Cerebral Monitoring in Cardiac Surgery: Sensitivity of Hb Co-variations and Individual Components

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Introduction

- Near-infrared spectroscopy (NIRS) monitoring of cerebral oxygenation has been well described and utilized clinically.[1]
- In an accompanying submission, we demonstrated that devices having only a small number of optodes are unlikely to provide reliable representations of cerebral perfusion or to detect hemodynamically significant events, underscoring the merit of adopting high-density optode arrays.
- In this report we examine the strategies used for analysis and interpretation of data obtained by NIRS tomography with high-density optode arrays.
- We compared methods of examining hemoglobin (Hb) signals individually,[2] versus exploring the spatial and temporal components of the co-variations among oxygenated (Hb_{oxy}), deoxygenated (Hb_{deoxy}) and total (Hb_{total}) Hb,[3] in terms of their effectiveness in detecting the cerebral hemodynamic responses associated with intraoperative clinically significant changes in blood pressure.
- We present evidence documenting that the considered co-variational (c-v) analysis approach provides an enhanced capability, with a substantially reduced rate of false positive results, for detection of clinically significant hemodynamic events, compared to similar analyses based on the individual Hb signals (i.e., the standard approach).

Subject	Gender	Age	Surgery	Measurement Duartion	Hemodynamic Event
1	F	65	CABG – Off-pump converted to on-pump beating heart	5h 18m	VF arrest / crash on CPB
2	F	73	GABG – Off-pump	5h 38m	VF / Cardioversion
3	M	67	AVR – On-pump	3h 00m	Cardiac Cannulation
4	F	58	GABG – On-pump	4h 32m	Initiation of CPB
5	F	58	GABG – On-pump	3h 27m	Low CPB flow rate
6	F	27	AVR – On-pump	4h 44m	Retrograde Autologous Priming of CPB

Table 1. Clinical information for the study participants. Abbreviations: AVR = aortic valve replacement, CABG = coronary artery bypass graft, CPB = cardiopulmonary bypass, VF = ventricular fibrillation.

Methods

- Two-wavelength time series data were collected (NIRx DYNOTcompact) from six patients during heart surgery (Table 1), using the multi-channel optode arrays shown in Fig. 1.
- Previously described methods[4] were used to reconstruct three-dimensional images of the Hb states: (Hb_{oxy}, Hb_{deoxy} and Hb_{total}).
- Using the definitions indicated in Table 2, each image pixel was assigned to one of six co-variation (c-v) states that correspond to different conditions of O_2 supply/demand balance, for each image time frame.[3]
  - Additional information that the c-v decomposition make available is illustrated in Fig. 2, using data from a forearm imaging study.
- The Hb and c-v state data were subsequently processed to yield multiple image metrics that involve elements of the spatial and temporal information domains derived from time periods corresponding either to clinically significant hemodynamic events or to control (i.e., clinically unimportant) intervals.
  - A clinically significant hemodynamic event was defined as a change in mean arterial pressure (MAP) >20 mm Hg, with the episode lasting more than 2 min, and a control period by a change in MAP < 5 mm Hg.
  - The metrics examined were the spatial mean (SM) value and spatial standard deviation (SSD) of the Hb_{oxy}, Hb_{deoxy}, Hb_{total} and Hb O_2 saturation (O_2Sat) time series, as well as the time-varying percentages of image volume (Vol%) occupied by each of the six c-v states.
- A total of 248 time-dependent metrics were computed; 216 of these correspond to metrics derived from c-v state analysis, while the remaining 32 correspond to metrics obtained from analysis of individual Hb states (conventional approach); at least one interval of each type (minimum = 1, maximum = 7) was chosen for each subject.
- Receiver Operating Characteristic analysis[5] was performed to determine which metrics can distinguish between control and event time intervals (true positive results), and which reveal differences between pairs of control intervals (false positive results).
- The number of metrics with a statistically significant ability (α = 0.05) to discriminates between segments was recorded, using the "score method"[6] to estimate the confidence intervals.

Hemoglobin State	State 1	State 2	State 3	State 4	State 5	State 6
Hb_{oxy}	–	–	–	+	+	+
Hb_{deoxy}	–	+	+	+	–	–
Hb_{total}	–	–	+	+	+	–
	Balanced	Uncomp. O_2 debt	Comp. O_2 debt	Balanced	Uncomp. O_2 excess	Comp. O_2 excess

Table 2. Concentration changes relative to a temporal mean value, associated with Hb levels influenced by autoregulation.

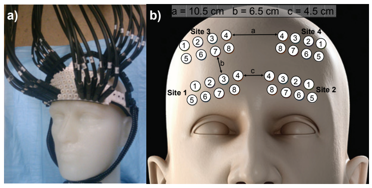


Figure 1. a) Photograph of headgear with the four-site optode array; b) Diagram of the optode arrangements in each site, and their inter-site distances.

