

# CEREBRAL OXIMETRY: A REPLACEMENT FOR PULSE OXIMETRY?

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## **Abstract**

Cerebral oximetry has been around for some 3 decades but has had a somewhat checkered history regarding application and reliability. More recently several monitors have been approved in the United States and elsewhere and the technique is emerging as a useful tool for assessing not only adequate cerebral oxygenation but also tissue oxygenation and perfusion in other organs.

## **Conflict of Interest**

The author has no financial relationships with any of the products discussed and has not received any funding for production of this paper.

## **Introduction**

Cerebral oximetry has been studied for over thirty years<sup>1</sup> and has been commercially available to clinicians for over two decades<sup>2</sup>. But, while pulse oximetry has been a standard of care for decades, only recently has cerebral oximetry been not only extensively studied but also adapted to investigate changes in oxygen delivery to the brain and how the monitor may be used as a “first alert” of impending organ dysfunction in other parts of the body<sup>3</sup>. It is a noninvasive technology using near-infrared spectroscopy (NIRS) to monitor regional cerebral tissue oxygen saturation (rSO<sub>2</sub>). NIRS has been widely used for assessing cerebral tissue oxygenation in a variety of populations including the fields of neonatology, anesthesiology, neurology, and cardiac surgery.

## **Mechanism of action**

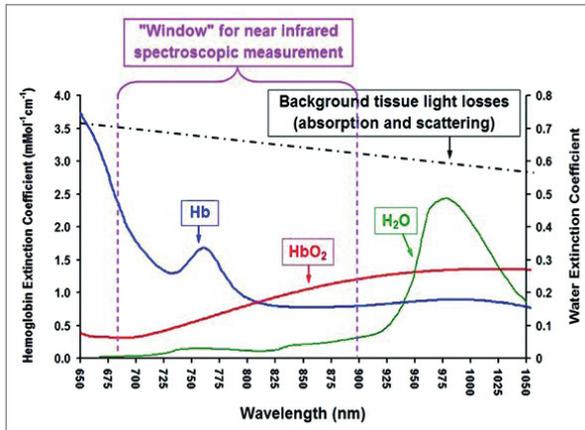
Cerebral oximetry estimates regional tissue oxygenation by transcutaneous measurement of the cerebral cortex, an area of the brain that is most susceptible to changes in oxygen supply and demand and has limited oxygen reserve. Measurement is based on the ability of light to penetrate the skull and determine hemoglobin oxygenation according to the amount of light absorbed by hemoglobin (near-infrared spectroscopy, NIRS)<sup>4</sup> (Fig. 1) Unlike pulse oximetry, NIRS cerebral oximetry uses 2 photo-detectors with each light source, which allows selective sampling of tissue beyond a specified depth beneath the skin. Near-field photo-detection can then be subtracted from far-field photo-detection to provide selective tissue oxygenation measurement. Adhesive pads are 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.

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Fig 1

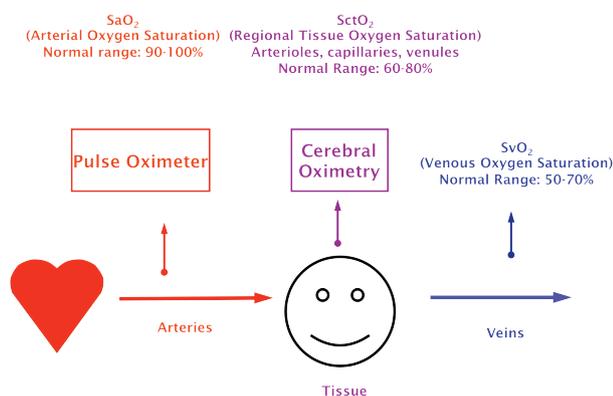
Near-infrared light passes readily through skin and skull and is absorbed by biological molecules in the brain. A spectroscopic window exists in the wavelength range of 660-940nm. (figure courtesy of G Fischer MD)



Tissue sampling by cerebral oximetry is mainly from venous (70-75%) rather than arterial (25%) blood and is independent of pulsatile flow (Fig. 2). Monitoring is non invasive and can provide an early warning of decreased oxygen delivery. Many cardiothoracic and vascular anesthesiologists have adopted the technique to provide continuous intraoperative insight into brain perfusion and oxygenation dynamics.

