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# Optimizing Unanesthetized Cerebral Oxygen Consumption Measures: Comparison of NIRS and MRI Approaches in Neonates with Congenital Heart Disease

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**Abstract:** Cerebral perfusion in neonates with congenital heart disease is a clinical concern. Combined measures of MRI and NIRS can provide complementary information to improve monitoring. We compare multimodal measures of cerebral hemodynamics in this group.  
**OCIS codes:** (300.6340) Spectroscopy, infrared; (170.2655) Functional monitoring and imaging; (170.0110) Imaging systems

## 1. Introduction

Moderate to severe congenital heart disease (CHD) affects 6/1000 live births, with severe CHD resulting in adverse neurodevelopmental outcomes in over 50% (1). The etiology of neurodevelopmental disorders is unknown but evaluation of the hemodynamic state of CHD infants pre- and post-surgically has become a focus with cerebral metabolic rate of oxygen consumption (CMRO<sub>2</sub>) identified as a key parameter for clinical evaluation (2-5). Jain et al. (4) demonstrated correlations between magnetic resonance imaging (MRI) and near-infrared spectroscopy (NIRS) measures of CMRO<sub>2</sub> pre-surgically when measured simultaneously in anesthetized neonates. We present NIRS and MRI-based measures of cerebral hemodynamics (OEF, CBF and CMRO<sub>2</sub>) in nine stable neonates with CHD. NIRS and MRI measures were performed without anesthesia and within one day from each other. Measures obtained with both modalities are compared to literature values.

## 2. Methods

**Subjects:** Nine infants (age=4.8±2.5 days) were recruited at Boston Children's Hospital after IRB approval and parental consent. MRI and NIRS measurements took place in the pre-operative period.

**Data acquisition:** Frequency-domain NIRS (FD-NIRS) and diffuse correlation spectroscopy (DCS) systems were used for the optical measurements (6). The FD-NIRS system has two banks of laser diode sources operating at 8 wavelengths (667-825nm) and two PMT detectors. The sources are modulated at 110 MHz, and the detectors at 110 MHz + 5 kHz for heterodyne detection at 5 kHz. The DCS system has a long coherence length laser source (785 nm) and four APD detectors. An eight-channel correlator is converts the detected light at each DCS channel into temporal intensity autocorrelation functions. Absorption ( $\mu_a$ ) and scattering ( $\mu_s$ ) coefficients were measured with FD-NIRS. Oxygenated (HbO<sub>2</sub>) and deoxygenated (HbR) hemoglobin were derived from the absorption coefficients using hemoglobin extinction coefficients reported in the literature. Cerebral oxygen saturation was computed as  $SO_2 = HbO_2 / (HbO_2 + HbR)$ . For DCS, each measured intensity autocorrelation function was fit to obtain a blood flow index (CBF<sub>i</sub>) using the semi-infinite solution to the correlation diffusion equation for a homogenous medium (6, 7). Individual  $\mu_a$  and  $\mu_s$  at 785 nm were used in the fitting. The MRI protocol included: Structural MEMPRAGE; time of flight angiogram (MRA) positioned to include the circle of Willis and the neck; velocity encoded phase contrast image positioned manually based on the MRA perpendicular to the basilar artery and interior carotid arteries (TE/TR=4.67/16.65ms, resolution=0.5x0.5x4.0mm, velocity encoding=100cm/s); T-relaxation under spin tagging (TRUST) positioned 15 mm above the confluence of the sinuses perpendicular to the superior sagittal sinus (TE/TR=15/5000ms, resolution=2.3x2.3x5mm, inversion time=1025ms, tagging width=50mm, tagging gap=15mm) (8). Venous oxygen saturation (SvO<sub>2</sub>) was calculated from T<sub>2</sub> using a published calibration (9).

