Blood Pressure-Related Hemodynamic Shifts in the Cerebral Cortex During Cardiac Surgery

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Abstract

Near-Infrared spectroscopic (NIRS) cerebral oximetry is currently employed to monitor intraoperative brain perfusion. Novel analyses presented here are part of a continuing study aimed at identifying differences between the sensing capabilities of large-area optode arrays and smaller arrays that are commercially available. Data were recorded from six patients undergoing cardiac surgery, using a continuous-wave, NIRS Diffuse Optical Tomography imager that sampled two wavelengths (760 and 830 nm) at 8 Hz, with 30 optodes arranged to yield 211 channels grouped into four distinct sites over the frontal and pre-frontal cortex regions. A total of 13 hypotensive events, defined as a drop and subsequent recovery in mean arterial pressure (MAP) of at least 20 mmHg for 90 seconds, and 24 control time periods of similar duration, were used in the analysis. Spearman correlation coefficients between MAP and oxygenated hemoglobin (Hb_{oxy}), for each data channel, showed a significantly different between control and event time periods ($p<0.001$). Additionally, channel-MAP correlations were significantly different among sites, for both control ($p<0.04$) and event ($p<0.03$) periods. A sensitivity analysis was performed that compared the magnitude of change during each event in each detector channel, for both Hb_{oxy} and oxygen saturation (HbO_2Sat). While a large fraction of the array (on average, 81%) was sensitive to the hypotensive events, only a few channels had responses of pronounced magnitude. To achieve sensitivity in 50% of the channels, the response threshold must be set to 22% of the maximum change, demonstrating a spatially heterogeneous response. Such heterogeneity is unlikely to be revealed by a small array.

Introduction

- Neurocognitive deficits are a common side effect of surgery, especially cardiac (Moller 1998 and Savino 2008)
- Many hemodynamic alterations during surgery affect MAP and subsequent brain perfusion
- Some of these shifts may be dramatic, dropping tens of mmHg in just a few seconds and reaching MAPs as low as single digits
- NIRS monitoring of cerebral oxygenation has been well described and utilized clinically (Wolf 2007 and Murkin 2007)
- Local brain responses to these perturbations have not been completely characterized
- Without a full understanding of how the brain responds, it is unlikely that a proper monitoring scheme can be developed
- In this study we show that cerebral responses to hemodynamic shifts exhibit substantial spatial heterogeneity, such that current small-array devices (Fischer 2008) may not be adequate for monitoring

Methods

- 2 wavelengths (760 nm and 830 nm) of time series data were collected from 6 patients during heart surgery, using arrays shown in Fig. 1, which yield 211 source-detector pairs (channels).
- Modified Beer-Lambert Law was used to compute estimates of oxygenated and deoxygenated hemoglobin (Hb_{oxy} and Hb_{deoxy}) (Schmitz 2005).
- Control time intervals are defined as periods of about 1.5 minutes duration, wherein patient was hemodynamically stable – MAP changes <3 mmHg, very little if any pharmacologic or physical manipulation.
- Event time periods also are ~1.5 minutes long. Acute hypotension is defined as a drop in MAP of more than 25 mmHg below the MAP level at the start of the period.
- Pearson correlation coefficients calculated between all pairs of detector channels
- Spearman correlation coefficients calculated between each channel and MAP
- We used linear mixed effects models, which allowed modeling of Spearman data with correlated observations. Type = 1 for control and type = 2 for event trials.
  - Let Y_{ijkl} be the mean Spearman correlation for the i^{th} subject, at site j, for type k, in the l^{th} trial

$$Y_{ijkl} = \mu + \alpha_j + \beta_k + (\alpha\beta)_{jk} + t_{il} + e_{ijkl} \quad \text{(EQ 1)}$$

  - In EQ 1, μ is the overall mean, α_j is a fixed effect of site j, β_k is a fixed effect of type k, $(\alpha\beta)_{jk}$ is a fixed interaction effect between site j and type k, and t_{il} is a random effect for trial l and subject i, and e_{ijkl} is the error term.
- Amplitude analyses – quantitative comparisons of the signal changes in all detector channels during an event period or during a control period – were done for both Hb_{oxy} and HbO_2Sat to simulate the sensitivity and specificity of a low-density array.

