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Use of Near-Infrared Spectroscopy in the Management of Patients in Neonatal Intensive Care Units – An Example of Implementation of a New Technology

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1. Introduction

Near-infrared spectroscopy (NIRS) is a spectroscopic technique which uses the NIR region of the electromagnetic spectrum to gain information about natural samples through their absorption of NIR light. This method is used in several branches of science. In medicine, it was first used in adult patients, who were placed on by-pass during cardiac surgery to follow cerebral oxygenation, cerebral rSO2 (rSO2-c,) and thereby perfusion and metabolism of the brain. Its many other possibilities soon became apparent. Although the brain remains the main organ of interest in patients of all ages, other tissues are being studied as well. Aside from cardiac surgery clinicians in specialties such as sports medicine, plastic surgery (to assess flap viability), and neonatology apply NIRS in clinical settings. (Feng et al., 2001)

By the late 1980's the first studies on monitoring of regional oxygenation in the neonatal brain were published. (Delpy et al., 1987; Edwards et al., 1988) In 2004 on average one new article on NIRS was published in Pub Med every day. (Ferrari et at, 2004) Monitoring of vital signs in the ICUs has scientific and patient care related goals. One may be able to gain better understanding of physiology and be alerted to changes in patient status to be able to respond immediately.

The vulnerability of the neonate, especially of the newborn brain, to changes in oxygenation is an ever present concern as it is linked to long-term outcome. For that reason neonatologists are obligated to find ways to monitor their patients to be ahead of evolving pathology and avoid the severe impact of negative events.

As early as 1999 the NINDS and NIH hosted a workshop for experts in the fields of neurology and neonatology to discuss the use of NIRS for cerebral monitoring in infants. The panel determined that the best NIRS instrument should be selected and used in longitudinal, blinded studies. Obtained data would need to be compared with short term, intermediate and long term outcomes. The questions the panel suggested to investigate were the predictive value of NIRS and its usefulness in leading to timely interventions and prevention of long term injury. (www.ninds.nih.gov/news_andevents/proceedings/

nirswkshop1999.htm) Once NIRS monitors became commercially available a few animal and many clinical trials were conducted. The clinical investigations were for the most part small, brief observational prospective studies. Also NIRS was introduced into daily practice by others at that time, years before normative data and validation studies had been obtained.

There is great potential to use the NIRS technology in the neonatal intensive care unit (NICU) since it is a portable, continuous, non-invasive bedside monitoring technique. Following the development of small and skin friendly sensors and FDA approval of some NIRS monitors for use in neonates, both research and clinical use of NIRS in the NICU increased exponentially. The number of research projects over the last 5-10 years is large. However, the trials, while dealing with questions important to understanding physiology and clinical care in the NICU, are small and almost exclusively conducted at single centers. Often no more than 10-20 patients are being followed. Very large NIRS related studies enrolled 40-90 patients. Many of the observations reported are of brief sampling periods, sometimes being no more than spot samples.

This chapter is a limited overview for non-clinicians such as engineers and science students, or clinicians who want to learn about a medical application of NIRS. The recent introduction of the NIRS technology into neonatal medicine is used as an example of how a new device came into use into use in the clinical setting over the last decade. Main areas of clinical use and supporting studies will be mentioned. Limitations of NIRS technology and controversies as well as future directions will be addressed. With the abundance of available literature this chapter cannot claim to be a reference. This is an exciting and rapidly advancing field with new studies published even as this article was sent to press. This chapter will demonstrate how a new technology is adopted into medical care, in this case the NICU.

1.1 Materials

Pub Med and Google have been queried regarding NIRS in NICUs, abdominal/splanchnic, cerebral and renal measurements, utility, and of NIRS use as prognosticator.

