Cerebral Oximetry: A “First Alert” Indicator Of Adverse Outcomes

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Introduction

Near-infrared spectroscopy (NIRS) based cerebral oximetry has been adopted by many cardiothoracic and vascular anesthesiologists to provide continuous intraoperative insight into brain perfusion and oxygenation dynamics.

Cerebral oximeters use near infrared light of various wavelengths to determine regional hemoglobin oxygen saturation (rSO2) in the frontal lobes. This is accomplished with adhesive pads applied over the frontal lobes that both emit and capture reflected near-infrared light passing through the cranial bone to and from the underlying cerebral tissue.

Beyond providing continuous insight into regional oxygenation of the brain, NIRS cerebral oximetry may allow clinicians to use the brain as an index organ which represents the adequacy of tissue perfusion and oxygenation of other vital organs, a concept that is well-supported by multiple clinical outcome studies of this monitor.

Additionally, it is of potentially striking importance to note that recently analyzed data from the Society of Thoracic Surgeons (STS) National Database strongly suggest that the intraoperative use of NIRS cerebral oximetry in cardiac surgical patients frequently (23%) served as a “first alert” indicator of an intraoperative dynamic that could lead to a potential adverse clinical outcome.

Given the large scale on which this monitoring modality has been adopted by adult and pediatric cardiothoracic and vascular anesthesiologists, the published validation studies of NIRS cerebral oximetry technology, the multiple supportive clinical outcome studies as well as the recently available STS data, renewed attention to the use of this monitor appears indicated.

This manuscript is written to provide a clinician’s perspective focused on augmenting understanding of the clinical validity and applicability of this monitor for cardiothoracic and vascular surgical patients and to consider expanding its regular use to other populations of anesthetized patients.

NIRS Cerebral Oximetry - Overview

NIRS cerebral oximetry has been studied for over thirty years (Jobsis, 1977) and has been commercially available to clinicians for over two decades (McCormick et al., 1991).

Presently there are four commercially available United States Food and Drug Administration (FDA) cleared cerebral oximeters that include the Somanetics INVOS, CASMED Fore-Sight, OrNim Cerox, and Nonin Equanox (listed in the chronological order in which they were FDA cleared). All four are indicated for use as monitors of brain oxygenation.

Additionally, the U.S. FDA recently allowed the claim that rSO2 monitoring with the Somanetics’ INVOS device improved outcome in patients > 2.5 kg who were at risk for reduced or absent blood flow in any monitored tissue (K082327).

NIRS cerebral oximetry functions on the premise that the translucent cranium permits the transmission of both near-infrared and infrared light to and from the underlying cerebral vascular tissue. The monitor specifically analyzes the hemoglobin contained in pulsatile and nonpulsatile blood within venous, arterial and capillary vessels that have a diameter of < 100 microns (Ferari et al., 2004).

Oxygenated and deoxygenated hemoglobin absorb light at different wavelengths, allowing differentiation of these two forms of hemoglobin. The adhesive pads applied to hairless skin over the frontal lobes contain light-emitting diodes (LED), or laser light sources in one manufacturer’s device, as well as light sensors. Light source wavelengths, sensor characteristics and computational algorithms are specific to each manufacturer, but all four commercially available devices have the same goal which is to determine the rSO2 in the frontal lobes, not in the skin or cranium.

NIRS Cerebral Oximetry – Clinical Use

NIRS cerebral oximeters function, in part, based on the knowledge that approximately 75% of the blood in this region is venous or capillary in nature and thus, produce saturation values that are venous-weighted. Normative cerebral rSO2 values are published for each manufacturer’s device (e.g., the Somanetics INVOS 5100 normal value for an adult cardiac surgical patient is 67±9%). While manufacturer’s recommendations vary, it appears prudent to establish bilateral room air baseline rSO2 values prior to the induction of general anesthesia. Since the devices are sensitive to light contamination (i.e. light piping if hair is present within the light pathway or contamination of rSO2 signal if the sensors are exposed to ambient room lighting), caution should be taken to securely adhere the pads to the skin. They should also be periodically observed, since skin perspiration or physical tension on the attached pads may partially detach the pad.

