MRI based Quantification of Global Cerebral Metabolism in Neonates with Congenital Heart Defect

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Introduction: Periventricular leukomalacia (PVL), a type of hypoxic ischemic injury, is the most common cerebral pathology observed in neonates with congenital heart defects (CHD) [1]. While the exact reason for this type of white matter injury is unclear, hemodynamic and metabolic dysregulation is thought to play a role [2]. We utilized a previously described non-invasive magnetic resonance (MR) method that can measure global bi-hemispheric cerebral venous oxygen saturation (S_vO_2) and cerebral blood flow (CBF) simultaneously [3, 4]. The two measurements can be combined using Fick's law to yield global cerebral oxygen metabolism ($CMRO_2$) in absolute physiological units. The goal of this work was to illustrate the feasibility of MR susceptometry based oximetry to quantify S_vO_2, CBF and $CMRO_2$ in absolute physiological units at rest and in response to hypercapnia in neonates with CHD. The latter was evaluated to assess the dynamic range of the method and cross-validate MR based hemodynamic measurements with more clinically widespread optical methods. Additionally, pre-operative hemodynamic parameters were correlated with the incidence of PVL postoperatively.

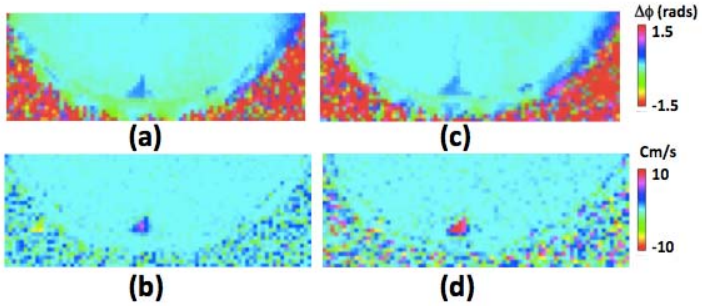

Figure 1**: Phase difference images used for calculating S_vO_2 and velocity maps in SSS at rest **(a,b)** and in response to hypercapnia **(c,d).

N=35	Baseline	Hypercapnia	p value
S_aO_2 (%)	90 (7.8)	84.6 (11.0)	0.0142
S_vO_2 (%)	55.6(12.0)	67.2(12.3)	<0.0005
CBF (ml/min/100g)	10.1 (9.4)	25.9 (18.4)	<0.0005
$CMRO_2$ (μmol/100g/min)	25.2 (17.3)	24.4 (20.5)	0.4187

***Table 1**: Median and interquartile range of various hemodynamic parameters measured at baseline and in response to hypercapnia.*

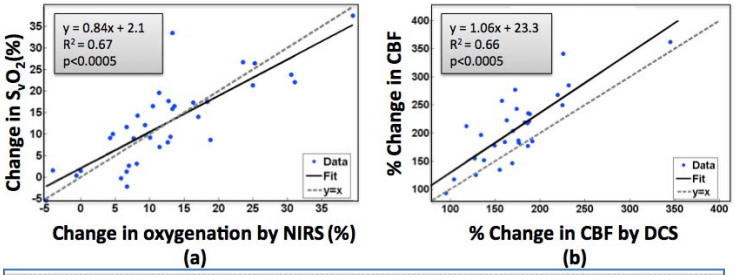

***Figure 2**: Correlation between MR and optical measurements of changes in **(a)** oxygenation and **(b)** flow. Y axis represents MR measurements and X axis optical measurements. The dotted gray line represents the line of identity.*

Methods: 35 full term infants with a diagnosis of complex CHD were recruited. The study was performed under general anesthesia on the morning of the patient's scheduled cardiac surgery. After a 30-minute baseline period of ventilation with FiO_2 of 0.21, CO_2 was added to the air mixture to achieve an $FiCO_2$ of 0.03. MRI and optical measurements were acquired simultaneously before and at the end of the hypercapnic period. All scans were conducted on a 1.5 T Avanto MRI located next to the operating room and intensive care unit. An interleaved GRE sequence consisting of four interleaves was used for simultaneous measurement of S_vO_2 in the superior sagittal sinus (SSS) using MR-susceptometry based oximetry and CBF using PC MR [4]. Scan parameters: FOV =112 × 112 × 5 mm^3, voxel size = 0.8 × 0.8 × 5 mm^3, flip angle = 25°, TR=35ms, VENC = 10cm/s (normocapnia) and 20 cm/s (hypercapnia), NEX=3, total scan time ~ 1 minute. Additional T_1, T_2 and diffusion weighted images were acquired and a clinical neurologist reviewed all images for the presence of PVL. An average neonatal brain mass of 300g was assumed and normalized to the volume drained by SSS (~60%) to express CBF and $CMRO_2$ in conventional units. For optical measurements, diffuse correlation and near infrared spectroscopies were used to evaluate tissue blood flow and oxygenation levels, respectively [5].

Results and Conclusion: In line with the known vasodilatory effect of hypercapnia, an increase in CBF and S_vO_2 was observed (***Figure 1***). A summary of various hemodynamic parameters measured at baseline and in response to hypercapnia is shown in ***Table 1***. A significant correlation between MR and optics measured changes in oxygenation and blood flow during hypercapnia was observed (***Figure 2***). Low venous oxygen saturation in the sagittal sinus pre-operatively was associated with worse PVL injury post-operatively (p = 0.033) (***Figure 3***).

In conclusion, we demonstrated the feasibility of conducting MR based hemodynamic measurements in neonates with complex CHD. Measured CBF and $CMRO_2$ values were substantially lower than in adults [2,3]; however in good agreement with those observed in preterm infants who also have a high incidence of PVL [6]. The measurements demonstrated a significant correlation with optical methods and agreed well with expected physiological changes in response to hypercapnia. Additionally, our results illustrate the potential utility of preoperative hemodynamic measurements as predictors of postoperative injury. These results highlight that MRI based measurements of cerebral hemodynamics can serve as a valuable adjunctive tool to evaluate and manage critically ill infants with CHD.

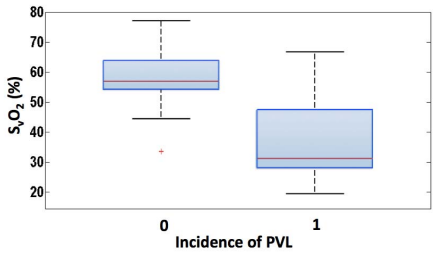

***Figure 3**: Box plot representing the association between venous oxygenation and incidence of PVL. 1 represents worsened PVL (>150 mm^3).*

References: [1]Volpe, J.J. Pediatr Res, 2001; 50(5): 553-62. [2] Licht, D. et al., J Thorac Cardiovasc Surg 2004; 128(6): 841-9. [3] Jain, V. et al., JCBFM 2010;1598-1607. [4] Jain, V. et al., JCBFM 2011; 31(7): 1504-12. [5] Durduran et al.,JBO 2010; 15(3):037004. [6] Altman, D.I. et al., Pediatrics 1993:92 (1): 99-104.