**Measurements of brain metabolism:** Oxygen extraction fraction was computed as  $OEF = (SaO_2 - SvO_2) / SvO_2$ , where SaO<sub>2</sub> was measured with a pulse oximeter. Cerebral metabolic rate of oxygen consumption was computed as

$CMRO_2 = 1.39 \times SaO_2 \times [Hb] \times CBF \times OEF$ , where [Hb] is the hemoglobin concentration measured from blood samples.

### 3. Results

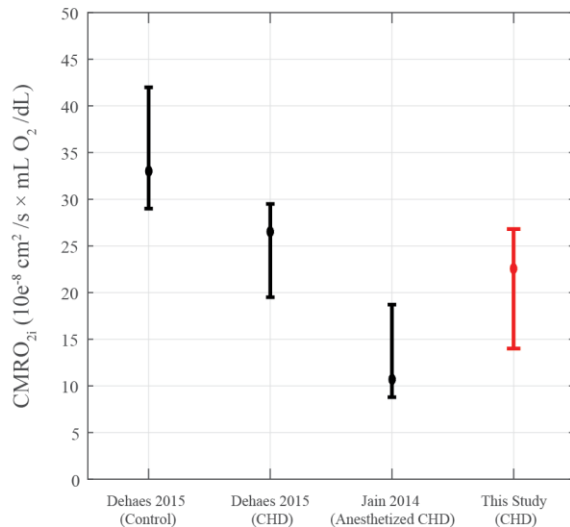
Figures 1 and 2 show  $CMRO_2$  comparisons between our results and the literature. Figure 3 shows the correlation between  $SvO_2$  and OEF measured by FD-NIRS and MRI.

### 4. Discussion

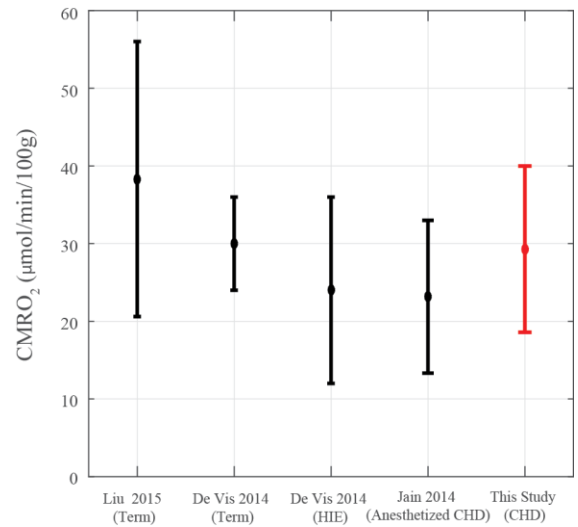
Compared to previous studies, our FD-NIRS/DCS results show decreased  $CMRO_2$  in CHD relative to controls (10), but higher  $CMRO_2$  than anesthetized subjects (4) (Figure 1). A similar trend is observed with our MRI results, showing a decreased  $CMRO_2$  relative to healthy subjects examined with a similar technique (8), and slightly higher  $CMRO_2$  than in anesthetized subjects (4, 11) (Figure 2).  $SvO_2$  and OEF measurements correlate across modalities ( $r^2=0.596$ ,  $p=0.015$  for  $SvO_2$ ;  $r^2=0.525$ ,  $p=0.027$  for OEF) suggesting that these measures capture similar information and/or are relatively stable in this cohort (Figure 3). However, there was no significant correlation between DCS and MRI measurements of CBF. Several possibilities could explain the discrepancy: 1. Measurements were not performed simultaneously and subjects with CHD have fluctuating physiology even when stable. 2. Sample size was limited as neonates needed to be stable and asleep to have a successful MRI scan. 3. MRI and NIRS rely on different models and assumptions that could lead to different measurement biases. We studied stable preoperative neonates without anesthesia and although the sample size was small the results compare well to other within modality measures (Figures 1, 2). Thus, we suspect the discrepancy between modalities is due to different biases, particularly in CBF measures, which have a direct effect on  $CMRO_2$ . MRI CBF measurements are based on large cerebral artery blood volume inflow, whereas NIRS measurements are based on microvascular red blood cells (RBC) flow.