Fig. 2

Cerebral oxygenation values are between arterial and venous levels. (Figure courtesy of G Fischer MD)



Presently four commercially available cerebral oximeters have been approved by the United States Food and Drug Administration (FDA) for adult use: Somanetics INVOS, CASMED Fore-Sight, OrNim Cerrox, and Nonin Equanox. The Somanetics' INVOS device has also been shown to improve outcome in patients >2.5 kg who were at risk for reduced or absent

blood flow in any monitored tissue.

Normal cerebral rSO<sub>2</sub> 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%). Bilateral room air baseline rSO<sub>2</sub> values should be established prior to the induction of general anesthesia or measurement by secure adherence of the pads to the skin. Values must be interpreted in the context of available clinical information as many factors alter measurements including cardiac output, blood pressure, hypo/hypercapnia, arterial pH, inspired oxygen concentration, temperature, local blood flow, hemoglobin concentration, hemorrhage, embolism, pre-existing disease (e.g., cerebral infarction) and position changes among others. With so many variables there is as yet no gold standard test to unequivocally validate that cerebral oximetry reflects regional oxygenation of frontal lobe cerebral tissue. Also, given that the technology of the several devices differs, individual validation is required. It may be reasonable to suggest that invasive and direct measurement of regional tissue oxygen pressure (tiPO<sub>2</sub>) might be equivalent to rSO<sub>2</sub> but these are not the same parameters although some correlations may exist.

The adequacy of global oxygen delivery depends also on central venous saturation. Traditional techniques required the placement of invasive central venous access devices. A recent study of 40 patients compared two non-invasive technologies for the estimation of regional venous saturation (reflectance plethysmography and NIRS), using venous blood gas analysis as the gold standard.<sup>5</sup>In the first group a reflectance pulse oximeter probe was placed on the skin overlying the internal jugular vein. In the second group, a cerebral oximeter patch was placed on the skin overlying the internal jugular vein and overlying the ipsilateral cerebral hemisphere. Oxygen saturation estimates from both groups were compared with measured saturation from venous blood. Correlation was statistically significant for near infrared spectroscopy, but not for transcutaneous regional oximetry. Placement of cerebral oximetry patches directly over the internal jugular vein (as opposed to on the forehead) appeared to approximate internal jugular venous saturation better, suggesting this modality may offer additional clinically useful information regarding global cerebral oxygen supply and demand matching.

These findings have also been confirmed by Marimon et al in a study of 20 pediatric patients undergoing cardiac surgery.<sup>6</sup> Cerebral oximetry and somatic renal oxygen saturation correlated significantly with continuous oxygen saturation from a central venous catheter.

## Applications

Beyond providing continuous insight into regional oxygenation of the brain, cerebral oximetry may allow clinicians to use the brain as an index organ that points to the adequacy of tissue perfusion and oxygenation of other vital organs, a concept supported by multiple clinical outcome studies<sup>3,7,8</sup>. Data from the Society of Thoracic Surgeons (STS) National Database strongly suggest that the intraoperative use of cerebral oximetry in cardiac surgical patients frequently (23%) served as a “first alert” indicator of an intraoperative dynamic that could lead to a potentially adverse clinical outcome in both adult and pediatric patients. This Society (STS) collects the world’s largest database for cardiothoracic cases with more than 500 participating centers contributing procedural data for over 3.77 million cardiothoracic surgical procedures ([www.sts.org](http://www.sts.org)). Seven cerebral oximetry-related data fields are presently being collected. (Fig. 3) One and two collect right and left pre-anesthesia induction baseline rSO<sub>2</sub> values. Three and four relate to both left and right cumulative saturation values below the threshold (baseline-25%). The cumulative values are captured as the area under the curve (AUC) and include 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 (left-sided) oxygen desaturation of 15% below the

critical lower threshold for a total of 10 minutes for the entire surgical procedure then the left sided AUC value would be 150 min •%. Five and six fields record rSO<sub>2</sub> values that are present at skin closure. The final variable asks if the use of rSO<sub>2</sub> monitoring during the procedure was a first indicator, or “first alert” of an intraoperative event that could lead to a potential adverse outcome. These newly captured rSO<sub>2</sub>-related data fields will provide further insight into the clinical utility of rSO<sub>2</sub> monitoring.

