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## CEREBRAL OXIMETRY: A REVIEW OF NIRS DEVICES

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### ABSTRACT

Continuous real-time monitoring of the adequacy of cerebral perfusion provides important therapeutic information in a variety of clinical settings. An imbalance between cerebral oxygen supply and demand can lead to cerebral hypoxic/ischemic injury. Lower levels of cerebral oxygenation have been associated with increased neurocognitive dysfunction, a higher incidence of major organ morbidity, worse outcomes and extended hospital length of stay. The current clinical availability of several non-invasive near infrared spectroscopy based cerebral oximetry devices represents a potentially important development for the detection of cerebral ischemia. This review aims to give an introduction to the basic principles of cerebral oximetry and offers an overview of currently available devices for monitoring cerebral tissue oxygen saturation.

**Keywords-** *Near Infrared Spectroscopy (NIRS), Oxygenated Hemoglobin (HbO<sub>2</sub>), Deoxygenated Hemoglobin (Hb), Cerebral tissue hemoglobin oxygen saturation (SctO<sub>2</sub>)*

### I. INTRODUCTION

Measurements of cerebral oxygenation are useful in assessing the balance between cerebral metabolic supply and demand. Various techniques are available to monitor different aspects of cerebral activity which includes electroencephalogram (EEG), brain saturation via jugular bulb oximetry (SjVO<sub>2</sub>) and near infrared spectroscopy (NIRS)(1). Cerebral activity monitoring during surgical procedures is not new. NIRS cerebral oximetry has been studied for more than 30 years (2) and has been commercially available to clinicians for more than two decades(3). SjVO<sub>2</sub> is a direct invasive method to measure cerebral tissue oxygen saturation(SctO<sub>2</sub>). In contrast, cerebral oximetry with NIRS offers a noninvasive, easy to use and continues to gain acceptance as a crucial monitoring tool in critical care environments(4). NIRS has been widely used for assessing SctO<sub>2</sub> in a variety of populations including the fields of neonatology, anesthesiology, neurology and cardiac surgery(5,6). Cerebral oximetry allows for assessment of adequacy of cerebral perfusion and is used to detect cerebral hypoxia during surgical procedures and various complex conditions which may lead to neurological injuries, neurocognitive decline and increased length of stay.

Cerebral oxygenation and perfusion are important clinical parameters, since hypoxia is the primary cause of neurological injuries. These parameters may help guide intraoperative monitoring during procedures associated with neurological complications. While stroke and cognitive dysfunction are complications of many surgical procedures, the incidence following cardiac surgery remains highest with rates of approximately 3-6% and 30-50% respectively(7). Consequently, prompt identification of cerebral hypoxia before irreversible injury occurs is paramount. Multiple etiologies have been proposed for these neurological disorders. Microembolism, macroembolism, hyperperfusion, or some combination of these are the most likely the reasons. In all of these scenarios, the final pathway is tissue ischemia which results in neuro degeneration.

NIRS is used to assess cerebral tissues and involves the use of near infrared (NIR) light of various wavelengths to determine SctO<sub>2</sub> in the frontal lobes. NIR light can penetrate through the brain without harmful ionization(8). This is accomplished with forehead probe positioned over the frontal lobes that both emit and capture reflected NIR light passing through the cranial bone to and from the underlying cerebral tissue. In the NIR region, there are many light absorbing chromophores, but only three are important in respect to oxygenation. They are the oxygenated hemoglobin (HbO<sub>2</sub>), deoxygenated hemoglobin (Hb) and cytochrome oxidase(CtOx). Hb and HbO<sub>2</sub> are found inside the red blood cells and CtOx is the enzyme which is located in the mitochondrial membrane. The concentration of CtOx in living tissue is usually atleast an order of magnitude below that of Hb(9). Therefore, its contribution is often neglected.

Measurement of cerebral oxygenation using NIRS technique is based on a light absorbent law called Lambert-Beer's law which states that for an absorbing compound dissolved in a non-absorbing medium, the attenuation (A) of an incident light is proportional to the concentration of the absorbing compound in the solution (c) and the optical pathlength (d)(10).

$$A = \log(I_0/I) = \epsilon.c.d$$

where  $I_0$  is light intensity incident on the medium,  $I$  is light intensity transmitted through the medium,  $\epsilon$  is the specific extinction coefficient of the absorbing compound. This law allows to calculate an estimate of the Hb and HbO<sub>2</sub> in the interrogated tissue.