1.2 Technology and measurements

The principle of how NIRS works in humans was excellently summarized by Cohn:

Near-infrared spectroscopy has been used as a tool to determine the redox state of light-absorbing molecules. This technology is based on the Beer-Lambert Law, which states that light transmission through a solution with a dissolved solute decreases exponentially as the concentration of the solute increases. In mammalian tissue, only three compounds change their spectra when oxygenated: cytochrome *aa3*, myoglobin, and hemoglobin. Because the absorption spectra of oxyhemoglobin and deoxyhemoglobin differ, their relative concentrations within tissue change with oxygenation, and the relative concentrations of the types of hemoglobin can be determined. Because NIRS measurements are taken without regard to systole or diastole, and because only 20% of blood volume is intra-arterial, spectroscopic measurements are primarily indicative of the venous oxyhemoglobin concentration. In the near infrared region (700 –1,000 nm), light transmits through skin, bone, and muscle without attenuation. (Cohn et al., 2003) There are several FDA approved

NIRS monitors with somewhat different technology and algorithms available commercially (Wolf & Greisen, 2009) to measure the venous weighted regional oxygen saturation (rSO2) or tissue oxygenation index (TOI).

Due to the small size and the thin covering layers of tissue of both term and preterm neonates, r-SO2/TOI measurements at a depth of 2-3 cm can reach brain, kidney, gut/ splanchnic circulation, liver and muscle. The access to these critical organs promises valuable physiologic information through monitoring by NIRS. Measurements of several sites can be recorded simultaneously. (Hoffman et al., 2003; McNeill et al., 2010, 2011)

NIRS measurements are organ specific and regional (rSO2), reflecting perfusion and metabolism by non-invasive measurement in real-time. They are not temperature, pulsatility or flow dependent. Thus they may offer advantages over traditional measures of perfusion such as capillary refill, blood pressure, and urine output, lactate, venous and arterial O2 which tend to alert the clinician once the disease process is further progressed. R-SO2 measurements cannot stand alone. While they may often be the first sign of change, they need to be interpreted in the context of other measurements such as mean arterial blood pressure (MABP), pulse oximetry (O2sat), blood gases, additionally in the research setting with measurements of cerebral blood flow (CBF) and cerebral blood volume (CBV). Evaluation of the link between the venous weighted NIRS readings and peripheral pulse oximetry, a measure of arterial O2, gives insight into oxygen supply and demand. Using a simple equation, the fractional extraction of oxygen (FTOE = SaO2-rSO2/SaO2) oxygen consumption can be calculated and oxygen supply can be assessed. (Lemmers et al., 2006)

1.3 Validation

NIRS was implemented by many enthusiastic clinicians without a vast body of previous research evidence. This phenomenon may be representative of an era of limited funding for larger studies linked with the promise of a non-invasive "safe" monitoring technology.

Before human application the initial research applying NIRS to measure rSO2 technology in the medical field occurred in the laboratory: One of the first examples of validation used a phantom brain model in which O2, N2, and CO2 content of a blood perfusate could be altered during measurements. The results correlated with findings in animal models. (Kurth et al., 1995) Later NIRS was further validated for the neonatologist in a newborn piglet model. The carotid, renal and mesenteric arteries were occluded and reperfused. These interventions led to rapid, simultaneous changes in rSO2 of the affected end-organs. (Wider, 2009) Furthermore, there have been validations in patients during intensive care, extra-corporeal membrane oxygenation (ECMO) and cardiac surgery by comparing central blood samples with NIRS values. (Abdul-Khaliq et al., 2002; Benni et al., 2005; Nagdyman et al., 2004; Rais-Bahrami K et al, 2006; Weiss, 2005) Menke found reproducibility to be good as well. (Menke et al., 2003). The accuracy of data is impacted by light scattering, hemoglobin concentration and chromophores such as melanin and bilirubin. In the presence of a thicker overlying tissue layer, such as severe subcutaneous edema or excess subcutaneous fat, it may be impossible for the NIR light beam to reach the target organ. In the newborn modest changes in weight have a small effect on abdominal measurements while changes in hemoglobin over the first weeks of life can change measurements by 30-50%. (Ferrari et al.,

2004; Madsen et al., 2000; McNeill et al., 2010, 2011; Wassenaar et al., 2005) NIRS measurements may differ between probes. (Sorensen et al., 2008)

1.4 Safety and feasibility

Commercially available sensors for neonates have become well tolerated due to smaller size and being lined with a skin friendly adhesive. To provide further skin protection in extremely premature patients probes can be attached to a light-permeable skin barrier without interference with measurements. (McNeill et al., 2010, 2011)

1.5 Monitoring

Organs which can be monitored in neonates are brain, kidney, gut, liver and muscle. This chapter will comment on the most commonly used sites– the brain, kidney and gut.