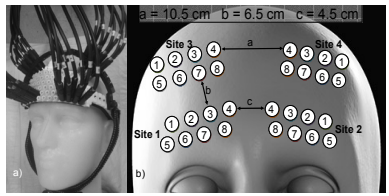

Figure 1. a) Photograph of headgear with the four-site optode array; b) Diagram of the optode arrangements in each site, and the inter-site distances.

Results

Summary: Brain is regionally heterogeneous across sites

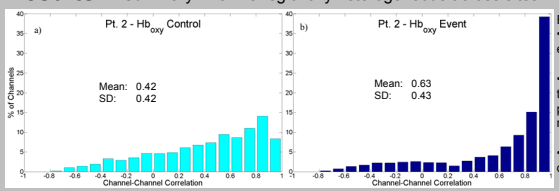

Figure 2:
- Data shows one control and one event time period from one patient
- Inter-channel correlations show that most pairs of channels are positively correlated but values ranged from -1 to +1.
- Higher mean correlation values during hypotensive event periods.

Figure 2. Correlation histogram of 4 site array (Pearson).

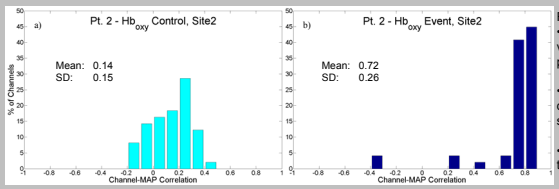

Figure 3:
- Low channel – MAP correlation values (about 0) during control time periods
- Higher channel – MAP correlations during hypotensive events at each site ($p<0.001$)
- Our array is sensitive to central tendencies of MAP changes

Figure 3. Correlation histogram of single site (Spearman).

Results 2

Sensitivity Analysis Mimicking Real-Time Monitoring:

- Found first drop of greater than 20 mmHg, spanning ~30 time frames, in the MAP tracing [Fig. 5(a)].
- Averages of each channel's Hb_{oxy} tracing were computed, for the 10 time frames following the rapid decrease in MAP, and for the 25-35 time frames preceding the drop [Fig. 5(b)].
- The post-drop average was subtracted from the pre-drop.
- Data plotted as percent of channels where Hb_{oxy} change exceeded a selected threshold, versus the threshold value.
- The event-interval differences were compared to the Hb_{oxy} differences computed for all possible control-period time windows having the same ~30 time-frame separation (~60 comparisons per control time period).

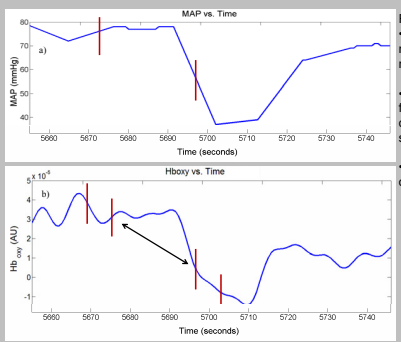

Figure 5:
- Time found when first drop of >20 mmHg happened (Panel a) – marked with red lines
- Panel b shows the Hb_{oxy} tracing for the channel that produced one of the largest changes in Hb_{oxy} signal for that time period.
- Time points from 5(a) used to obtain values of Hb_{oxy} for analysis

Figure 5 . Tracings of MAP and Hb_{oxy} versus time during acute hypotension

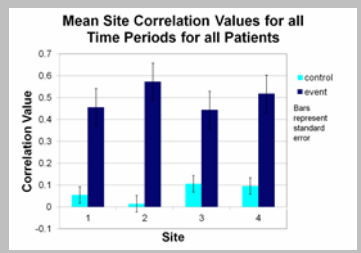

Figure 4:
- Means from all 24 control and all 13 event time periods are utilized.
- Controls and events significantly different $p<0.001$
- Indicates there are inter-site differences.

