MCN for Neonatology
West of Scotland
Neonatal Guideline

Near Infra Red Spectroscopy (NIRS)
Guidance for use in neonates

This guidance is for medical staff and nursing staff working in Neonatal Intensive Care settings within the MCN for Neonatology, West of Scotland. This document is intended to be primarily educational but also to provide a safe framework for the use of NIRS in the Neonatal Unit (NICU) in selected clinical areas.
NIRS is a novel bedside non invasive continuous clinical monitor. Whilst providing an exciting new bedside technology on the NICU, caution must be exercised because of the potential for skin damage, variation between probe algorithms and limited clinical trial evidence to support routine use. However in some patients, when considered with standard monitoring, it can provide very useful additional information about vital end organ perfusion and adequacy of the circulation.

Indications
NIRS provides continuous non invasive assessment of regional tissue (mixed arterial and venous) oxygen saturation which can provide additional information about adequacy of organ perfusion and metabolic demands in the intensive care setting. The current indications for use in NICU include:

1. Preoperative management of infants with major congenital heart disease
2. Peri operative care of infants requiring PDA ligation
3. Neonates on ECMO
4. Neonates with Vein of Galen Aneurysmal Malformation (VGAM) in the peri operative period
5. Adjunctive assessment of HIE

Whilst it is possible that the use of NIRS will be extended to novel areas in the future, including assessment of hypotension and PDA in premature infants, this is currently the subject of clinical trials. Routine use in the NICU is not advised at present.

Background
Near Infra red spectroscopy utilises low intensity near-infrared light that has the ability to penetrate biological tissues including bone. This allows continuous non invasive assessment of Hb oxygen saturation using technology similar to that used in pulse oximetery. However, instead of working on the arterialised waveform, oxygen saturations are assessed in tissue vascular beds at a fixed depth. This permits assessment of the capillary beds and provides a mixed arterial and venous saturation that is typically predominantly (75%) venous in origin. This information can be used to assess the adequacy of tissue oxygen delivery and is analogous to measuring systemic venous oxygen saturations (SvO_2) via the internal jugular vein or SVC; a standard of care in paediatric and adult intensive care departments. There have been numerous validation studies in animals and humans demonstrating that cerebral NIRS offers a non invasive alternative SvO_2 (1, 2). Because probes can be applied to any area of the body they can be used to describe **regional saturations (rSO_2).** An alternative descriptive terminology used in some systems is the **Tissue Oxygenation Index (TOI)**. In GGC neonates results are then described as regional saturations with a suffix being inserted after "S" to indicate which region studied. The regions considered in this document are **$rScO_2$ (cerebral saturations), $rSrO_2$ (renal saturations), $rSs0_2$ (somatic saturations).**

Normal and critical values
NIRS measurements have been validated in both animal and human studies, including the adult and paediatric population (1, 2). Normative values have been described for the neonate in numerous observational studies in "well" premature neonates. They are presented as percentages but the upper value for most probes is set at 95%.
Cerebral saturations, summarised in the Table 1 from Van Bel et al (3) are considered to be statistically normal if lying between 55 and 85%. These are the range of values currently in use for a large European multicentre trial, SafeBoosC, studying the effects of NICU interventions on cerebral saturations perfusion (4).

Table 1 (reference 3)

Study patient group	$rScO_2$	Patient numbers	Study author
Adults	67 (+/-8) 66 (+/-8)	n=94 n=19	Misra Yoshitani
Full term neonates/ infants Day 12 Day 4.5	 61 (+/-12) 63 (+/-12)	 n=155 n=20	 Weiss Dullenkopf
Preterm neonates (GA< 32 weeks) Day 1 Day 2 Day 3 Day not specified >Day 7 Day 1 Day2 Day3	 57 (54-66) 66 (62-82) 76 (68-80) 75 (+/-10.2) 66 (+/-8.8) 70 (+/-7.4) 71 (+/-8.8) 70 (+/-7.8)	 n=15 n=253 n=40 n=38	 Naulaers Sorrenson Lemmers

Lower cerebral limits
The absolute threshold associated with sustained neurological damage for an individual patient is impossible to predict. Piglet work demonstrates sustained cerebral levels (**$rScO_2$**) of 35% are harmful but are time dependant requiring several hours to result in behavioural histological brain changes (5). Extrapolation from this and adult work have resulted in a standard critical threshold of 40% for **$rScO_2$**being adopted.