The changing status of the continuously generated bilateral rSO2 values are repeatedly interpreted in the context of all available clinical information and hence never considered in a vacuum. There are a number of physiologic variables that are known and/or expected to affect the observed rSO2 values.

These include, but are not limited to, the following: cardiac output, pulmonary function, PaCO2, arterial pH inspired oxygen concentration, cerebral metabolism,

cerebral temperature, local arterial blood flow, adequacy of local venous effluent, adequacy of local arterial autoregulation, hemoglobin concentration, pre-existing tissue dysfunction (e.g., cerebral infarction) within the monitored site and any mechanical perturbation (e.g., turning the head to an extent that occludes cerebral arterial inflow or direct mechanical compression of an arterial or venous vessel) that may affect blood flow in or out of the monitored tissue bed.

Further, there are numerous clinical procedure-related variables that may affect observed rSO2 values (e.g., inadvertent placement of an intra-aortic balloon pump into the left common carotid artery, arterial perfusion cannula malposition, or iatrogenic aortic dissection creating occlusion of either common carotid artery), especially in patients that do not possess a complete Circle of Willis. The gamut of procedure-related events that can adversely affect cerebral oxygenation are not limited to cardiothoracic surgical procedures.

General surgery patients can also experience events that rSO2 monitoring may herald. These include, but are not limited to, acute reductions in oxygen carrying capacity or intravascular volume (i.e. hemorrhage), hypoxemia, acute intraoperative arterial vascular occlusions (i.e. embolic events), acute venous vascular occlusions (i.e. hematoma related to vascular access attempts), acute cardiovascular collapse (i.e. CO2 venous embolus) and occult reductions in cardiac output (i.e. intraoperative myocardial infarction).

NIRS Cerebral Oximetry – Validation

With the potential for so many variables to affect the observed rSO2 values, clinicians are compelled to consider the experimental evidence which validates that this monitor reflects rSO2 values. Unfortunately, there is no index, or gold standard invasive, or noninvasive, test to unequivocally validate that NIRS cerebral oximetry reflects regional oxygenation of frontal lobe cerebral tissue.

Further complicating the validation of this monitor is the fact that the technology existing among the four commercially available devices differs significantly and hence positive, or negative, validation studies of one device are not necessarily transferrable to the other three. Of note is the fact that a large majority of the validation and clinical trial work present in the peer-reviewed literature was generated with the Somanetics INVOS device, the first commercially available device of its kind in the U.S. market.

At first thought on this topic, one would consider that the invasive, direct measurement of regional tissue oxygen pressure (i.e. tiPO2) could address this question of validation. However, it is clear that tiPO2 is not the same parameter as rSO2, and thus no absolute, direct correlations can be expected to exist. Interestingly, there is supportive evidence from human clinical studies of tiPO2 and rSO2 performed with the INVOS device demonstrating that apparent correlations exist between these two different and distinct indexes of cerebral oxygenation (Holzschuh et al., 1997; Brawanski et al., 2002).

With consideration that no single gold standard test exists to assess brain oxygenation, one of the more pertinent validation studies performed assessed the

relationship between rSO2 values and jugular venous bulb saturations (SjvO2); this study was also conducted with the INVOS device in healthy volunteers. In this study, Kim and colleagues studied the correlations between SjvO2 values (obtained from a right-sided retrograde jugular venous catheter placed with its distal tip at the level of the jugular venous bulb) and imultaneously obtained right-sided frontal lobe rSO2 and SaO2 (obtained from a radial arterial catheter) values.

Two sets of experiments were conducted, one in which the PetO2 (hypoxia) was varied during normocapnia and a second set during which the same variations were repeated while etCO2 was actively increased above (i.e. hypercapnia) their established normal room air values. In these experiments the correlation of SjvO2 and rSO2 was observed to be stronger (r = 0.84) than between SjvO2 and SaO2 (r = 0.78) during isocapnic hypoxia (established by increasing etCO2 either 2 mmHg or 7 mmHg above resting baseline values; Kim et al., 2000).

A more complex experiment performed in a small cohort of head trauma patients (n = 8) compared the observed values of rSO2, SjvO2 and tiPO2. These investigators concluded that all three of these parameters represent different physiologic measurements of cerebral oxygenation and in their experiment all three variables were observed to exhibit similar patterns of change when the FiO2 was varied.