2. Cerebral NIRS

The neonatal period is a unique time in life as the infant undergoes dramatic physiologic changes during transition from intra- to extra-uterine life, which involve hemodynamics and affect oxygenation, reflected in rSO2. Due to its vulnerability the neonatal central nervous system is the main area of interest for measurements of oxygenation. The majority of articles written on the clinical use of NIRS in neonates include reports on cerebral measurements (c-rSO2 or cerebral Tissue Oxygenation Index (TOI)).

2.1 Effect of gestational and postnatal age

The largest body of research investigates cerebral NIRS values. Reports regarding effects of gestational age (pre-term, term, post-term) and postnatal/chronologic age on NIRS values are conflicting.

In a study by McNeill, which was blinded to caregivers and sampled from birth for a maximum of 21 days, baseline rSO2 for preterm infants (gestational age of 29-34 weeks) differed from established pediatric norms, while values for term neonates in the first days of life did not (McNeill et al., 2010, 2011). The observation by McNeill (McNeill et al., 2010, 2011) that cerebral NIRS decreases over time are supported by Roche-Labarbe's findings following weekly spot samples during the first 6 weeks obtained with a different study protocol and different NIRS equipment. (Roche-Labarbe et al., 2010, 2011) Both observations contradict Lemmers' study in which twice daily 60 minute sampling periods found no observed change. (Lemmers et al., 2006)

Naulears found an increase in cerebral oxygenation in premature infants during the first three days. In this study sampling periods were 30 min. NIRS recordings occurred with a different instrument. (Naulaers et al., 2002) Meek's earlier report from 1998 in ventilated babies used NIRS and found an increase in cerebral blood flow over time. (Meek et al., 1998)

A study measuring rSO2-c in transition after delivery found by minute 3 that rSO2 increased and reached a plateau by minute 7. (Urlesberger et al., 2010)

More recently, Takami followed cerebral TOI in extremely low birth weight infants (ELBWs) at 3-6h followed by samples every 6h up to 72h. He observed a decrease in measurements until 12h, then an increase that correlated with similar changes in SVC flow. (Takami et al., 2010).

When reviewing this literature regarding the contradicting study results, possible explanations present themselves: Patient populations are not identical. Protocols vary from study to study. Different sampling times may play an important role in influencing results, especially when spot samples versus long-term continuous data were collected. If studies were not blinded, care giving and subsequently observations might have been influenced. The use of different monitors and probes and probe placement may further lead to different results. Studies were small and data inconclusive. There was some agreement regarding abnormally low values being linked to poor outcome. (Dullenkopf et al., 2003; Sorensen et al., 2008; van Bel et al., 2008; Wolf & Greisen, 2009, also see cerebral hypoxia)

2.2 Variability

Variability is the change in percent of rSO2 away from a calculated baseline. It can be followed over time to know how much time the rSO2 was above or below baseline. The baseline differs from patient to patient. Variability is an area of interest and needs further investigation: Cerebral daily variability is small. Large changes (>20%) off the baseline would raise concern for acute clinical change. (McNeill et al., 2010, 2011) Change in variability may be an indicator of infection (Yanowitz et al., 2006). The change in baseline over the first weeks of life, which is observed in preterm infants, may represent ongoing developmental maturation independent of feeding status. (McNeill et al., 2010, 2011)

2.3 Peripheral blood pressure and oxygenation, impact on autoregulation

In the research setting cerebral blood flow and blood volume measurements, oxy- and deoxy hemoglobin and fractional extraction of oxygen (FTOE) as well as blood gas samples from central catheters added to detailed understanding of physiology.