The Duke Clinical Research Institute (DCRI) examined the STS Adult Cardiac Surgery Database cerebral oximetry parameters collected from January 2008 through December 2009 specifically enquiring if item 7 were a “first alert”. This analysis established that in 23% (8,406 of 36,548) of procedures, the use of cerebral oximetry provided the first indication of impending potential clinical problem<sup>3</sup>. The statistical analysis is ongoing.

Several large clinical trials of cerebral oximetry have been conducted. In a retrospective study of 2,279 cardiac surgical patients, Goldman et al assessed two groups of patients<sup>9</sup>. Only group 1 employed rSO<sub>2</sub> monitoring. Significant reduction of stroke (0.97% rSO<sub>2</sub> group vs. 2.5% control;  $p < 0.044$ ), postoperative mechanical ventilation time (6.8% rSO<sub>2</sub> group vs. 10.6% control;  $p < 0.0014$ ) and the length of postoperative hospital stay ( $p < 0.046$ ) were established in the monitored group. The most notable differences in these outcomes were found among the New York Heart Association Class I patients, indicating that monitoring benefits not only the sickest patients. Prospective, randomized controlled trials examining the effects of employing rSO<sub>2</sub> monitoring in cardiac surgical patients also have been conducted. Murkin et al examined the results in patients in whom

Fig 3

*The Society of Thoracic Surgeons (STS) National Database Fields related to cerebral oximetry*

Cerebral Oximetry: Data Collection from the Society of Thoracic Surgeons

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

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

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

Cerebral Oximeter Provided the First Indication: Yes /No

saturations fell below 75% of preoperative levels and were treated and compared the outcome to patients who were not treated.<sup>7</sup> Patients in the control group had longer intensive care unit stays ( $p = 0.029$ ) than in the active treatment group. Morbidity and mortality were significantly lower in the treatment group than that observed in the control group ( $p = 0.048$ ). More recently, Baraka has also commented on the efficacy of cerebral oximetry monitoring during cardiopulmonary bypass<sup>10</sup>.

Pedrini et al indicated the potential reliability of cerebral oximetry monitoring during carotid endarterectomy under general anesthesia, using a cutoff of -25% or a cutoff of -20% for prolonged hypoperfusion in a study of 473 patients with a mean age of 73<sup>11</sup>. Three patients presented with transient ischemic deficits at awakening but there were no cases of death or stroke. Shunting was required in 41 patients; in 30 the decision was made based on initial rSO<sub>2</sub> and in 11 after decrease of rSO<sub>2</sub> intraoperatively. Using the area under the curve analysis, for a >25% reduction from baseline, sensitivity was 100% and specificity was 91%.

Other studies in general surgery and geriatric patients have found similar improvement when rSO<sub>2</sub> falling below 75% of baseline was aggressively treated<sup>8</sup>. Control patients experiencing intraoperative cerebral desaturation had significantly longer PACU stays and lower postoperative day seven mean Mini-Mental Status Exam score ( $p = 0.02$ ) compared with patients who were treated for desaturation. Another study by Tang et al of 76 patients undergoing thoracic surgery with single lung ventilation showed that early cognitive dysfunction related positively to intraoperative decline of rSO<sub>2</sub><sup>12</sup>. In fact more than 600 peer-reviewed retrospective studies, prospective observational studies and case reports attest to the clinical value of rSO<sub>2</sub> monitoring in critical care operative situations<sup>3</sup>.