They concluded that measuring multiple variables of cerebral oxygenation (i.e. rSO2, SjvO2 and tiPO2) provided the best insight into whether there was an actual change in cerebral oxygenation. The authors further concluded that improvement in a single index of cerebral oxygenation cannot be assumed to accurately reflect an improvement in brain oxygenation (McLeod et al., 2003).

Validation work that assessed the relationships between observed rSO2 values and hematocrit and hemoglobin concentration has been performed (Kishi et al., 2003; Han et al., 2004). No linear relationship between measured hematocrit and rSO2 values appears to exist above a hematocrit of greater than 30%. However, apparent relationships between rSO2 values and a measured
hematocrit less than 30% have been established and likely indicate declines in cerebral oxygenation when oxygen carrying capacity is reduced (Han et al., 2004).

NIRS Cerebral Oximetry – Clinical Outcomes

Given the well-established complexity encountered in validating the use of NIRS cerebral oximetry, clinicians have turned to conducting clinical trials of this monitor to test its clinical utility. These clinical trials have produced tangible and relevant results, providing reinforcement to the earlier validation studies. In a large, retrospective study involving a cohort of 2,279 cardiac surgical patients, two groups were assessed. In one group (treatment, n = 1,034), patients that underwent cardiac surgical procedures employing cerebral oximetry with an associated standardized interventional protocol were assessed. In a second group serving as a recent historical control (n = 1,245), patients undergoing similar procedures without the use of cerebral oximetry were assessed. The patients in the rSO2 monitoring group were observed to have significant reductions in the incidence of stroke (0.97% rSO2 group vs. 2.5% control; $p < 0.044$), the incidence of prolonged (i.e. > 24 hours) postoperative mechanical ventilation time (6.8% rS2 group vs. 10.6%

control; $p < 0.0014$) and the length of postoperative hospital stay ($p < 0.046$). Of great interest in this study was the fact that the most notable differences in these three significant outcomes were found among the New York Heart Association Class I patients. This fact suggests that it is not just the sickest patients who benefit from the use of NIRS cerebral oximetry monitoring (Goldman et al., 2004).

Prospective, randomized controlled trials examining the effects of employing rSO2 monitoring in cardiac surgical patients also have been conducted. Murkin et al. (2007) examined two groups of patients that were both monitored with the INVOS rSO2 device. In the first group (treatment, $n = 100$), the rSO2 results were open to the clinicians and a standardized intervention protocol was employed to treat observed desaturations below 75% of the preoperative established baseline values. In the second group (control, $n = 100$), the rSO2 data were blinded to clinicians. Patients in the control group had significantly greater area-underthe- curve (AUC) desaturation values (> 150 minute • %) ($p = 0.014$) and longer intensive care unit stays ($p = 0.029$) than in the active treatment group. Further, the observed morbidity and mortality (as assessed by the composite outcome of death, myocardial infarction, stroke, postoperative ventilation greater than 48 hours and reoperation for hemorrhage) was significantly lower in the treatment group than that observed in the control group ($p = 0.048$).

A prospective, randomized clinical outcomes study of NIRS cerebral oximetry using the INVOS has demonstrated the utility of this monitor in general surgery patients. Casati et al. (2005) studied a cohort of geriatric, abdominal surgery patients (total, $n = 122$) in which the members of one group were randomized to rSO2 monitoring with a standardized intervention protocol (treatment, $n = 56$). Members of a second group (control, $n = 66$) were monitored with a cerebral oximeter, but the results were blinded to the clinicians. The control group had a significantly larger mean AUC value ($p = 0.017$) compared with the active treatment group which represented excursions of greater magnitude and duration (i.e. minute • %) for time spent below 75% of the preoperatively established baseline value. Control patients experiencing intraoperative cerebral desaturation had significantly lower postoperative day seven mean Mini-Mental Status Exam score ($p = 0.02$) compared with patients who were treated for desaturation in the active treatment group. Additionally, patients in the control group experiencing cerebral desaturation also had significantly longer post-anesthesia care unit length of stay ($p = 0.01$), as well as significantly longer hospital length of stay (control, 25 days vs. treatment, 10 days; $p = 0.007$) compared with treated patients.