## II. PRINCIPLE OF CEREBRAL OXIMETRY

Cerebral oximeters consist of the basic components such as light source to deliver light of a known wavelength to the tissue, a light detector to measure the intensity of light exiting the tissue and a process to translate changes in light intensity to a SctO<sub>2</sub> value(11,12). It uses the physical principle of light transmission, absorption and reflection to noninvasively measure the concentration of Hb and HbO<sub>2</sub> within brain tissue, thus providing a continuous measure of cerebral oxygenation.

This technique employs principle of optical spectrophotometry which exploits the fact that biological material including skull is relatively transparent in the NIR range and therefore NIR light can easily penetrate several centimeters through cerebral tissue(13). Light transmission depends on a combination of reflectance, scattering and absorption effects (14). Reflectance is primarily a function of the angle of the light beam to the tissue surface, while scattering decreases with increasing wavelength, favouring transmission of shorter NIR light (650- 1100 nm). Absorption occurs at specific wavelengths, determined by the molecular properties of the materials in the light path. Above 1300 nm, water absorbs all photons over a pathlength of a few millimetres, while below 700 nm, increasing light scattering and intense absorption bands of hemoglobin prevent transmission. In the 700-1300 nm range, however, NIR light penetrates tissue several centimeters.

Hb and HbO<sub>2</sub> absorb light at different wavelengths, allowing differentiation of these two forms of hemoglobin (Figure1). Tissue absorption of NIR light is primarily determined by hemoglobin and since Hb and HbO<sub>2</sub> have different absorption capacities, the degree of oxygenation, i.e. the relation between Hb and HbO<sub>2</sub> within the tissue can be determined(15).

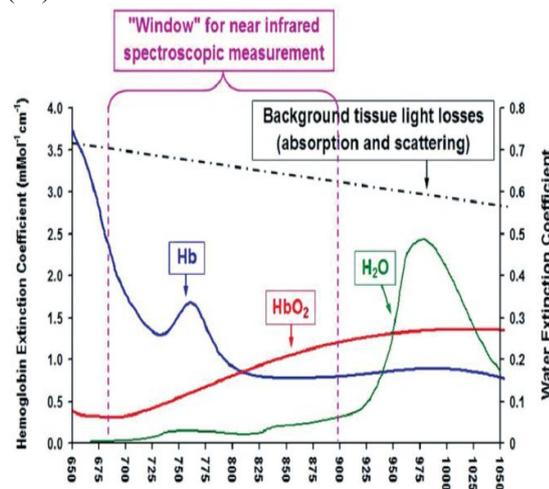


Fig.1 Light absorption spectra of Hb and HbO<sub>2</sub>(16)

Measurement of SctO<sub>2</sub> is determined by using a specially designed forehead probe. This probe comprise adhesive pad applied to hairless skin over the frontal lobes which contain light emitting diodes (LEDs) or laser light sources and two (or more) sensors placed several cm's apart. Light sources emit photons in the NIR spectrum capable of tissue penetration of several centimeters through the cranial bone to the underlying cerebral tissue. This light is partly reflected, partly redirected, scattered and absorbed. The light scattered within the brain tissue follows a predictable path that resembles a "banana like" or curvilinear arc within the tissue(17). Because of this scattering, the photons detected by the sensor close to the emitter have passed through shallow layers of the head i.e. skin and skull, while the photons detected by the sensor farther from the emitter have gone through the deeper layers i.e. the skin, skull, muscle tissue and brain tissue. The first detector (scalp sensor) captures the saturation level from extracerebral tissue and gives a superficial signal. The second detector (brain sensor), allows the analysis of a deeper signal from brain tissue as shown in Figure 2. The device uses mathematical algorithms based on the Lambert-Beer's law subtracting the superficial signal from the deeper signal to give only the value of SctO<sub>2</sub>(18) which will result in a balance between O<sub>2</sub> supply and consumption.

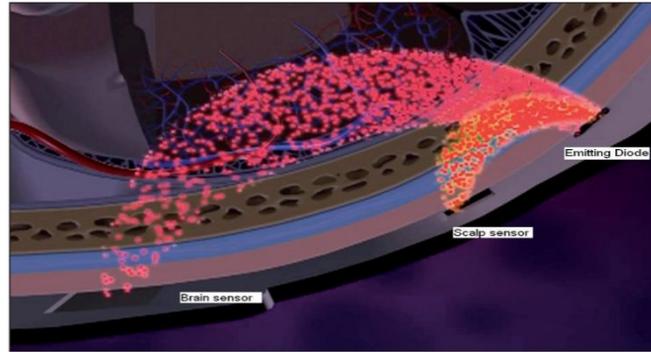


Fig.2 Technology of brain oximetry allows sampling of brain tissue from two photodetectors, each with light sources penetrating to different depths (19)