Adequate O2 delivery to the brain tissue is most critical. Assessment of O2 delivery and consumption help understand clinical scenarios and their underlying pathophysiology: At the bed side this evaluation can occur by following changes in cerebral rSO2, changes in BP, oxygenation and peripheral blood gases. The below clinical scenarios for monitoring are amongst the more common:

Cerebral autoregulation is a homeostatic phenomenon controlled by the main capacitance vessels in the cerebral circulation. Through dilatation and constriction of these vessels cerebral blood flow and cerebral rSO2 or TOI are maintained at a steady level over a range of changing mean arterial blood pressures (MABP). This range is narrower in neonates, particularly in preterm infants. Cerebral pressure-passivity or loss of autoregulation is associated with low gestational age, low birth weight and systemic hypotension in a large study of 90 patients. (Soul et al., 2007)

If rSO2 or TOI changes correlate with the wave form of MABP autoregulation is lost. Swings in peripheral perfusion will be mirrored in cerebral blood flow and regional saturation readings. This phenomenon, when profound, carries an increased risk for intra-ventricular hemorrhage (IVH) and peri-ventricular leucomalacia (PVL) in preterm infants and generally a poor prognosis for neurodevelopment outcome. The more swings or changes in mean arterial pressure (MAP) and NIRS coincide and mirror each other, the more the waves are in concordance. Several studies link concordance with a more unfavorable prognosis and a higher likelihood of death. (Caicedo et al., 2011; DeSmet et al., 2010; Greisen & Borch, 2001;

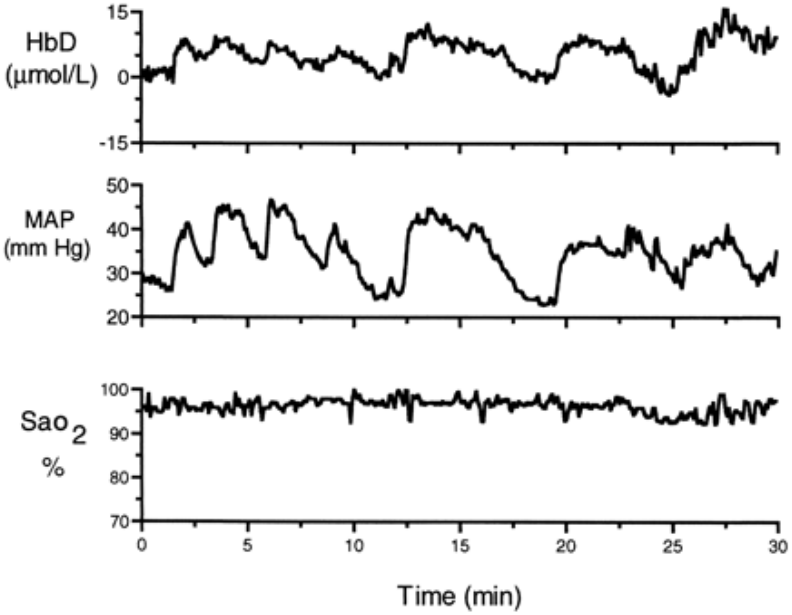

Fig. 1a. Example 1: Patient with loss of autoregulation and concordance of MAP and NIRS measurement of intravascular oxygenation (HbD). This patient had an unfavorable outcome.

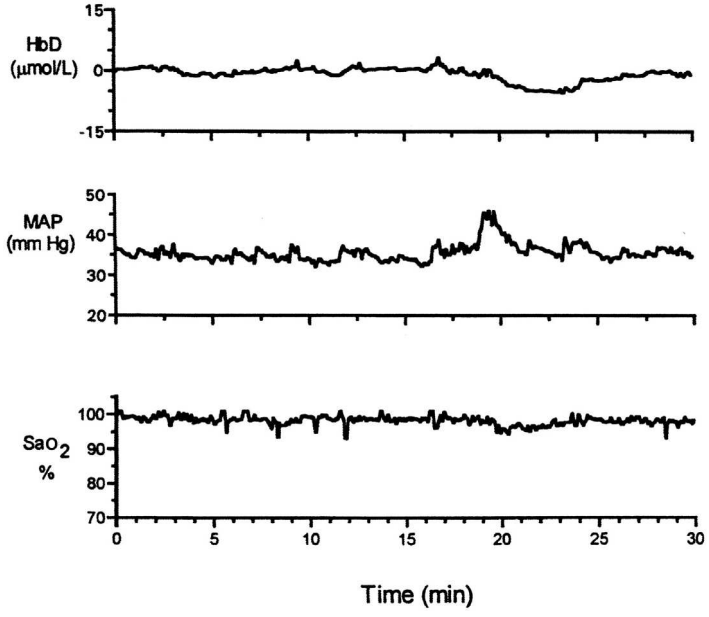

Fig. 1b. Example 2: Maintenance of autoregulation (Tsuji, 2000)