A substantial literature now evidences the potential clinical benefit of NIRS surgical/critical care monitoring. It includes more than 600 peer-reviewed retrospective studies, prospective observational studies and case reports with the first FDA cleared NIRS cerebral oximeter alone.

Society of Thoracic Surgeons National Database

The Society of Thoracic Surgeons (STS) maintains the world’s largest cardiothoracic database, the STS National Database.

The STS National Database provides a means by which to build and continuously

monitor quality assurance among cardiothoracic surgical programs in the United States. Currently there are more than 500 participating centers contributing procedural data to this repository and recent counts indicate that it houses data for over 3.77 million cardiothoracic surgical procedures. The data reporting and management methods are rigorous, which adds to the strength of this database. Given the broad number of data fields that are collected, combined with the large number of reporting centers, this database provides the ability to address several cardiothoracic-related clinical queries that otherwise might not be possible because of the time consumptive and costly nature of employing prospective methodologies to answer these same questions. From 1994 to date, over forty publications have come from the STS National Database and have appeared in peer-reviewed professional journals as well as textbooks. Additionally, the ability of the STS National Database to individually risk-stratify perioperative patients based on the collective power of this data repository is highly accurate and beneficial to clinicians.

The STS National Database supported risk-stratification tool is available free of charge to clinicians and the public on the STS website (www.sts.org).

Society of Thoracic Surgeons National Database – NIRS Cerebral Oximetry

Recently, the STS National Database began harvesting optional data fields related to the intraoperative use of NIRS cerebral oximetry in adult cardiac patients. A total of seven NIRS cerebral oximetry-related data fields are presently being captured (see Figure 1). The fields are comprised of six continuous variables (i.e. numerical) and one subjective, dichotomous variable (i.e. yes or no). The first two of the six continuous variables relate to left and right pre-anesthesia induction baseline rSO2 values. The second two continuous variables relate to both left and right cumulative saturation values below the (baseline – 25%) threshold. The cumulative values are captured as the AUC values which are represented by a dual-dimension parameter including both the time spent below the lower threshold as well as the magnitude of these excursions; thus, the units of AUC are minute • %.

For example, if a patient had a unilateral (right-sided) oxygen desaturation of 10.5% below the critical lower threshold for a total of only 6 minutes for the entire surgical procedure while cerebral monitoring was occurring then the right sided AUC value would equal 63 min • % (see Figure 2). The last two continuous variables simply capture the left and right rSO2 values that are present at skin closure. Under most conditions the AUC values represent the time interval between anesthetic induction and skin closure. The dichotomous variable which is captured is intended to establish if the use of rSO2 monitoring during the procedure was a first indicator, or “first alert” of an intraoperative event that could lead to a potential adverse outcome. Similar to the well-established utility of the STS National Database to provide useful insight into the factors that influence the quality of outcomes among cardiothoracic patients, it is possible that these newly captured rSO2-related data fields will provide further insight into the clinical utility of rSO2 monitoring.

Cerebral Oximetry: Optional Harvest

Pre-Induction Baseline Regional Oxygen Saturation: Left: _____ (%) Right _____ (%)

Cumulative Saturation Below Threshold: Left: _____ (minute-%) Right _____ (minute-%)

Cerebral Oximeter Provided The First Indication: Yes No

Skin Closure Regional Oxygen Saturation: Left: _ _ ___ (%) Right _____ (%)

Figure 1. Cerebral oximetry data fields from the STS National Database data collection tool displaying the seven optional harvest fields.

Figure 2. Screenshot from the Somanetics INVOS monitor where the red circle accentuates the area under the curve for both time and magnitude spent below the right sided threshold rSO2 value.