### III. CLINICAL UTILITY OF CEREBRAL OXIMETRY MONITORING

NIRS based cerebral oximetry is used in monitoring of cardiovascular surgery, traumatic brain injury, cerebrovascular diseases, cerebral palsy etc. In addition to this, it provides a sensitive index of cerebral hypoxia, which is one of the main causes of brain injury(20,21).Neurocognitive dysfunction occurs in aortic surgery patients which is likely due to brain ischemia during cardiac surgery. In cardiac surgery, use of cerebral oximetry has been shown to significantly reduce adverse clinical outcomes, including permanent stroke and to improve economic outcomes via decreased ICU and hospital stays(22-24).

SctO<sub>2</sub> values are important to clinicians because it permits early detection of cerebral hypoxia and guides therapy to restore it. Cerebral hypoxia is a leading cause of irreversible neurological injuries and occurs in many surgical and clinical situations. If left unchecked, it may lead to adverse clinical outcomes such as short or long term brain damage, paralysis, disabilities or death(25,26).

Cerebral oximetry is used to avoid catastrophic events. It is used to prevent cerebral desaturation occurred due to hypocapnia, which led to cerebral vasoconstriction and hypoperfusion and other undetected clinical events that could result in injury or death. Therefore, real-time monitoring of brain ischemia during any of the above conditions using cerebral oximeter is crucial in critical conditions.

### IV. EVOLUTION OF CEREBRAL OXIMETRY

Presently there are four NIRS based commercially available United States Food and Drug Administration (FDA) cleared cerebral oximeters that are marketed as of the publication date. These include Somanetics INVOS (Figure3),Casmed FORESIGHT (Figure4),Ornim CerOx (Figure5) and Nonin EQUANOX (Figure6) (listed in the chronological order in which they were FDA cleared).All these devices are portable, non-invasive and easy to use in operating room, neurocritical care, trauma units, ICU etc. These devices are developed to monitor SctO<sub>2</sub> to detect changes in the concentrations of HbO<sub>2</sub> and Hb and provide information to guide the timely initiation of interventions and therapies to protect the brain from hypoxia.

Although all commercially available cerebral oximeters use same components but there appears to be some difference in approach between these devices. Each device employs different light sources (LEDs vs Lasers),different numbers of wavelengths and different computational algorithms but all with the same goal of most accurately determining SctO<sub>2</sub> values in the cerebral tissue. Based on the distribution of arterial and venous blood in the brain tissue, SctO<sub>2</sub> is calculated according to a ratio of the arterial to venous saturation.



Fig. 3 INVOS Cerebral Oximeter(27)



Fig.4 FORE-SIGHT Cerebral Oximeter(27)



Fig.5 CerOx Cerebral Oximeter(28)



Fig.6 EQUANOX Cerebral Oximeter(28)

The INVOS device was the first FDA approved cerebral oximeter. It has been commercially available since 1993. According to the FDA cleared indications for use, this device only provides trend monitoring of hemoglobin oxygen saturation of blood in the brain of an individual(29). It is also the most widely used regional oximeter in the world. It is the only oximeter that display four channels simultaneously, enabling the clinician to conveniently track multiple cerebral as well as somatic (body) tissue oxygen saturations. It provides real-time data about a patient’s site-specific levels of oxygenation in the brain and other vital organs. This system provides clinicians with reliable, timely and actionable monitoring to help avoid adverse events and improve patient care and outcomes. It provides monitoring of changes in regional oxygen saturation ( $rSO_2$ ) of blood in the brain or other body tissues beneath the sensor for effective oxygen monitoring in adults, children, infants and neonates. It uses disposable user and patient friendly sensors which makes monitoring of ischemic threats to the brain and body safe and easy, while supplying the information the care team needs to assess and intervene accordingly. The sensors are applied to the skin’s surface and can be applied on upto four site-specific areas chosen by the care team. The sensor contains two wavelengths of infrared light (730 and 810 nm) from LEDs (30) and two light detectors at fixed distances from the light source. Using a subtraction algorithm, it is used to assess cerebral oxygenation. By reporting venous weighted  $rSO_2$  in tissue directly beneath the sensor, this reflects oxygen remaining after tissue demand has been met. Decreases in this venous reserve indicate increased ischemic risk and compromised tissue perfusion. The INVOS technology enables clinicians to detect physiologic changes in saturation and cerebral perfusion in order to make timely, critical lifesaving decisions for improved patient outcomes. In neonates, infants and children, cerebral and somatic  $rSO_2$  provide noninvasive indications of oxygen changes in the cerebral and peripheral circulatory systems and may provide an early indication of oxygen deficits associated with impending shock states and anaerobiosis. The INVOS Analytics

Tool allows users to review the data, generate a detailed analysis of the clinical case and illustrate the nuances of rSO<sub>2</sub> in various clinical scenarios.