Hahn et al., 2010; Lemmers et al., 2006; Morren et al., 2003; Munro et al., 2004, 2005; O'Leary et al., 2009; Seri, 2006; Tsuji et al., 2000; Wong et al., 2008) In a recent study 23 infants with a mean gestational age of 26.7 +/-1.4 weeks were observed with NIRS. They were found to have periods of loss of cerebral autoregulation which were more profound with lower, longer lasting MABPs. There was no correlation with head ultrasound (HUS) findings as measure of short term outcome. (Gilmore et al., 2011)

A study followed changes in cerebral NIRS in ventilated preterm infants and found frequent periods of loss of autoregulation. (Lemmers et al., 2006). Vanderhaegen stresses the important contribution of pCO2 to cerebral blood flow, which may possibly override autoregulation. (Vanderhaegen et al., 2010) Hoffmann manipulated pCO2 in neonates undergoing cardiac surgery to improve cerebral blood flow. (Hoffman et al., 2005) According to another study by Vanderhaegen in 11 ELBWS blood glucose may play a role in influencing oxygenation. (Kurth et al., 1995)

2.4 Cerebral hypoxia

Cerebral hypoxia is a feared event as it translates to long-term morbidity and mortality. There is not enough data available linking a specific duration of hypoxia and levels of rSO2 or TOI while in the NICU with outcomes. There are no absolute numbers as reference in the human neonate. A piglet study from 2007 demonstrated changes seen on brain autopsy 72h after the animal spent 30 min. with rSO2-c of <40%. (Hou et al., 2007) It is not certain whether observations of concerning low levels of r-SO2/TOI in cardiac patients (Dullenkopf et al., 2003; Sorensen et al., 2008; van Bel et al., 2008; Wolf & Greisen, 2009) apply to infants with other diagnoses.

2.5 Cerebral hyperoxia

Cerebral hyperoxia in the critically ill neonate may occur by 2 mechanisms: either as hyper-oxygenation during the reperfusion phase of severe hypoxic ischemic encephalopathy most commonly occurring in neonates after perinatal birth depression or from decreased brain metabolism as seen in critical patients when blood flow is uncoupled from O2 (Toet, 2006; Wolf & Greisen, 2009). Either scenario is concerning for a poor long-term prognosis. The overall clinical situation needs to be taken into consideration as cerebral rSO2 in well preterm neonates has also been reported to be high in the first days of life. (Sorensen et al., 2009).

3. Renal NIRS

Renal rSO2 is higher than cerebral rSO2. McNeill reported that trends in cerebral and renal NIRS during the first 21 days of life mirror each other. Short-term and long-term variability of r-SO2 is small. Saturation changes exceeding >20% from baseline would be reason for concern and may indicate compromised perfusion. Several investigators report use in patients with shock or during surgery. Measurements of the renal rSO2 give insight into peripheral perfusion in general and into renal end-organ function. Using renal rSO2 in conjunction with cerebral rSO2 has been reported to give more and sometimes earlier insights into evolving pathology such as shock. (Cohn et al., 2003; Hoffman et al., 2003, 2004) See figure 2.