### Outside of the Operating Room

Although rSO<sub>2</sub> monitoring has been used mainly in the operating room, Padmanabhan et al reported a procedural emergency room study in 2009<sup>13</sup>. Poor correlation between NIRS cerebral oximetry, pulse

oximetry and capnography was shown in 100 children between the ages of 9 months to 18 years. Various agents were used including ketamine, fentanyl, dexmedetomidine and propofol. Changes in rSO<sub>2</sub> occurred in 2.1% of patients and were associated with changes in SPO<sub>2</sub> 23% only of the time and changes in ETCO<sub>2</sub> 29% of the time. Very few hypoxic events resulted in changes in rSO<sub>2</sub> but most of the changes in rSO<sub>2</sub> were not accompanied with any changes in cardiorespiratory parameters. However, most of the children were otherwise healthy and deemed suitable for off site sedation. It would appear that rSO<sub>2</sub> is a more sensitive measure of cerebral oxygenation than pulse oximetry but isolated decreases in rSO<sub>2</sub> in children may not correlate well with short or long-term neurologic complications. Clearly more studies are indicated.

Other studies in children have compared tissue oximetry in somatic sites to that of the cerebral cortex. Mitnacht summarized recent developments and available data on the use of NIRS in children at risk for low perfusion, postulating that during states of low cardiac output, cerebral blood flow and thus cerebral NIRS may be better preserved than in somatic tissue sites<sup>14</sup>. Sites other than the frontal cerebral cortex (e.g. abdomen, flank, and muscle) have been investigated for a possible correlation with invasive measures of systemic perfusion and oxygenation. The abdominal site seems preferable to the flank site NIRS (kidney region) application. Thus, to increase the sensitivity, specificity, and positive predictive value of tissue oximetry to detect systemic hypoperfusion, multisite NIRS such as a combination of cerebral and somatic site NIRS has been suggested. NIRS has also been used to assess systemic perfusion in patients undergoing first-stage palliation for hypoplastic left heart syndrome. Multi site measuring is in the early stages and certainly more investigation is indicated as NIRS has been shown predictive in the detection of low-flow states (low cardiac output).

In the field of trauma, cerebral oximetry may also have found a place. Tausky et al compared NIRS cerebral oximetry with CT perfusion in 8 brain injured patients and found that mean cerebral blood flow measured by CT perfusion was 61ml/100gm/min for the left side and 60ml/100g/min on the right

side<sup>15</sup>. Mean NIRS values were 75 on the right and 74 on the left. Linear regression analysis demonstrated a statistically significant probability value ( $p = 0.0001$ ) comparing NIRS frontal oximetry and CT perfusion-obtained CBF values. Other investigators have used cerebral oximetry as an additional monitor in trauma patients at the scene and during transport in 33 road ambulances and 32 helicopters<sup>16</sup>. For outdoor monitoring, adequacy of signal was around 50% which improved to 100% during road transport and 86% during helicopter transport. The authors felt that not only was cerebral oximetry possible but it added valuable information.

The feasibility of evaluating the role of cerebral oximetry in predicting return of spontaneous circulation after cardiac arrest was examined by Nasir et al<sup>17</sup>. Patients with return of spontaneous circulation after in-hospital arrest had significantly higher overall mean rSO<sub>2</sub>; patients with return of circulation had an rSO<sub>2</sub> above 30% for >50% of the time of resuscitation. Non-survivors had rSO<sub>2</sub> <30% for >50% of the time. Also, survivors had a significantly higher change in rSO<sub>2</sub> from baseline as compared to non-survivors (310% vs. 150%).

In yet another study outside of the operating room, Rifai et al monitored 30 patients in cardiac failure<sup>18</sup>. All patients had New York Heart Association (NYHA) functional class I to III. All patients were on cardiac failure medical therapy. rSO<sub>2</sub> measurements were recorded from the left and right forehead simultaneously. The mean rSO<sub>2</sub> value was 67.4% (range, 47.6%-76.3%), while the mean peripheral tissue saturation SPO<sub>2</sub> was 97% (range, 92%-100%). The mean difference between cerebral and peripheral tissue oxygenation (SpO<sub>2</sub>-rSO<sub>2</sub>) was 29.2% (range, 19.2%-51.4%). There was also a significant positive correlation between rSO<sub>2</sub> and mean arterial blood pressure (0.55,  $P < .01$ ). Statistically significant lower rSO<sub>2</sub> values were observed in patients with diabetes ( $P = < .026$ ) and in patients with dyslipidemia. Thus rSO<sub>2</sub> may be an important biomarker to measure in patients in cardiac failure and may be a useful indicator of target organ perfusion.

