Near-infrared spectroscopy (NIRS) monitoring in contemporary anesthesia and critical care

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Abstract: Near-infrared spectroscopy (NIRS) is a non-invasive technology that continuously monitors regional tissue oxygenation. Originally used for assessment of oxygen saturation of the brain, its use has now been expanded to evaluation of oxygenation of tissues other than the brain. There is also growing evidence for the larger applicability of NIRS as an estimate of systemic venous saturation in correspondence with the adequacy of the circulatory status. New and promising advances may further this technology to become part of our standard armamentarium, in order to optimize patient care in daily anesthesia practice. The present paper briefly reviews the basic principles of operation, the inherent limitations of the technology and the clinical data that have been acquired with NIRS monitoring in the broad field of acute clinical medicine.

Key words: NIRS; spectroscopy; cerebral oxygenation; monitoring.

INTRODUCTION

The primary goal in the hemodynamic management of patients undergoing surgery is to preserve oxygen delivery at a level sufficient to cover all metabolic needs. Nowadays, anesthesiologists can rely on a variety of monitoring tools to quantify cardiovascular performance and global oxygen delivery. However, regional oxygen status of individual organs may vary significantly and local oxygen deficiencies may go unnoticed until functional organ damage becomes evident. Techniques to monitor regional tissue oxygen status would therefore add significant value to our current armamentarium, particularly for patients at increased risk for vital organ ischemia due to a specific surgical procedure or pathophysiological condition.

The first attempt to monitor human tissue oxygenation non-invasively dates back to 1874 when the German physiologist Karl von Vierordt showed that the amount of red light transmitted through a hand decreased after it was made ischemic (1). His pioneering studies were essentially ignored for half a century until it was again reported that the variable transmission of red and infrared light through a human ear reflected changes in blood oxygenation (2). The first small portable oximeter was developed in 1942 by Glen Milliken (3), although the device was used only as an experimental tool in the aviation and the physiology laboratory. The concept of cerebral near-infrared spectroscopy (NIRS) originated with the observations of Jobsis (4) who irradiated a cat’s head with near-infrared light and found that the intensity of the transmitted light varied with the oxygen metabolic state of the brain.

NIRS was originally introduced in clinical practice for the assessment of cerebral oxygenation in preterm infants (5). It was also welcomed with enthusiasm in cardiac and neuroanesthesia but its utility, particularly in the latter field of application, was seriously challenged by a series of reports on false positive as well as false negative readings. The technique was further discredited by anecdotal papers illustrating that NIRS oximeters generated near normal values when the probes were placed on an empty human skull filled with blood-soaked gauzes (6) or even on a pumpkin (7). Even today these papers are quoted to question the validity of NIRS monitoring in anesthesia. However, a fair understanding of the assumptions and limitations of NIRS technology suffice to understand that such observations are indeed possible yet do not invalidate the use of NIRS to quantify changes in the oxygen status of human tissue.

The interest in NIRS as a monitoring tool in anesthesia has revived over the past few years and several systems have now been approved for clinical use. In the present paper we briefly review the
basic principles of operation, the inherent limitations of the technology and the clinical data that have been acquired with NIRS monitoring in the broad field of acute clinical medicine.

PRINCIPLES OF OPERATION

The physical and mathematical basis for NIRS is provided by the Beer-Lambert law, which states that the quantity of light absorbed by a substance (A) is directly proportional to the specific absorption coefficient of the substance at a particular wavelength (□), the concentration of the substance (c) and the path length of the light through the solution (l) \( A = □ c l \) (8). The relative transparency of biological tissues to near-infrared light enables light photons to pass through the tissues, where they are attenuated due to a combination of absorption and scattering. NIRS technology is based on the assumption that the quantity of scattering remains constant and that changes in attenuation result solely from changes in absorption. Among several light absorbing substances (chromophores), only hemoglobin chromophores are present in variable concentrations. Other chromophores are assumed to be constant over the period of monitoring. Oximetry relies on the fact that absorption of near-infrared light at specific wavelengths is different in deoxygenated hemoglobin (Hb) when compared with oxygenated hemoglobin (O2Hb) (Fig. 1). NIRS devices use near-infrared light at two or more specific wavelengths to differentiate between O2Hb and HHb. Similar to the principles used in pulse oximetry, the device measures the amount of light absorbed at these specific wavelengths and calculates the relative contribution of O2Hb and HHb. The resulting ratio of O2Hb to total Hb (expressed as a percentage) represents the oxygen saturation of tissue under the sensor.