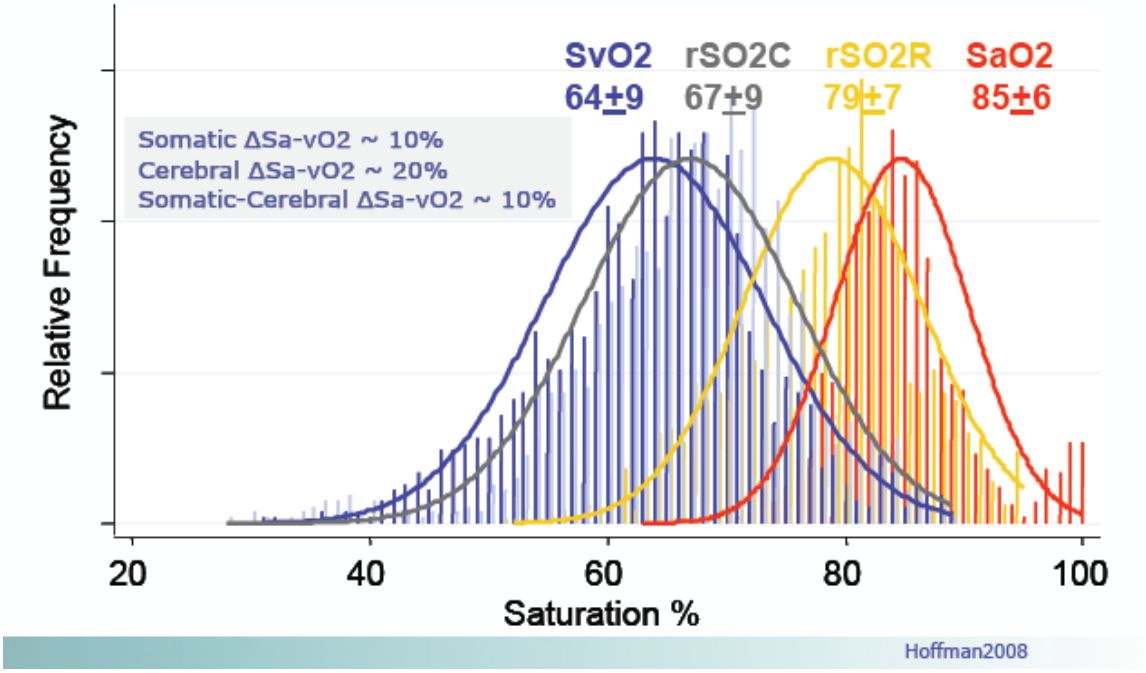
Higher cerebral limits (HIE)
Conversely, whilst rSo2 falls if there is inadequate oxygen delivery, rSo2 will rise if there is increased oxygen delivery or reduced oxygen consumption. This is rarely of concern unless there has been a possible significant organ hypoxic ischaemic event with subsequent loss of metabolically active tissue. This is relevant following hypoxic ischaemic encephalopathy(6), where levels > 80% after 24 hours of age measured with small adult probes, have been significantly associated with adverse neurological outcomes. Further information and references are given under **neonatal research** but currently we would recommend that cerebral NIRS may provide additional useful information after 24 hours of age but should not replace CFAM. The potential advantage with NIRS may be that unlike CFAM readings are less affected by cooling and anticonvulsants. If cerebral NIRS is being used to help gather prognostic information after HIE we would recommend using the **small adult probe**.

Calculating Fractional Tissue Oxygen Extraction (FTOE).
To investigate the balance between oxygen delivery and oxygen consumption, FTOE can be calculated as: (SaO2_rSO2)/SaO2. An increase reflects increased oxygen extraction by the tissues, whereas a decrease suggests less utilization or increased delivery of oxygen.
A simpler measure of **arterial venous oxygen saturation difference** can be calculated (pSaO2 – rSO2). A typical arterial venous difference is less than 10% and rising gaps should prompt clinical review.