NIRS Cerebral Oximetry – A First Alert Indicator: Analysis of the STS National

Database Presently, cerebral oximetry data from tens of thousands of patients have been collected into the STS database and a formal initial query that may reflect the utility of this data has been launched. The Duke Clinical Research Institute (DCRI) performed a query of the STS Adult Cardiac Surgery Database cerebral oximetry parameters (Figure 1) that were collected from January 2008 through December 2009. DCRI is wellqualified to perform this type of analysis and have been the Data Warehouse and Statistical Coordinating Center for the STS National Database since 1999. Further, DCRI has vast experience with database management within their own center and their team is also well-practiced at extracting clinically useful information from large databases in a meaningful and statistically appropriate way, so that peer reviewed publications can be generated that address various complex medical questions.

In this query, the data field that sought information on rSO2 monitoring as a first indicator was assessed. Specifically, analysis of the dichotomous variable (i.e. “yes” versus “no”) indicating if cerebral oximetry monitoring served as a first indicator of an intraoperative event (i.e. technical problem or physiologic change) that could potentially lead to an adverse outcome was conducted. This analysis established

that in 23% (8,406 of 36,548) of procedures, the use of cerebral oximetry provided the first indication to an impending potential clinical problem.

While statistical analysis is not yet complete on these figures, it is expected, given the large sample size, that the results will be highly statistically significant. The validity and potential clinical significance of this preliminary query are supported by several facts.

One, there is ample foundational basic science and clinical validation work published in the peer-reviewed professional literature that strongly suggests that the use of NIRS cerebral oximetry can rapidly herald interruption of regional cerebral blood flow (Brawanski et al., 2002; Kim et al., 2000; McLeod et al., 2003).

Two, peer-reviewed literature from the human research arena including clinical trials and case reports greatly supports the notion that the use of NIRS cerebral oximetry can improve patient outcomes for those undergoing surgical procedures (Murkin et al., 2007; Goldman et al., 2004; Casati et al., 2005).

Three, the fact that this query represents the work of an experienced team of database managers and statisticians (i.e. DCRI) leaves little doubt that the technical aspects of how this data query was performed would be very difficult to challenge.

Four, routine use of NIRS cerebral oximetry technology has become a widely practiced standard of care for patients undergoing complex cardiovascular procedures, especially those involving the use of deep hypothermic circulatory arrest.

NIRS Cerebral Oximetry – Expanded Use

The published validation and clinical outcome studies of NIRS cerebral oximetry strongly suggest that this monitor has the potential to provide a measurable clinical benefit to cardiovascular and thoracic, as well as other, surgical patient populations. As previously cited, Murkin et al. (2007) and Casati et al. (2005) demonstrated a significant clinical outcomes benefit in adult cardiac and geriatric, abdominal surgical patients. Increasing patient age, acuity and the associated limited organ functional reserve are well-established trends in contemporary surgical and anesthesia practices.

Thus, NIRS cerebral oximetry is poised to provide anesthesia care providers with a noninvasive tool to continuously monitor cerebral tissue oxygenation in the increasingly aged and acutely ill patients that we encounter in the current clinical setting. As with cardiac and major abdominal cases, it is possible that this monitoring modality has the potential to improve clinical outcomes in gastric, orthopedic, neurosurgical, gynecologic, pediatric, urologic and essentially any general surgical patient population. It is clear from the existing clinical trials data related to rSO2 monitoring that the well-protected brain may act as index organ of how well all of the vital organs are perfused and oxygenated.

A review of the previously cited clinical trials revealed that the outcome benefits of its use are seen in reduced post-anesthesia care unit length of stay, reduced

incidence of stroke, reduced intensive care unit length of stay, reduced postoperative mechanical ventilation time and in a reduction of the composite outcome of death, stroke, myocardial infarction, postoperative ventilation > 48 hours and reoperation for hemorrhage. Clearly these various outcomes measures are not directly associated with just adequate cerebral protection, but their correlations have been well published.

Many potential clinical scenarios exist wherein NIRS cerebral oximetry can provide the first alert indication of a potential adverse outcome in anesthetized patients. The recently available DCRI query of the STS adult cardiac surgical database revealed reporting centers indicated that in a striking 23% of procedures rSO2 monitoring served as a first alert indicator of a potential adverse clinical outcome.

The clinical benefits of using a monitoring tool such as NIRS cerebral oximetry are likely presently underutilized in anesthetized patients and the expanded use of this technology should continue to be an active area of investigation in our specialty.

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