Jobsis (4) used transmitted light in his original experiments. Light was applied to one side of the body and received on the other side. However attenuation of light due to absorption and scattering restricts usage of this method to very thin and transparent areas of the body such as the earlobe or finger. For that reason, reflected light rather than transmitted light is being used to study absorption of light in larger tissue samples. Reflectance probes locate the light emitter and detector adjacent to one another. The light takes a “banana-shaped” pathway through the tissues, with the depth of photon penetration proportional to the source-detector separation (principle of spatial resolution) (Fig. 2).

In order to compensate for superficial tissue, which is not the tissue of interest, differentially spaced light detectors are used. Owing to the principle of spatial resolution, the closer receiver will measure more superficial tissue while the distal optode measures both superficial and deeper tissue. After subtraction of the interference from superficial tissues – the mathematical details of which are not provided by the manufacturers – oxygenation in the deeper tissues is derived.

ASSUMPTIONS AND LIMITATIONS

As with any monitoring system it is essential for the clinician to understand its underlying
technology, including the limitations, and the assumptions made to translate a physical quantity into a clinically meaningful parameter.

First of all, NIRS does not quantify oxygen molecules but calculates the ratio of light absorbencies at predefined wavelengths. External light sources may cause significant artefacts and careful shielding of the probes is therefore important. Theoretically any substance to which NIRS is applied can generate a value on the monitor. In fact, the technology is being used for more than 20 years now in the agricultural, chemical, and pharmaceutical industries, e.g. to determine the freshness of food.

Secondly, the algorithms used to calculate oxygen saturation assume a fixed distance for light to travel through the sampled area (the optical pathlength). However, different tissue components produce very different amounts of photon scattering and absorption. As a result, variations in probe positioning (9) as well as interindividual variations in the composition of tissue may result in 10 to 15% variability of the true optical pathlength measurement (10). In fact, for cerebral NIRS, the influence of extracranial tissue and blood on the optical pathlength is not known (11). It is therefore impossible to completely eliminate the potential interference of changes in extracranial flow on cerebral NIRS readings. The significant inter-individual biological variability in tissue composition causes a wide variation in ‘normal’ baseline values of volunteers. Therefore NIRS devices are best used as trend monitors. Rather than to base therapeutic decisions on absolute numbers, it is safer to rely on proportional changes of an individual’s baseline value as a basis for clinical decision making. Although individual manufacturers claim that some monitors provide reliable absolute values which can be applied universally, this statement lacks any scientific basis. In fact, to subscribe such a statement, validation studies would be required to compare NIRS data to invasive measurements of oxygen saturation in tissue samples obtained directly from the brain. Such studies have not yet been performed.

Third, the physiological correlate to which tissue saturation measurements obtained with NIRS relate, remains a matter of debate. NIRS measurements are continuous, i.e. not time-gated with respect to the cardiac cycle. Furthermore, the interrogated tissue sample contains all the different vascular components and represents a mixture of arterial, capillary and venous oxygen saturations. In contrast, pulse oximetry incorporates the variation in optical density during the cardiac cycle which enables it to define the systolic fraction of the signal. It calculates the ratio between systolic and diastolic absorption values to determine arterial oxygen saturation. In contrast to NIRS, pulse oximeters have been subjected to a calibration procedure. During calibration, readings from pulse oximeters are being compared to simultaneously obtained arterial blood samples from volunteers who undergo a controlled desaturation (down to values of 70% \( \text{SaO}_2 \)). For NIRS measurement, the precise contribution from the various vascular beds is not known but is assumed to represent a 30/70 ratio (or 20/80) of arterial to venous components (12). However, relative changes in blood volume of the venous or arterial compartment can influence cerebral saturation independently, without a true change in saturation of either. A simple example of this is a change from the head-elevated Fowlers’ position to the head-down Trendelenburg position (13).