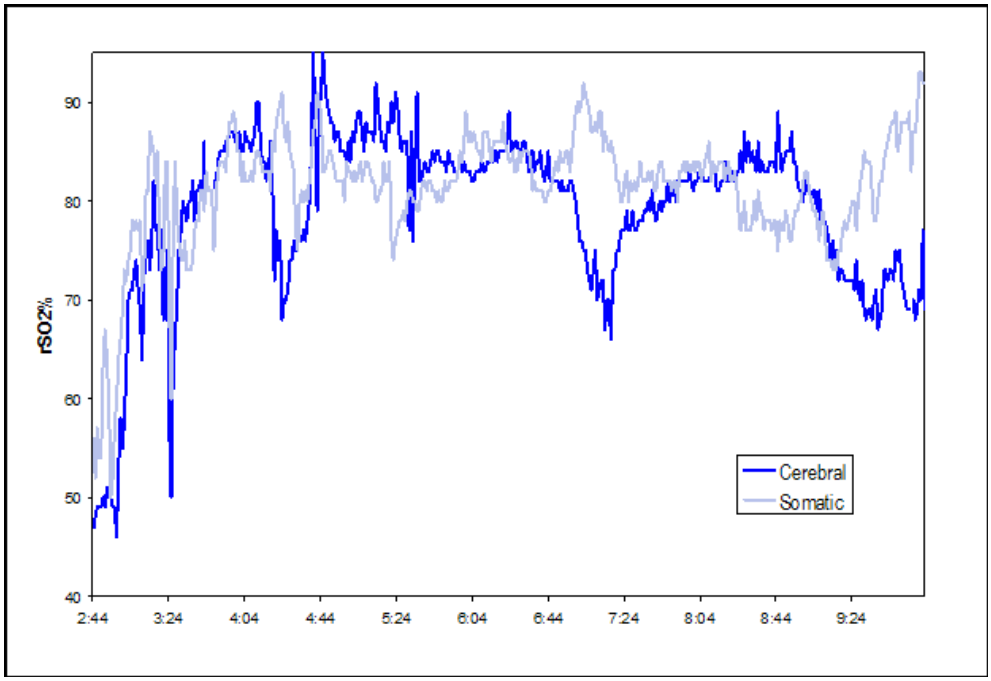

Fig. 2. Two-site NIRS trends from a patient undergoing resuscitation from hypovolemic/septic shock. Early aggressive resuscitation with fluid and epinephrine to normal regional rSO2 values restored urine output. The effect of changes in pCO2 on cerebral blood flow are evident at 0700. The mirror changes in cerebral and somatic rSO2 suggest that total cardiac output was relatively limited but that the distribution changed.(Hoffman et al., 2007)

4. Splanchnic (gut) NIRS

Monitoring the GI tract as opposed to monitoring the brain or kidneys is more complex since the gut is a hollow or gas and stool filled, moving structure, in close proximity of stomach and bladder, which could affect its position and functioning. Proper probe placement may therefore be a challenge. In addition movements of the baby and pull on electrodes are more likely. A recent small study by Gillam-Krakauer et al. using Doppler confirmed that splanchnic NIRS reflects bloodflow to the small intestine. (Gillam-Krakauer et al., 2011)

McNeill's study of splanchnic/abdominal rSO2 in healthy preterm infants between day 0 and day 21 found that baseline changed over time. Overall abdominal rSO2 values were significantly lower than cerebral and renal values. The baseline increased over time. When comparing patients born at 32 and 33 weeks to those born at 29 and 30 weeks gestation, higher weekly means were observed in the 2nd week of life in the older group. (McNeill et al., 2010, 2011)

These changes too may indicate regional developmental maturation. For abdominal rSO2 long- and short-term variability is much higher and exceeds 20%. It may be associated with

clinical and caregiving events and warrants further investigation/characterization. (McNeill et al., 2010, 2011)

Cortez found higher splanchnic rSO2-s and variability to be associated with a healthy gut, whereas infants with necrotizing enterocolitis, a condition of devastating bowel inflammation, had low splanchnic rSO2s and decreased variability. (Cortez et al., 2010, 2011)

5. Clinical events observed with NIRS

To further demonstrate the extent of topics and studies, examples of some clinical scenarios are listed. Referenced articles date back to 2000. The articles quoted are found in the bibliography. They are representative of the scope of interest.

5.1 Unstable neonates

Respiratory distress (Lemmers et al., 2006; Meek et al., 1998)

ECMO (Benni et al., 2005; Rais-Bahrami et al., 2006)

Pediatric Surgery (Dotta et al., 2005)

Cardiac disease pre-, intra, post op (Abdul-Khaliq et al., 2002; Hoffman et al., 2003; Johnson, 2009; Kurth et al., 2001; Li et al., 2008; Redlin et al., 2008; Seri, 2006)

Patent Ductus Arteriosus (Hüning et a., 2008; Keating et al., 2010; Lemmers et al., 2008, 2010; Meier et al., 2006; Underwood et al., 2006, 2007; Vanderhaegen et al., 2008; Zaramella et al., 2006)

