Post-Surgical Cerebral Autoregulation in Neonates with Congenital Heart Defects Monitored With Diffuse Correlation Spectroscopy

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Abstract: Following cardiac surgery, cerebral blood flow changes in neonates with congenital heart defects are measured using diffuse correlation spectroscopy. Using statistical correlations with mean arterial pressures, we explore an "autoregulation index" to define periods of impaired autoregulation.

OCIS codes: (170.3880) Medical and biological imaging, (170.5380) Physiology, (170.1610) Clinical applications.

1. Introduction

Approximately 6-8 in 1,000 infants born each year are diagnosed with congenital heart defects (CHD), a third of whom require major surgical repair in the first month of life. Recent advances in cardiac surgery for severe CHD have minimized infant mortality. Thus, clinicians are now focusing on the prevention of neurologic injury and the improvement of neurocognitive outcome in these high-risk infants. Studies conducted with magnetic resonance imaging (MRI) indicate that the incidence of neurological injury increases substantially after cardiac surgery[1, 2]. We hypothesize that disruptions of cerebral autoregulation in the post-operative period may contribute to brain injury in these infants. Cerebral autoregulation, loosely defined as the ability to maintain adequate and constant cerebral blood flow (CBF) despite changes in systemic blood pressures, is very difficult to measure non-invasively due to limitations in CBF measurements. To assess hemodynamic autoregulatory changes, researchers have used transcranial Doppler measurements of blood flow velocity in the main cerebral arteries, near infrared spectroscopy (NIRS) measurements of cerebral blood volume, tissue oxygen saturation, and/or hemoglobin difference as a surrogate for CBF. Using NIRS, Brady *et al.* have pioneered a real-time technique to assess autoregulatory failure using measures of tissue oxygen saturation (StO_2) [3]. They compute a 300 second moving window Pearson's correlation coefficient between arterial blood pressure and StO_2, coined the cerebral oximeter index (COx), which they update every 60 seconds. Using a predefined threshold for COx, they have had success in both animal and human models in identifying time periods of impaired autoregulation, i.e. times in which systemic blood pressure and CBF exhibit a strong positive correlation [4]. The main weakness of this technique is the use of StO_2 to infer the behavior of cerebral blood flow instead of monitoring CBF directly.

Following the spirit of Brady *et al.*'s methods, we propose the use of diffuse correlation spectroscopy (DCS), a novel, non-invasive optical technique capable of directly measuring relative changes in CBF in a continuous fashion, as a means to assess a cerebral autoregulation index in neonates following cardiac surgery. DCS [5] has shown promise as a monitor of relative changes in cerebral blood flow (rCBF) [6, 7]. Like NIRS, DCS employs near-infrared light to probe the dynamics of deep tissues. However, DCS detects changes in CBF *directly* by monitoring temporal fluctuations of scattered light. It does not rely on tracers or measurements of tissue oxygenation to indirectly infer information about CBF. Finally, in contrast to Doppler ultrasound, DCS provides information about *microvascular* as opposed to macrovascular hemodynamics.

To date six subjects diagnosed with complex congenital heart defects, either hypoplastic left heart syndrome (HLHS) or transposition of the great arteries (TGA) have been recruited and monitored with DCS in the cardiac intensive care unit for twelve hours immediately following return from cardiac surgery. Herein we describe our optical and vital signs data acquisition and analysis techniques, and we employ DCS to quantify duration and magnitude of impaired autoregulatory capacity in these neonates using the methods outlined in [3].

2. Procedure

With institutional review board approval, all newborn infants with CHD admitted to the cardiac intensive care unit (CICU) at The Children's Hospital of Philadelphia (CHOP) were evaluated for study inclusion. Inclusion criteria included full term age (gestational age 40±4 weeks), an intention to undergo surgery with cardiopulmonary bypass (CPB) with or without deep hypothermic circulatory arrest (DHCA) and medical stability for 24 hours prior to surgery. Infants were excluded if they had a history of neonatal depression (5 minute APGAR<5 or cord pH<7.0) or a pre-operative cardiac arrest requiring chest compressions. Subjects with HLHS treated with hypercarbia for pulmonary over-circulation were also excluded.

On return from cardiac surgery, vital signs monitors were secured and the optical probe was placed on the forehead. For data analysis purposes, vital signs, including heart rate, systolic, diastolic, and mean arterial blood pressure, temperature, respiration rate, blood oxygen saturation, and right atrial pressure, were recorded via Moberg Devices Component Neuromonitor Systems at a rate of 0.5 Hz. Manual time-stamps were placed to co-register the optical and vital sign data. A hybrid NIRS/DCS optical device constructed in our lab (described previously [8]) acquired oxygenation and cerebral blood flow data at a rate of 0.13 Hz. The optical probe was repositioned on the forehead routinely every two hours, or as needed in the case of poor signal quality or movement of the child. All patients were monitored for 10 to 12 hours after returning from surgery.