Finally, one of the major criticisms against the use of NIRS as a neuromonitor is that marked decreases in cerebral oximetry may occur without apparent resultant neurologic damage. It should be clear that low cerebral saturations reflect an oxygenation imbalance, indicating a potential risk of ischemia, but does not necessarily indicate tissue damage. The transition to irreversible injury depends on both the severity and duration of hypoxia. On the other hand, the measurements obtained with NIRS are regional, and strictly confined to the zone beneath the sensor. Clinically relevant focal cerebral ischemia in a brain area remote from the monitored area may easily go unnoticed. These limitations undoubtedly explain the relatively low sensitivity and specificity reported for carotid endarterectomy (14).

**Clinical Considerations in NIRS Monitoring**

To obtain an individual reference baseline value, NIRS monitoring is best initiated before preoxygenation and anesthesia induction. Self-adhesive sensors containing the infrared light source and light detectors are fixed on one or both sides of the forehead. The values reported for regional cerebral oxygen saturation (\( r\text{SO}_2 \)) are 71 ± 6% in young healthy adults (15) compared with 67 ± 10% in cardiac surgery patients (16). In most clinical studies cerebral desaturation is defined as a 20% reduction from baseline values or an absolute decrease below 50% (16). At present, the critical threshold requiring intervention is not yet known. Therefore it is important to assess changes in oxygen saturation
over time and to relate these changes to specific events.

Figure 3 illustrates NIRS monitoring during anesthesia for defibrillator implantation. During anesthesia induction (Fig. 3A) an increase in rS\text{O}_2 is seen due to preoxygenation and suppression of cerebral metabolism. To test proper functioning of the defibrillator, ventricular fibrillation was induced, resulting in immediate and profound cerebral desaturation (Fig. 3B). After restoration of circulation by defibrillation rS\text{O}_2 instantly normalized.

A clinical algorithm to correct for decreases of rS\text{O}_2 values is depicted in table 1. In case of decrease, first step is to rule out technical or mechanical causes. Verify that the sensors are well positioned, because an inappropriately applied sensor will capture ambient light and may display a wrong value. Then rule out technical and mechanical causes of hypoperfusion. During extracorporeal circulation, a malpositioned arterial or venous cannula may compromise cerebral perfusion pressure, resulting in immediate cerebral desaturation. Proper repositioning of the cannula instantaneously leads to effective restoration of rS\text{O}_2 (Fig. 4). Since the introduction of NIRS in cardiac surgery, it turned out that NIRS is often the first and only indicator of cannula malpositioning (17), which strongly suggests that the incidence and impact of cannula misplacement have been underestimated in the past.

Once technical and mechanical problems have been excluded, the next step is to optimize those factors that influence NIRS values. A change in NIRS values can be caused by a wide variety of pathophysiological conditions since every parameter that affects oxygen balance, both supply and demand, will change tissue oxygen saturation. Cerebral oxygen delivery can be increased by optimizing cardiac output and increasing arterial oxygen content (P\text{aO}_2, Hb).

Considering hemoglobin is an important determinant of tissue oxygenation, low rS\text{O}_2 values may be related to low hemoglobin levels. Some investigators have proposed using rS\text{O}_2 as a transfusion trigger (18, 19). However, transfusion will not invariably increase rS\text{O}_2 (20), considering hemoglobin is only one determinant of tissue oxygenation and since blood processing may reduce hemoglobin oxygen-carrying capacity by up to 90% (21).

Because the cerebral circulation is very responsive to changes in carbon dioxide (CO$_2$), deliberate hypercapnia will increase rS\text{O}_2. In a patient with normal CO$_2$ reactivity, cerebral blood flow changes 1-2 ml/100g/min per mmHg CO$_2$ change (22).