Figure 4. Mean channel-MAP Spearman correlations.

Type	Site	Vs Site	Estimate (Y-Y Eq 1)	StdErr	P
control	1	2	0.04	0.03	0.23
control	1	3	-0.05	0.03	0.13
control	1	4	-0.04	0.03	0.22
control	2	3	-0.09	0.03	0.0075
control	2	4	-0.08	0.03	0.017
control	3	4	0.01	0.03	0.77
event	1	2	-0.11	0.06	0.059
event	1	3	0.01	0.06	0.84
event	1	4	-0.06	0.06	0.32
event	2	3	0.12	0.06	0.037
event	2	4	0.05	0.06	0.37
event	3	4	-0.07	0.06	0.23

Table 1:
- Means were placed into mixed model (EQ 1) to determine inter-site differences
- Red highlights the sites that are statistically different.
- Site 2 has lower correlations than Sites 3 and 4 during control time periods, and Site 2 has higher values than Sites 1 and 3 during event periods.

Table 1. p-values for the mixed model comparison of sites

Summary of Principal Findings:

- **Threshold for Event Sensitivity**: Mean 22% (11-45%). Percentage of the maximal amplitude difference at which the threshold would have to be set for a majority (50%) of channels to register the change (Fig. 6).
- **False Positive Rate**: Mean 6% (0.5-22%) At the 22% threshold, about 6% of the channels are sensitive during control period (Fig. 6).
- **False Negative Rate**: Mean 19% (4-22%) Channels that registered no change or even an *increase* in Hb_{oxy} values during acute hypotension events, (Fig. 6).
- **Site Heterogeneity**: The channels that produce the largest change for one event period are often not the same that produce the largest change in others.

Figure 6. Selected extreme results of the amplitude analysis.

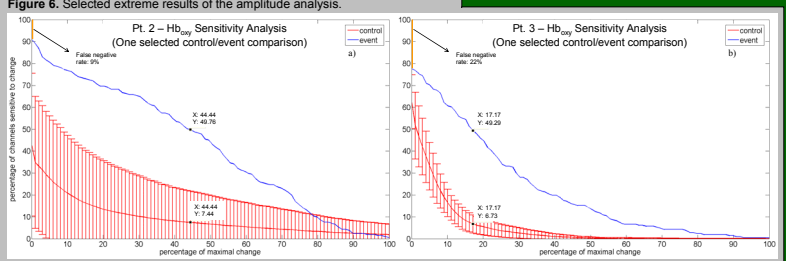

Figure 6:
- Blue lines represent one event time period
- Red lines represent one control period. Error bars on the red lines show the standard deviation across all possible ~30 time-frame windows (roughly 60 windows).
- This analysis utilizes all 211 channels, current arrays would only utilize 2 or 4 channels
- Sensitivity findings summarized above

Conclusions

- Channel-channel correlations show that **positional heterogeneity** is present at all times.
- Changes in channel-MAP correlations between control and event periods show that a large-area NIR monitoring device is **sensitive to central tendencies** of hemodynamic shifts.
- The **differences in channel-MAP correlation across sites** may be a function of anatomy, normal patient physiology (such as autoregulation), or pathology.
- Sensitivity analysis shows **difficulty determining *a priori*** where to put a small array to properly detect all significant hypotensive changes
- Even though the **false-positive rate** for any one control time period may be low, these periods constitute a large fraction of intraoperative time, meaning many false positives would occur.
- The observed degree of spatial heterogeneity during the acute hypotension events considered here implies that it is **unlikely that a small-array device would be adequate** for intraoperative monitoring of cerebral oxygenation.

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Acknowledgements

This work was supported under grant nos. R21NS067278-01A1, R42NS050007-03 and 5R44NS049734-03 to Randall L. Barbour and Daniel Lee; and by the New York State Department of Health.