Concerned about the incidence of cerebral injury following shoulder surgery in the beach chair position, the American Society of Anesthesiologists established

a registry in 2012 to gather information about this critical complication. Murphy et al collected data on 124 patients undergoing elective shoulder arthroscopy in the beach chair (61 subjects) or lateral decubitus (63 subjects)<sup>19</sup>. Anesthetic management was standardized in all patients. Baseline heart rate, mean arterial blood pressure, arterial oxygen saturation, and rSO<sub>2</sub> were measured before patient positioning and then every 3 minutes for the duration of the surgical procedure. rSO<sub>2</sub> values below a critical threshold ( $> \text{or} = 20\%$  decrease from baseline or absolute value  $< \text{or} = 55\%$  for >15 seconds) were defined as a cerebral desaturation event (CDE) and treated using a predetermined protocol. Anesthetic management was similar in the beach chair and lateral decubitus positions. Intraoperative hemodynamic variables did not differ between groups. rSO<sub>2</sub> values were lower in the beach chair group throughout the intraoperative period ( $P < 0.0001$ ). The incidence of CDEs was higher in the beach chair group (80.3% vs. 0% in the lateral decubitus position group), as was the median number of CDEs per subject (4, range 0-38 vs. 0, range 0-0 lateral position group, all  $P < 0.0001$ ). Among all study patients without interscalene blocks, a higher incidence of nausea (50.0% vs. 6.7%,  $P = 0.0001$ ) and vomiting (27.3% vs. 3.3%,  $P = 0.011$ ) was observed in subjects with intraoperative CDEs compared with subjects without CDEs. This study alone would suggest that cerebral oximetry monitoring be included for all patients to be operated in a beach chair position, especially if some level of hypotension is added.

### Possible conditions for errors in interpretation

It should, however, be noted that rSO<sub>2</sub> may not provide early warning of a low hematocrit immediately after initiation of hypothermic coronary artery bypass in cardiac surgery as demonstrated by Sung et al in a study of 151 surgical patients<sup>20</sup>. Also, interdevice technologic differences may impose potential variation in the ability to accurately acquire brain oxygenation signals. In twelve healthy volunteers each of three NIRS devices were randomly applied to the forehead<sup>21</sup>. Then, a circumferential pneumatic head cuff was positioned such that when inflated, hypoxia-ischemia would be produced in the extracranial

scalp tissue beneath the NIRS cerebral oximeters. Comparisons among the three devices indicated that the induction of extracranial hypoxia-ischemia resulted in a significant reduction in regional cerebral oxygen saturation measurements in all three NIRS devices studied. Thus extracranial contamination appears to significantly affect NIRS measurements of cerebral oxygen saturation. However, while the authors suggest that the clinical implications of these apparent inaccuracies require further study, they note that the oxygen saturation measurements provided by cerebral oximetry do not solely reflect that of the brain alone.

### **Concluding Comments**

These and other studies in a wide range of patient populations and ages indicate that cerebral oximetry has the potential to provide a measurable clinical benefit not only in cardiovascular and thoracic procedures. An aging population with decreasing organ functional reserve is an increasing part of anesthesia practice. This, to date underutilized, monitor can provide anesthesiologists with a noninvasive tool to

continuously monitor cerebral tissue oxygenation and has the potential to improve clinical outcomes in gastric, orthopedic, pediatric, urologic and essentially any general surgical patient population both in and out of hospital. The brain may act as an index organ of how well all of the vital organs are perfused and oxygenated.

Finally it might be noted that on at least two occasions to the author's knowledge, cerebral oximetry has featured in medical malpractice cases. In the first one, the anesthesiologist informed the surgeon (and also documented his remarks) that the rSO<sub>2</sub> had decreased on several occasions after cross clamping of the carotid but had rebounded with fluid administration. The surgeon declined to insert a shunt. The patient suffered mild hemiparesis postoperatively. In a second case, the rSO<sub>2</sub> declined 40% for about 30 minutes during carotid endarterectomy and no action was documented. The patient suffered a stroke. In one case the anesthesiologist was helped and in the other he was not although in both situations, it was argued that rSO<sub>2</sub> is not the standard of care... but that may soon change.

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