Theoretically, cerebral blood flow should be constant when cerebral perfusion pressures range between 50 and 150 mmHg. However, this concept of cerebral autoregulation is increasingly questioned, since there is an enormous individual variation in the autoregulation limits (23), and multiple causes during surgery might impair cerebral autoregulation such as hypothermia, vasoactive drugs, anesthetics, endothelial dysfunction and inflammatory responses (24, 25). It was shown that

![Figure 3](image_url)

**Fig. 3.** — Time plot of cerebral oxygen saturation (rS\text{O}_2) from the left (grey line) and right (black line) frontal cortex. Case: Implantation and testing of defibrillator. A: Anesthetic induction. B: Ventricular fibrillation.
NIRS has the potential to identify impaired cerebral autoregulation and to detect otherwise unnoticed cerebral hypoperfusion (26, 27).

If a reduction in rS\textsubscript{cO}\textsubscript{2} values is observed despite optimization of cerebral oxygen delivery, steps to decrease cerebral oxygen consumption can be taken such as brain cooling and increasing anesthetic depth.

In summary, decreasing NIRS values undeniably reflect a deterioration of the oxygen delivery-demand balance which should trigger a search for potential causes and provide an early opportunity for therapeutic correction.

**Clinical studies**

There is an exhaustive and still growing body of literature concerning the use of NIRS in clinical anesthesia. Whereas initial research focused on the use of NIRS as a mere brain monitor in neurosurgery and cardiovascular surgery, now interest extends to other surgical areas and to the evaluation of oxygenation of tissues other than the brain.

**Neurosurgery/neurointensive care**

The reliability of NIRS in this setting has been seriously questioned. In conditions where the brain is threatened, light absorption and scattering is highly variable, making accurate quantification impossible (28). Importantly, MAEDA et al. (29) found cerebral oxygenation values ranging from 0.3% to 95% in 214 human cadavers. The variation was dependent on the total hemoglobin content, cause of death, and cadaver-storage conditions. Obviously, these data indicate that NIRS would not qualify to assess cerebral death.
Cardiac surgery

As the incidence of neurologic complications is particularly high in patients undergoing cardiac operations (30, 31), the potential to monitor the brain in a simple, non-invasive way was appealing for anesthesiologists managing cardiac surgery patients. In congenital heart surgery, most centres have adopted NIRS very quickly as standard of care. Because changes in cerebral hemodynamics and oxygenation are common during pediatric cardiac surgery, putting these children at risk for brain damage, real-time neurological monitoring is considered as an integral part of neuroprotective strategies for pediatric cardiac patients. A growing number of case reports describe the early detection of potentially catastrophic events by NIRS monitoring, which likely prevented brain injury (32-34). In addition, the potential for instantaneous hemodynamic evaluation and timely intervention has been proven invaluable during high risk pediatric cardiac surgery (35).

The interest in NIRS extended soon from congenital to adult cardiac surgery. In several observational studies, routine use of perioperative cerebral oximetry monitoring in patients undergoing cardiac surgery has been demonstrated to reduce neurological complications (36-38) and to shorten hospital stay (39). However, to justify new technology it is important to prove that interventions based on this technology effectively improve clinical outcome. Currently, three interventional trials in the domain of cardiac surgery and anesthesia have addressed this question.

The first one, from Goldman et al., compared 1245 patients who underwent cardiac surgery before cerebral oximetry was incorporated, with 1034 patients in whom rS\textsubscript{O}\textsubscript{2} was maintained near to each patient’s pre-induction baseline (40). The latter group had fewer permanent strokes (0.97% vs 2.5%), shorter ventilation times, and decreased hospital stay. The weakness of this study is its non-randomized and retrospective design.