Results

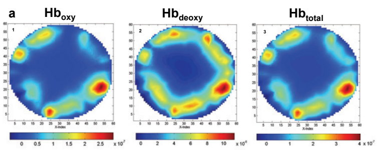
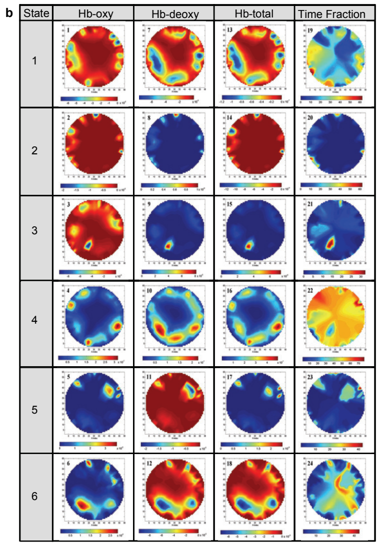


Figure 2. (a) Conventional reconstructed images of Hb_{oxy}, Hb_{deoxy}, Hb_{total}, in an 2D section through a volunteer's forearm, at a time frame representative of the entire baseline time series. All three images are qualitatively similar, with superficial veins dominating the signal in every case. Deeper lying dynamic features are present but obscured by the larger-amplitude superficial information. **(b)** Columns 1-3: The same image data as in (a), but fractionated according to which one of the 6 c-v states (Table 2) is present in each pixel during the selected time frame. (That is, each pixel is set to a value of 0 if the c-v state is different from the one indicated in the row heading.) In this representation, features that were obscured in conventional analysis are unveiled. Furthermore, anatomical features can be tentatively assigned a physiological significance, on the basis of which state reveals its presence. Column 4: time fraction images for each of the 6 c-v states. These spatial maps show how much time each pixel spends in a particular c-v state during the full course of the baseline time interval (approximately 500 time frames). This analysis is informative because it is amplitude-insensitive, provides a way of summarizing the information in any number of time frames with a small fixed number of spatial maps, and provides information on which tissue regions principally experience the physiological phenomena associated with each c-v state.



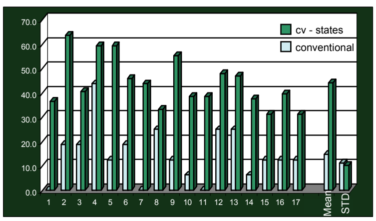


Figure 3. For each of the 17 clinically significant event time intervals: number of spatial mean-based metrics, expressed as percentage of theoretical maximum (i.e., 16 for the integrated Hb signals, and 96 for the c-v states), with statistically significant (α = 0.05) ability to distinguish the clinically significant and baseline time intervals. Also shown are the Mean and STD across all events.

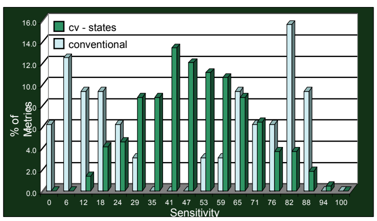


Figure 4. Diagnostic sensitivity histograms for the complete sets of conventional and c-v state-based metrics. Bar heights indicate the percentage of metrics that have the sensitivity values shown on the horizontal axis. The c-v metric distribution (min. = 12%, max. = 94%, avg. = 49%) is shifted rightward by a small amount in comparison to the conventional metric distribution (min. = 0%, max. = 88%, avg. = 46%) .

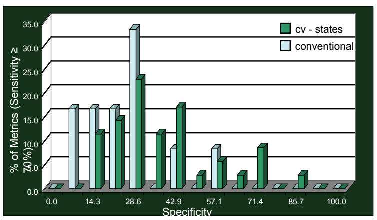


Figure 5. Diagnostic specificity histograms, for all conventional (n = 12) and c-v (n = 35) metrics having ≥ 70% sensitivity. Only one of the conventional metrics has specificity > 50%, and all are < 60%. In contrast, several c-v metrics have specificity > 70%, thereby meriting further study.

Discussion

- The percentage of event-sensitive SM-based c-v metrics is significantly greater than the corresponding percentage of SM-based conventional metrics (p = 4.3×10^{-9}, Fig. 3).
  - While the overall number of S-M c-v metrics is larger than the corresponding number of conventional metrics by a factor of 6 (Table 1), the number of *event-sensitive* cv-state metrics is greater than its conventional counterpart by a factor of 18.
  - The reason for our initial focus on SM-based metric is that these correspond to the only type of information that is obtained from FDA-approved devices comprising a single illumination site and a small number of detectors.
  - In contrast, both c-v analysis and the computation of SSDs require spatially resolved images as input.
    - The requisite real-time image reconstruction capability has been demonstrated previously.[7,8]
  - Thus optical tomography has an important advantage over simple cerebral oximetry, which does not provide the spatial variability information necessary for image reconstruction.
- Nearly half of the conventional-analysis metrics show very little sensitivity to the occurrence of clinically significant events (Fig. 4). The other half initially *seem to* perform comparably to the most sensitive c-v metrics.
  - However, only c-v metrics (Fig. 5) simultaneously yield potentially useful levels of sensitivity and specificity.
- In conclusion, our data provide credible preliminary evidence that the metrics obtained from analysis of the Hb image time series based on c-v states would be a more successful basis for an intraoperative monitoring tool, compared to evaluation of the same image data in terms of the conventional individual Hb signals (i.e., Hb_{oxy}, Hb_{deoxy}, Hb_{total}).

References

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Acknowledgements

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