.

Conclusion

We were able to demonstrate the simultaneous acquisition of optical and MR data on a rat animal model during a hypercapnic challenge. The salient features of the MR and optical measurement matched very well, and we were able to use one of the CO₂ transitions to calibrate the partial volume effect in DCS cerebral flow estimates, giving us confidence in the future ability of optical-only measurements to follow CMRO₂ changes in vivo.

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References

- [1] Boas, D.A., L.E. Campbell, and A.G. Yodh, Scattering and Imaging with Diffusing Temporal Field Correlations. *Phys. Rev. Lett.*, 1995, 75, p. 1855-1858.
- [2] Cheng, G., et al., In vivo cerebrovascular measurement combining diffuse near-infrared absorption and correlation spectroscopy. *Phys Med Biol*, 2001, 46(8): p. 2053-65.
- [3] Culver, J.P., et al., Diffuse optical measurement of cerebral blood flow, oxygenation, and metabolism in rat during focal ischemia. *J Cereb Blood Flow Metab*, 2003, 23(8): p. 911-24.
- [4] Durduran, T., et al., Diffuse optical measurement of blood flow in breast tumors. *Opt Lett*, 2005, 30(21): p. 2915-7.
- [5] Durduran, T., et al., Diffuse optical measurement of blood flow, blood oxygenation, and metabolism in a human brain during sensorimotor cortex activation. *Opt Lett*, 2004, 29(15): p. 1766-8.
- [6] Fisel, C.R., et al., MR contrast due to microscopically heterogeneous magnetic susceptibility: numerical simulations and applications to cerebral physiology. *Magn Reson Med*, 1991, 17: p. 336-347.
- [7] Detre, J.A. and D.C. Alsop, Perfusion magnetic resonance imaging with continuous arterial spin labeling: methods and clinical application in the central nervous system. *Eur J Radiol*, 1999, 30(2): p. 115-24.
- [8] Wang, J., et al., Pediatric perfusion imaging using pulsed arterial spin labeling. *J Magn Reson Imaging*, 2003, 18(4): p. 404-13.
- [9] Alsop, D.C. and J.A. Detre, Reduced transit-time sensitivity in noninvasive magnetic resonance imaging of human cerebral blood flow. *J Cereb Blood Flow Metab*, 1996, 16(6): p. 1236-49.
- [10] Wolhuis, R., et al., Determination of water concentration in brain tissue by Raman spectroscopy. *Anal Chem*, 2001, 73(16): p. 3915-20.
- [11] Culver, J.P., et al., Diffuse optical measurement of hemoglobin and cerebral blood flow in rat brain during hypercapnia, hypoxia and cardiac arrest. *Adv Exp Med Biol*, 2003, 510: p. 293-7.
- [12] Rosen, B.R., et al., Perfusion imaging with MRM contrast agents. *Magn Reson Med*, 1990, 14: p. 249-265.
- [13] Hamburg, L.M., et al., Continuous assessment of relative cerebral blood volume in transient ischemia using steady state susceptibility-contrast MRI. *Magn Reson Med*, 1996, 35: p. 168-173.
- [14] Delpy, D.T., et al., Estimation of optical pathlength through tissue from direct time of flight measurement. *Phys Med Biol*, 1988, 33: p. 1433-1442.