In the second interventional trial, Murkin examined perioperative major organ morbidity in a prospective, randomized blinded study of 200 coronary artery bypass patients (41). Hundred patients were randomized to intraoperative cerebral saturation monitoring with an active display and treatment intervention protocol, and 100 patients underwent blinded cerebral saturation monitoring. Significantly more major organ dysfunction (death, ventilation >48 h, stroke, myocardial infarction) was observed in the control group versus the intervention group.

In the most recent interventional trial, Slater et al. found that patients with a higher desaturation score (a score accounting for both depth and duration of desaturation) had a significantly higher risk of early postoperative cognitive decline and prolonged hospital stay (42). Due to poor compliance to the treatment protocol, Slater was not able to demonstrate that treatment of cerebral desaturation resulted in better outcome.

Carotid endarterectomy (CEA)

Perioperative stroke is a major risk of CEA. Stroke may be caused by hypoperfusion during cross-clamping of the internal carotid artery, or by embolism during insertion of a shunt. Many studies investigated the usefulness of NIRS to detect patients developing cerebral ischemia during cross-clamping, trying to define the indication for a shunt. Although several studies showed that rS\textsubscript{O}\textsubscript{2} during carotid cross-clamping decreased significantly more in patients who developed neurological symptoms (14, 43), defining a meaningful cutoff for decline in rS\textsubscript{O}\textsubscript{2} associated with neurologic threat is very difficult (44). The negative predictive value is high, but the positive predictive value is unacceptably low, hence cerebral oximetry cannot be relied on for decision making about placement of a shunt during CEA (45).

Noncardiac surgery

A large multicenter study (International Study of Post-Operative Cognitive Dysfunction (ISPOCD) (46) showed that after major non-cardiac surgery, postoperative cognitive dysfunction was present in 26% and 10% of the patients respectively at 1 week and 3 months after surgery. Although the etiology is not completely clear, it is assumed that unrecognized cerebral hypoperfusion can be implicated in a significant number of perioperative brain damage. Casati prospectively monitored rS\textsubscript{O}\textsubscript{2} in 122 elderly patients undergoing major abdominal surgery. Twenty% of the patients experienced a decrease in rS\textsubscript{O}\textsubscript{2} below 75% of baseline. Correcting low rS\textsubscript{O}\textsubscript{2} was associated with a lower incidence of immediate postoperative confusion and an earlier hospital discharge (47).

Other organ applications

The interest for using NIRS as a monitor of oxygen status in tissues other than the brain is growing. Regional saturation monitoring at somatic
sites has been advocated as an early warning system for changes in the oxygen supply-demand balance. As cardiac output falls, the sympathetic stress response raises vascular resistance, redistributing blood flow to the brain and heart, leaving other tissues – typically kidneys, liver, and intestines – at increased risk for silent ischemia. Currently, rSO$_2$ monitoring of kidneys (48), liver tissue (49, 50), splanchnic tissue (51) and muscles (52) are extensively being studied to evaluate their potential to detect perfusion deficits. Other promising applications of NIRS are prediction of splanchnic ischemia in neonates (53, 54), diagnosis of compartment syndrome (55), assessment of peripheral vascular disease (56), monitoring of free flaps (57) and monitoring of spinal ischemia during thoracoabdominal aneurysm repair (58). For all these applications it is important to realize that the mean depth of light penetration is proportional to the light source-detector distance, however the exact depth of penetration of near-infrared light is not known (59). For a number of applications there is little evidence yet to guarantee that the device truly interrogates the organ of interest. One of the concerns with these new applications is that changes in the oxygen status of non-vital organs may be a too sensitive marker for hemodynamic compromise and result in a large number of unnecessary interventions. Future work is needed to identify which of these applications are of benefit in clinical practice.