The optical probe consisted of two source-detector pairs, both separated 2.5 cm apart, one designated for NIRS measures of oxygenation, the other for DCS measures of rCBF. With this unique population in mind, we designed the probe to be flexible and only 2mm thick. It was secured to the forehead with an eye mask. Anatomical MRI scans reveal a combined skull, scalp, and cerebral spinal fluid thickness of 0.74±0.10 cm, thus the optical techniques were probing a region between 0.8-1.2 cm into the cortex.

3. Data Analysis

For all optical data analysis, we assumed a semi-infinite geometry. For NIRS, we calculated changes in oxy-, deoxy- and total hemoglobin concentrations using the modified Beer-Lambert law. Additionally, we quantified changes in the absorption coefficient of the tissue, and we incorporated these changes into our DCS analysis. For DCS, we used solutions of the electric field correlation diffusion equation to derive relative changes in cerebral blood flow. All relative changes were calculated by subtracting/dividing by the mean during the first five minutes after probe placement or readjustment.

Once relative changes in CBF and oxygenation were established, statistical correlation calculations were examined and cerebral autoregulation was assessed. For simplicity, we present only the correlations between mean arterial pressure (MAP) and rCBF. Following the steps laid out by Brady *et al.*, the entire time course of data (rCBF and MAP) was averaged over nonoverlapping 10-second intervals. A Pearson's correlation coefficient, dubbed the cerebral blood flow index (CBFx), was computed from consecutive, paired, 10-second means of rCBF and MAP from a 300 second window (30 data points). This 300 second window was then shifted 60 seconds and the CBFx was recalculated from the new overlapping time frame. An arbitrary CBFx threshold of 0.5 was assigned to designate impaired autoregulation.

4. Results

Data from six patients have been fully analyzed. Figure 1 shows samples of rCBF, MAP, and CBFx versus time for a small portion of the total 12-hour monitoring. The figure demonstrates rCBF following the trend of MAP around 3, 15, and 25 minutes, at which time CBFx rises, suggesting possible impaired cerebral autoregulatory abilities. Trends such as these are observed periodically throughout the monitoring period. To assess the extent of impaired autoregulation in each subject, the percentage of time spent above the CBFx threshold was also calculated (Figure 2). Subjects spent a median(range) of 4.9(17.6) percentage of time with CBFx above the threshold.

5. Conclusions

This abstract described the first steps of a novel application of measures of relative changes in cerebral blood flow obtained with diffuse correlation spectroscopy to assess cerebral autoregulation in infants with congenital heart defects following cardiac surgery. More patients and correlations with concurrent measurements of oxy- and deoxy-hemoglobin concentrations will permit further exploration of the utility of this new index.

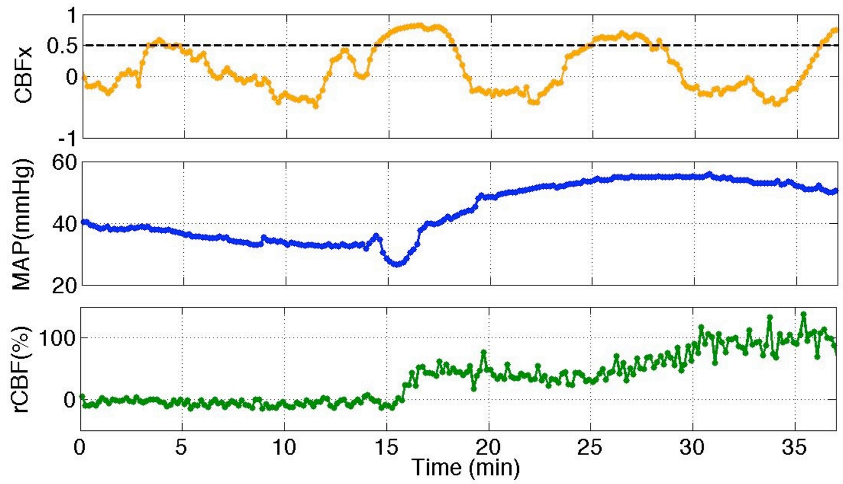

Figure 1 Sample time series of CBFx, MAP, and rCBF.

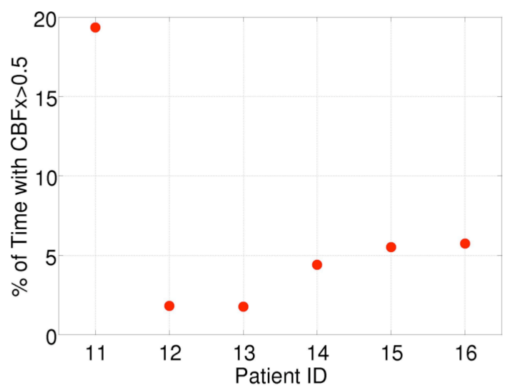

Figure 2 Percent of time in which CBFx was above our predefined threshold of 0.5.

6. References

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