CNS abnormalities HIE, PVL, PIH (Caicedo et al., 2011; De Smet et al., 2010; Morren et al., 2003; Munro et al., 2004, 2005; Wolf & Greisen, 2009; Wong et al., 2008)

Greisen & Borch , 2001; Hou et al. 2007; O'Leary et al., 2009; Sorensen & Greisen, 2009; Toet, 2006; van Bel F et al., 2008; Vanderhaegen et al., 2009, 2010; Weiss, 2005; Verhaen et al. , 2010; Wolf & Greisen , 2009)

Mechanical Ventilation (Noone et al., 2003; van Alfen-van der Velden et al., 2006; Verhagen et al., 2010)

Apnea (Payer et al., 2003; Yamamota et al., 2003)

Intensive Care (Limperopoulos et al., 2008)

Resuscitation (Baerts et al., 2010, 2011; Fuchs , 2011)

5.2 Care giving

Delivery room (Baenziger et al. ; Urlesberger et al., 2010)

Feedings (Baserga et al., 2003; Dave et al., 2008, 2009)

Blood transfusion (Bailey et al., 2010; Dani et al., 2010; Hess, 2010; van Hoften et al., 2010) *

Head ultrasound (van Alfen-van der Velden et al., 2008, 2009)

Kangaroo care (Begum et al., 2008)

Endotracheal tube suctioning (Kohlhauser et al., 2000)

CPAP (Dani et al., 2007; van den Berg et al.,2009, 2010; Zaramella et al., 2006)

Blood draws from umbilical artery catheters (Bray et al., 2003; Hüning et al., 2007; Roll et al., 2006; Schulz et al., 2003) **

Stimuli, Pain (Bartocci et al., 2001, 2006; Holsti et al., 2011; Liao et al., 2010; Ozawa et al., 2010, 2011; Slater et al., 2007)

Posture/Position (Ancora et al., 2009, 2010; Pichler et al., 2001)

NIRS/EEG (van den Berg et al., 2009, 2010)

5.3 Medications

Caffeine (Tracy et al., 2010)

Dopamine (Wong et al., 2009)

Epinephrine (Pellicer et al., 2005)

Ibuprofen (Bray et al. 2003; Naulaers et al., 2005)

Indomethacin (Dave et al., 2008, 2009; Keating et al., 2010)

Morphine/Midozalam (van Alfen-van der Velden et al., 2006)

Propofol (Vanderhaegen et al.,2009, 2010)

Surfactant (Fahnenstich et al., 1991; van den Berg et al., 2009, 2010)

***Blood transfusions** too are a routine part of NICU care. 3 studies found increases in rSO2-c following transfusion, in addition 2 of the authors reported increase in splanchnic oxygenation and lastly one of the studies found increased renal rSO2 as well. These findings are overall encouraging. Dani however questions whether the increases in rSO2 are reflecting benefits or administration of a pro-oxidant. Another author is attempting to identify the need for transfusion by calculating splanchnic-cerebral oxygen ratios. Infants with low ratios pre-transfusion are more likely to improve post-transfusion. (Bailey et al., 2010 ; Dani et al., 2010; Hess, 2010; van Hoften et al., 2010)

****Blood draws from umbilical artery catheters** decrease rSO2-c. Two reports conflict on whether volume or a rapid draw causes the decrease in rSO2. (Roll et al., 2006; Schulz et al., 2003)

6. Conclusions

NIRS is a fascinating technology with impressive potential. The opportunities to learn more about physiology and effects of therapy through monitoring with NIRS are limitless.

The literature reporting about NIRS in the clinical setting of the NICU is abundant. However published supporting scientific evidence for the use of NIRS in neonatology has limitations. There are no large multi-center collaborative studies. The advent of NIRS has

been affected by coinciding with the era of limited research funding for large clinical studies.

Studies are largely observational either observing a group of patients over time or following changes caused by therapeutic interventions (ECMO, heart surgery, transfusion, medications). Studies for the most part are small in patient numbers and short in time of observation. Study protocols observing the same phenomenon are often distinctly different from each other. Devices used may differ from trial to trial as well. All this can contribute to differences in study results. Due to the differences in study design meta-analysis, as an opportunity to obtain more robust results from a large number of trials and patients, may not be an option. Cerebral NIRS measurements are the most researched and incorporated into daily care. There is some consensus regarding critical lower limits of cerebral oxygenation (Wolf & Greisen, 2009; Wider, 2009). In addition the patient is accepted as his own control, using the NIRS monitor as a trend monitor. (van Bel et al., 2008).