### 5. Conclusions

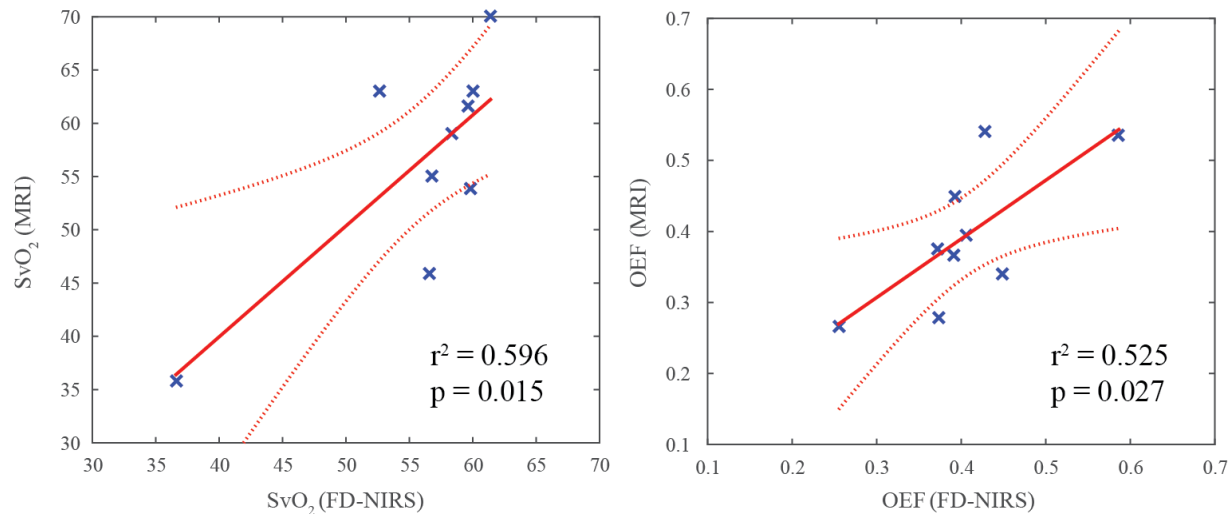
MRI and NIRS provide complementary methods for quantification of cerebral hemodynamics that if cross-validated would increase our confidence in both modalities and lead to more comprehensive bedside clinical monitoring. However, before data between these two modalities can be compared or combined, additional studies are needed to better understand the relationship between large vessel bulk flow and microvascular RBC flow.  $SvO_2$  and OEF measurements in our study are significantly correlated between modalities, but CBF, and therefore  $CMRO_2$ , are not in good agreement either due to differences in physiology or biases in these measurements.



**Figure 1:** Index of cerebral metabolic rate of oxygen consumption ( $CMRO_{2i}$ ) measured with FD-NIRS/DCS.  $CMRO_{2i}$  values are shown as median and interquartile ranges.



**Figure 2:** MRI-based  $CMRO_2$  comparison between this study and values reported in the literature.  $CMRO_2$  values are shown as mean and standard deviation.



**Figure 3:** Significant correlations were obtained between FD-NIRS and MRI measurements of SvO<sub>2</sub> and OEF, respectively. A linear regression model was estimated for each variable (the red solid line represents the best fit, while the dashed lines represent 95% confidence bounds).