In contrast to INVOS, FORE-SIGHT is a newer device to the market which is designed to measure absolute brain oxygen saturation. It is a non-invasive device that incorporates CAS Medical System's exclusive laser-light technology to project harmless NIR light through the scalp and skull and into the brain via a disposable sensor on the patient's forehead. Laser-Light technology incorporates a laser system that is designated as a Class 1 laser product by the FDA which is considered to be non-significant risk and non-hazardous device(31). This oximeter utilizes continuous wavelengths at 690nm,780nm,805nm and 850nm to determine SctO<sub>2</sub>.NIR light is allowed to penetrate the brain to measure mostly gray matter in the cerebral cortex(32). It operates on the principle that blood contains hemoglobin in two primary forms-HbO<sub>2</sub> and Hb. These two forms of hemoglobin absorb light in different measurable ways.SctO<sub>2</sub> levels are found by determining the ratio of oxygenated hemoglobin to total hemoglobin at the microvascular level (arterioles, venules and capillaries) in the region of the brain that is interrogated. It continuously monitorsSctO<sub>2</sub>which is a mixed oxygen saturation parameter and reflects a proportional mix of arterial (~30%) and venous (~70%) blood in the outlying regions of the brain. Laser light is projected into the brain in four precise wavelengths to capture information needed for an absolute indication of SctO<sub>2</sub> levels. Four precise wavelengths are needed to maximize the measurement accuracy of HbO<sub>2</sub> and Hb in determining SctO<sub>2</sub>, to compensate for wavelength dependent scattering losses and to account for interference from other background light absorbers such as fluid, tissue and skin pigmentation(33). Reflected light is captured by detectors positioned on the forehead probe for optimal signal collection and subtraction of interference from tissues outside the brain(34). After analyzing the reflected light, it displays the SctO<sub>2</sub> level on the monitor as an absolute number and provides a graphical representation of historical values.

The CerOx device consists of a stand alone bedside unit which is simple and easy to use that contains both electronics and optics required for non-invasive monitoring of vital signs of vital organs. This monitor unit provides a user friendly graphical display of current and historical patient data from two sensors simultaneously. The monitor unit is connected via electronic and optic cables to the sensors. The sensors are coupled to the skin using a single use adhesive. It provides physicians with the most advanced monitoring tools to help direct safe and decisive patient care when the perfusion of vital tissue is at stake. It has two products-the CerOx and the c-FLOW which are based on the patented Ornim's Ultrasound Tagged(UT) Light Technology and can be used in most areas where cerebral blood flow needs to be monitored. The UT Light technology utilizes weak acoustic beams to identify light emerging from deep tissue layers. This employs the combination of light and ultrasound to provide a non-invasive measure of rSO<sub>2</sub> and blood flow. It is unique among all other commercially available NIRS technologies, since it also analyzes the light speckle signal and does not rely solely on the intensity of light reaching the detector. The CerOx monitor is the only FDA-cleared device enabling continuous, non-invasive measurement of blood flow and oxygen saturation in real time which enables localized and quantitative measurements of physiological parameters within specific tissue regions. This allows neurosurgeons to act quickly and decisively to optimize hemodynamics in the critical care setting. UT Light technology utilizes laser light which is introduced into a tissue, much like other NIRS based cerebral oximetry devices. UT Light transmits a beam of light through tissue to measure the absorption of light by HbO<sub>2</sub> and Hb. The system tags the light with ultrasound beams enabling to bypass superficial tissue and measure absolute oxygen saturation levels within the monitored tissue. If the blood in the area marked by the ultrasound is red and oxygen-rich, it absorbs more tagged light. If the area is light and oxygen-poor, more tagged light is reflected back to the detector. In this way, oxygen levels can be measured precisely. The c-FLOW is a continuous, non-invasive monitor which enables physicians to monitor change since cerebral tissue blood flow that provides direct measurements of relative changes in tissue blood flow. It monitors regional microcirculatory blood flow in tissues by using sensors placed near the area of interest. It adds rapid, brief, focused pulses of ultrasound into the tissue over the volume of interest through which light passes. Propagating through tissue slower than the light does, these ultrasound pulses create an effect, similar to the Doppler Effect, on the light photons they encounter. As time progresses, the ultrasound pulse penetrates deeper into the tissue, and the phase of light emanating from this depth is shifted or tagged accordingly. The UT Light algorithm analyzes the Doppler shift of the tagged light signal to non-invasively determine a patient's blood flow in the microcirculation underneath the sensor. Using this tagging mechanism, light collected by the c-FLOW photo sensor can be filtered serially as a function of time, corresponding to relative depth, calculating flow can be done, focusing the measurement only at a determined volume. The blood flow is displayed numerically and graphically on the bedside monitor's screen. This increases the confidence that oximetry measurements derive from the desired volume such as the brain or muscle tissue, by reducing contamination from tissue layers. In other words, c-FLOW reads dynamic information rather than just the absorption. In addition to this, it can screen out flow signal that originates from non-cerebral tissue layers, focusing on a deeper region of interest that correlates with cerebral microvasculature.