For the future of NIRS monitoring in the NICU, it may be necessary for another NIH panel to be called to review the existing evidence obtained since the initial group met in 1999 and devise a hopefully low budget strategy to validate NIRS in the NICU further. Larger, randomized trials will be needed. Blinding would not be useful unless normative data is obtained. Unblinded studies would allow interventions based on NIRS measurements and observe possible benefits. An anecdotal example was a rotated ECMO cannula that led to a steep decrease in cerebral r-SO2 with all other vital signs remaining unchanged. The caregivers responded immediately avoiding adverse consequences. Greisen in a paper from November 2011 estimates one needs to study 4000 infants with cerebral oximetry to have the power to detect the reduction of a clinically relevant endpoint, such as death or neurodevelopmental handicap, by 20%. (Greisen et al., 2011)

In the meantime, NIRS monitors could be further improved to make interpretation of data easier:

While the information gained is tempting, interpretation of data takes experience. NIRS does not stand alone. It needs to be viewed in context of other occurring physiologic changes. Recently data collection and interpretation has been made easier and more precise by the increasing ability to synchronize collection of different data points and thus link NIRS observations, possibly from multiple channels, with vital signs, EEG, interventions, medications, stimulation and care giving events. At this point this technology is not generally available.

Eventually more channels to measure greater than 3 sites, allowing for more than one cerebral site plus somatic sites, may be needed.

Once norms are established for cerebral, renal and splanchnic sites, normal limits at each site for different gestational and postnatal ages could be indicated on the monitor. Alarms could signal when a patient's rSO2-c is outside the normal range. Variability could be reported both by percent change and change over time, also possibly in reference to gestational age for the observed organ. Incorporation of the ability for the monitor to calculate physiologic equations like FTOE or cerebral blood flow could give more value to NIRS monitoring.

Will those changes improve life and care in the NICU for patients and staff? Perhaps. Possibly clinicians find themselves confronted by unexpected physiology and new problems

to solve. Now it is time to prove benefits of using the NIRS technology by decreasing adverse events in day-to-day patient care and improving outcome.

Greisen summarized the current situation in an article published recently:

> *"On the one hand, cerebral oximetry can potentially become inexpensive as it is based on technology that can be mass produced. Also, the probe may be miniaturized and integrated with the electronics into a soft 'plaster' that may stick to the skin of the head of tiny infants and need little attention. Solid evidence of benefit to patients will create a large market. Evidence of benefit of an instrument using public domain technology can serve as a platform for healthy competition on user-friendliness and price. On the other hand, what will happen if the clinical use of cerebral oximetry is not developed in a rational, evidence-based format? Then it may become another randomly applied expensive technology. Cerebral oximetry will be supported by anecdotal evidence, expert opinion, active branding and marketing. The consequences include unnecessary disturbances and risks to a very vulnerable group of patients and depletion of scarce healthcare resources".*
>
> (Greisen et al., 2011)

In closing, this chapter is not a manual for patient management. It demonstrated the implementation of a new tool as well as the temptations and hurdles faced by investigators and clinicians using a new promising device, which the author herself understands from both observation and personal experience.

7. Acknowledgment

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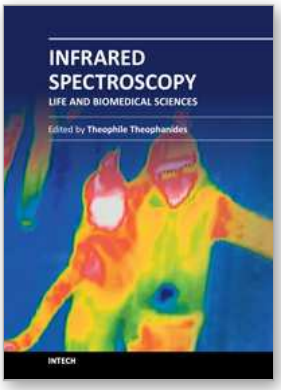

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This informative and state-of-the art book on Infrared Spectroscopy in Life sciences designed for researchers, academics as well as for those working in industry, agriculture and in pharmaceutical companies features 20 chapters of applications of MIRS and NIRS in brain activity and clinical research. It shows excellent FT-IR spectra of breast tissues, atheromatic plaques, human bones and projects assessment of haemodynamic activation in the cerebral cortex, brain oxygenation studies and many interesting insights from a medical perspective.

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