**CAN NIRS ADD SIGNIFICANT VALUE TO STANDARD ANESTHESIA MONITORING?**

Current standard anesthesia monitoring has two major drawbacks. Firstly, it provides a global assessment of the patient’s status, therefore vital organ ischemia may go unnoticed until functional organ damage becomes evident. Case reports of dramatic neurologic outcome after minor surgery in healthy patients (60) point out the compelling need for organ-specific monitoring. Despite its vital importance, the human brain remains a poorly monitored organ in clinical anesthesia. A second drawback is that the majority of variables monitored in contemporary anesthesia focus on oxygen supply (cardiovascular performance, hemoglobin and arterial oxygen content) but do not assess imbalances between oxygen supply and demand. The use of central and mixed venous oxygen measurements to assess oxygen consumption is gaining interest now in perioperative care (61). However current techniques for assessing venous oxygen saturation are invasive and therefore not used routinely in clinical anesthesia.

Initially, the interest in the use of cerebral oximetry focused on the detection of asymmetric changes, indicating a potentially catastrophic cerebral event. In recent years, a growing understanding of the physiological principles of NIRS led to a more complete appreciation of its potential. As stated earlier, rS.O$_2$ measured with NIRS primarily reflects venous oxygen saturation in the brain since the ratio of arterial to venous blood is about 30:70 (12). When cardiac output decreases progressively, cerebral autoregulation and preferential distribution of cardiac output to the brain preserves perfusion to the brain longer than perfusion to any other organ system. Consequently, decreases in cerebral venous oxygen saturation usually occur when global venous oxygen saturation is also deteriorating. Not surprisingly, NIRS-measured cerebral oxygen saturation was shown not only to correlate with oxygen saturation in blood obtained from the internal jugular vein (62), but also from the pulmonary artery (63) and superior caval vein (62, 63). In figure 5 is demonstrated how changes in mixed venous oxygen saturation are closely followed by changes in cerebral saturation. Even though perfusion of the brain is momentarily preserved when cardiac output declines, the brain appears to offer a “window” on global hemodynamics and NIRS seems to provide a non-invasive monitoring tool to assess global tissue perfusion. This notion is supported by the results of Murkin (41) who showed that optimizing cerebral NIRS also enhanced global tissue oxygenation, resulting in significantly less major (non-cerebral) organ morbidity.

**NIRS DEVICES**

Several NIRS devices for measuring cerebral oxygen saturation are commercially available, three of which are FDA-approved: INVOS 5100 (Somanetics Corporation, Troy, MI, USA), Foresight (CAS Medical Systems, Branford, CT, USA) and Equanox 7600 (Nonin Medical Inc., Minneapolis, MN, USA). NIRO-200NX (Hamamatsu Photonics Corp, Tokyo, Japan) is not FDA approved. Despite the identical basic technology using near-infrared wavelengths to detect changes in the concentration of O$_2$Hb and HHb, there are several technical differences, which are summarized in table 2. NIRO employs the technique of Spatially Resolved Spectroscopy (SRS), multiple closely spaced detectors to measure light...
attenuation as a function of source-detector separation) to measure tissue oxygen saturation and change in hemoglobin. Independently of the SRS method, NIRO measures changes in concentration of O$_2$Hb, HHb and total hemoglobin using the Modified Beer-Lambert method. INVOS, Foresight and Equanox use the Modified Beer-Lambert law to measure tissue oxygen saturation, and eliminate the contribution of extracerebral tissue by using the principle of Spatial Resolution (depth of photon penetration proportional to the source-detector separation). The NIRS devices also differ significantly in applied algorithms, most probably also in penetration depth, and therefore their comparability is not clear. To date there has been no direct comparison between the four technologies.

**Conclusion. NIRS: When and why should we measure?**

In an era where clinical outcome is increasingly determined by optimizing specific target organ function, there is a constant need for accurate and specific monitoring equipment during the critical perioperative period. Based on the direct relationship between cerebral oxygenation and neurological outcome, NIRS has been used to detect deficits...
in cerebral perfusion during complex cardiac and cerebrovascular procedures with varying success. More importantly, there is growing evidence for the larger applicability of NIRS as an estimate of systemic venous saturation in correspondence with the adequacy of the circulatory status. Due to the advantage of simple, continuous and non-invasive monitoring, NIRS has the potential to become a valuable tool to optimize patient care in our daily anesthetists practice.

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