The EQUANOX System was developed by Nonin Medical, Inc. It is completely non-invasive and measures rSO<sub>2</sub> by utilizing a patented technology with a dual emitter and dual detector sensor topology. Accurate measurements of rSO<sub>2</sub> provide clinicians with information needed to ensure patients receive appropriate intervention during surgery and in critical care settings. The emitters are LEDs which utilize four wavelengths of light -730nm,760nm,810nm,880nm to measure the balance of HbO<sub>2</sub> and Hb. The result is highly accurate measurements of patient's true arterial and venous saturation. The dual emitter and dual receiver sensor cancels out surface and shallow tissue variations allowing for a more targeted tissue reading. It provides improved isolation of targeted tissue compared to single emitter systems(35)and excellent repeatability when measuring rSO<sub>2</sub>(36). Most NIRS cerebral oximeters use a single emitter and two detectors for the optical measurements. The optical measurements from the shorter path (representing extracranial blood oxygen) is subtracted from the longer path (representing intracranial and extracranial blood oxygen) to give measurements for intracranial blood oxygen(37). Any surface and shallow tissue variation between the two detector sites introduces error into the measurement. The EQUANOX sensor differs from the INVOS and FORE-SIGHT sensors because it is equipped with dual emitter sites, enabling a crisscrossing in the transmission of the photons. This technology offers real-time management of patients at risk for oxygen saturation in the brain. Its near infrared optics and sensor architecture deliver greater accuracy and consistency than conventional NIRS cerebral technologies and provide stable, rapid and reliable signals by minimizing ambient light interferences. Compared to traditional NIRS technology, EQUANOX sensors are absolute and provide enhanced accuracy in rSO<sub>2</sub> measurements regardless of age or weight. With EQUANOX sensors, if rSO<sub>2</sub> values are below 60%, it is a clear indication that a patient may be in a critical oxygen reserve condition and immediate intervention should be considered. This unique sensor architecture effectively targets the cerebral cortex, eliminating surface artifacts that interfere with measurement accuracy(38).

## V. CONCLUSIONS

This review represents the detailed comparative performance analysis of cerebral oximetry technologies currently available commercially. The cerebral oximeters differ regarding the sensor technology and the processing algorithms used to calculate SctO<sub>2</sub>. Further research may expand the use of this promising monitoring modality to the place of a standard monitor during various complex surgical procedures.

Since the introduction of cerebral oximetry into clinical practice almost 30 years ago, there has been tremendous progress of the technology as well as the research in the field of cerebral oxygenation monitoring. Non-invasive cerebral oximetry represents a potentially important and broadly spread new monitoring modality. This modality of cerebral monitoring is most promising for the prevention and correction of cerebral desaturation. NIRS based cerebral oximetry appears to be an evolving technology which provides continuous intraoperative insight into brain perfusion and oxygenation dynamics. Obtaining adequate tissue oxygenation may prevent complications which may result from tissue hypoxia. It can be served as a first alert indicator of the intraoperative events that may lead to a potential adverse clinical outcome.

NIRS based cerebral oximetry has potential clinical benefits in a wide range of areas and conditions including resuscitation in shock and cardiac arrest, prehospital medicine including transportation of trauma or other critically ill patients, admitting to the emergency area, various kinds of urgent cardiac and non-cardiac surgical operations and during intensive care of critically ill patients. It has the potential to improve clinical outcomes in pediatric, orthopedic, gastric, urologic and essentially any general surgical patient population both in and out of the hospital.

It can be concluded that cerebral oximeter can be considered as a hemodynamic monitoring system since it uses an easy to apply and completely non-invasive technology to identify patients at risk for an adverse outcome in order to make timely, lifesaving decisions in the critical care setting.

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