## References

- Marino, B. S.; Lipkin, P. H.; Newburger, J. W.; Peacock, G.; Gerdes, M.; Gaynor, J. W.; Mussatto, K.; Uzark, K.; Goldberg, C. S.; Johnson, W. H.; Li, J.; Smith, S. E.; Bellinger, D. C.; Mahle, W. T. Neurodevelopmental Outcomes in Children with Congenital Heart Disease: Evaluation and Management: A Scientific Statement from the American Heart Association. *Circulation* 2012, 126, 1143–72.
- Limperopoulos, C.; Tworetzky, W.; McElhinney, D. B.; Newburger, J. W.; Brown, D. W.; Robertson, R. L.; Guizard, N.; McGrath, E.; Geva, J.; Annese, D.; Dunbar-Masterson, C.; Trainor, B.; Laussen, P. C.; Plessis, A. J. du Brain Volume and Metabolism in Fetuses with Congenital Heart Disease: Evaluation with Quantitative Magnetic Resonance Imaging and Spectroscopy. *Circulation* 2010, 121, 26–33.
- Sun, L.; Macgowan, C. K.; Sled, J. G.; Yoo, S.-J.; Manlhiot, C.; Porayette, P.; Grosse-Wortmann, L.; Jaeggi, E.; McCrindle, B. W.; Kingdom, J.; Hickey, E.; Miller, S.; Seed, M. Reduced Fetal Cerebral Oxygen Consumption Is Associated With Smaller Brain Size in Fetuses With Congenital Heart Disease. *Circulation* 2015, 131, 1313–1323.
- Jain, V.; Buckley, E. M.; Licht, D. J.; Lynch, J. M.; Schwab, P. J.; Naim, M. Y.; Lavin, N. a; Nicolson, S. C.; Montenegro, L. M.; Yodh, A. G.; Wehrli, F. W. Cerebral Oxygen Metabolism in Neonates with Congenital Heart Disease Quantified by MRI and Optics. *Journal of cerebral blood flow and metabolism : official journal of the International Society of Cerebral Blood Flow and Metabolism* 2014, 34, 380–8.
- Cheng, H. H.; Wypij, D.; Laussen, P. C.; Bellinger, D. C.; Stopp, C. D.; Soul, J. S.; Newburger, J. W.; Kussman, B. D. Cerebral Blood Flow Velocity and Neurodevelopmental Outcome in Infants Undergoing Surgery for Congenital Heart Disease. *The Annals of thoracic surgery* 2014, 98, 125–32.
- Durduran T; Choe R; Baker WB; Yodh AG. Diffuse optics for tissue monitoring and tomography. *Rep Progr Phys* 2010; 73: 1–43.
- Boas, D. A. and A. G. Yodh. Spatially varying dynamical properties of turbid media probed with diffusing temporal light correlation. *J. Opt. Soc. Am.* 1997, 14(1): 192–215.
- Liu, P.; Huang, H.; Rollins, N.; Chalak, L. F.; Jeon, T.; Halovanic, C.; Lu, H. Quantitative Assessment of Global Cerebral Metabolic Rate of Oxygen (CMRO<sub>2</sub>) in Neonates Using MRI. *NMR in biomedicine* 2014.
- Lu, H.; Xu, F.; Grgac, K.; Liu, P.; Qin, Q.; Zijl, P. van Calibration and Validation of TRUST MRI for the Estimation of Cerebral Blood Oxygenation. *Magnetic resonance in medicine: Official Journal of the Society of Magnetic Resonance in Medicine / Society of Magnetic Resonance in Medicine* 2012, 67, 42–9.
- Dehaes, M.; Cheng, H. H.; Buckley, E. M.; Lin, P.-Y.; Ferradal, S.; Williams, K.; Vyas, R.; Hagan, K.; Wigmore, D.; McDavitt, E.; Soul, J. S.; Franceschini, M. A.; Newburger, J. W.; Ellen Grant, P. Perioperative Cerebral Hemodynamics and Oxygen Metabolism in Neonates with Single-Ventricle Physiology. *Biomedical Optics Express* 2015, 6, 4749.
- De Vis JB, Petersen ET, Alderliesten T, Groenendaal F, de Vries LS, van Bel F, Benders MJNL, Hendrikse J. Non-invasive MRI measurements of venous oxygenation, oxygen extraction fraction and oxygen consumption in neonates. *Neuroimage [Internet]. Elsevier Inc.*; 2014 Mar 29; 95C:185–192. PMID: 24685437