Regional variations

In addition the variation between different organs and regional blood flow should be considered. Arterial blood should always have the highest oxygen saturation ($pSaO_2$) but for regional saturations the renal beds ($rSrO_2$) have the highest saturations (high blood flow and low metabolic demands) followed by cerebral saturations. This pattern is shown in Figure 1(kindly reproduced from Hoffman) in a series of children with congenital heart disease where **$rScO_2$** is represented in grey (rSO2C) , mixed venous saturations in blue (SvO2), renal saturations in yellow (rSO2R) and arterial saturations in red . Mesenteric or other somatic saturations, $rSs0_2$ are not included. Local experience suggests general abdominal saturations are highly variable and difficult to interpret.

Figure.1.



Neonatal research

Although long term evidence of benefit from specific NIRS based interventions are lacking, research is currently underway to looking at effects of reducing periods of cerebral hypo and hyperoxia. There is also a rapidly growing body of evidence suggesting that cerebral NIRS has potential utility in neonatology in a number of clinical areas. Case series studies of neonates with and without PDA demonstrate significantly lower cerebral saturations in PDA infants which disappear as the PDA closes with indomethacin (7). Significant changes have also been reported around PVH but not of sufficient sensitivity at present to guide intervention (8).

Cerebral NIRS has been demonstrated to be a strong predictor of adverse outcome following HIE in two publications using the small adult probe. Sensitivity is maximal from 24 – 72 hours and is not affected by therapeutic cooling (6,9). Sensitivity and specificity improves when utilised with CFAM (12) but may be particularly useful when CFAM is altered by cooling or sedation and anticonvulsant medications. After 24 hours of age, utilising small adult probes, the median value for patients with a favourable outcome is in the 70s whilst the median is in the mid 80s for those with adverse outcome (9). If cerebral NIRS is being utilised to assess the likelihood of a poor prognosis in HIE, we would recommend using the small adult probe. However, if the neonatal probe is utilised value > 90 are likely to be abnormal but should only be interpreted in conjunction with other assessment tools and imaging.

Although there is little neonatal research on the optimal care of babies with congenital heart disease there is evidence that preoperative NIRS monitoring improves preoperative stability and simplifies preoperative care(9). There are numerous case reports noting significant changes in abdominal NIRS associated with NEC but the utility of monitoring abdominal NIRS is not clear.

Clinical application

What should we interpret as abnormal?

Like $PSaO_2$ monitoring there are few absolute values. There is variation between probes and machines and although there is a statistical target range no absolute value to be avoided to minimise brain injury can be given. Therefore establishing a starting baseline and monitoring trends and patterns can be very valuable. All values have to be considered in conjunction with other clinical monitoring. The following provide guidance.

- Trends are very important: drop > 20% from baseline is significant and requires patient review
- Critical values: < 50% abnormal and < 40% considered critical
- Arterial venous saturation difference ($pSaO_2$ – rSO_2): normal 10-20%; widening gap and gap > 20% abnormal
- Cerebral saturations: normal 55% - 85% (> 80% suspicious of HIE with adult probes vs. > 90% with neonatal probes)
- Renal saturations: 5-10% > cerebral saturations. Loss of this relationship is abnormal except in some special cardiac cases.

What should be reviewed if regional saturations are below the normal range or trending downwards?

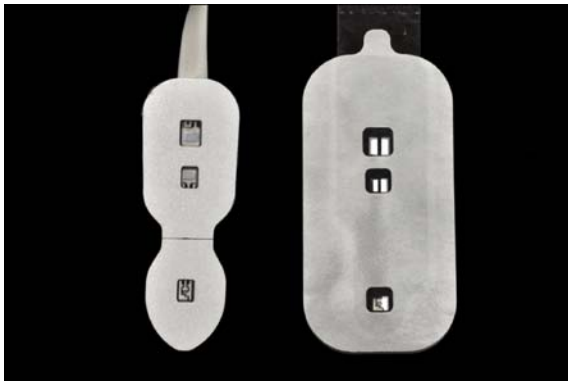
Regional saturations are very dependent on physiological variables which may not always noticeably affect pulse oximetery or even result in increases in arterial O_2 saturation. Abnormally low (rSO_2) should always prompt clinical review and consideration of the following:

- Haemoglobin – anaemia will reduce rSO_2
- Blood pressure – hypo or hypertension can reduce tissue perfusion and rSO_2
- Cardiac output – low output states reduce rSO_2
- Duct dependant circulations – duct constriction reduces rSO_2
- Single ventricle circulations or unbalanced circulations reduce rSO_2
- Agitation: consider adequate sedation if rSO_2 borderline
- Ventilation – excessive PIP and PEEP can reduce rSO_2
- Carbon dioxide – hypocapnia reduces cerebral perfusion and rSO_2
- Persistent PDA – PDA may be responsible for reduced $rScO_2$ (4)
- Neck cannula (ECMO) – obstruction can reduce rSO_2
- Cardiac tamponade (typically ECMO) can reduce rSO_2
- Cerebrovascular regulation – loss may reduce cerebral rSO_2.
- Hypoxic ischaemic injury with reperfusion after 24 hours may increase cerebral rSO_2

Equipment

Monitor: There are a number of systems available from different manufacturers. At present in GG&C neonatology, we are using the Invos Somanetics 5100 model. A manufacturer's guide to start up and care of the monitor is attached as Appendix 1. Images of the monitor are included below under "clinical examples".
The screen default displays 2 sensors as C (cerebral) and R (renal or somatic). These labels can be changed. Upper and lower limit warning lines are set at 90% and 40% but can be adjusted. A base line mean for the patient is calculated after monitoring is commenced and also traced. Adequacy of probe contact is indicated by 5 green boxes on the screen which should all be on. Events can be marked on the screen using neonatal and paediatric menus.

Probes:

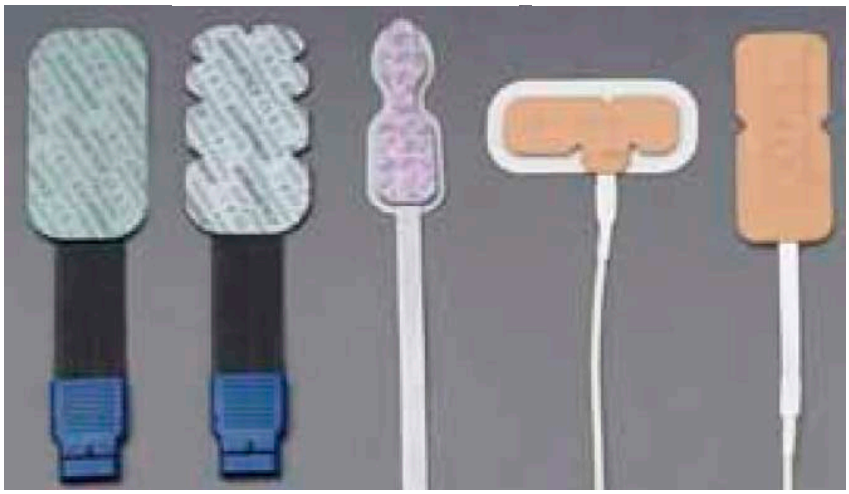


There are a number of different probes available from Covidien, designed for different patient size, for use with the Somanetics monitor. However they all have the same single light emitting diode and dual receptor photodiodes to distinguish light returning from deep and superficial tissues (Figure 2)**.** Data measurements from the by the probe are updated on the screen every 3 seconds.

Figure 2.

The range of probes, from small adult to neonatal, are pictured below (Figure3). Structurally the only difference between probes is the size of the adhesive area and flexibility. The upper limit reported on all probes is 95%. There is one key difference in algorithm between the small adult and all other probes in this range with the small adult probe reading approximately 10 – 15% lower than the neonatal probe. This is important as most research has been undertaken on neonates using the small adult probe. However in practice this is only critical if using the NIRS to screen for HIE when the neonatal probes may not have good specificity.

Small adult somasensor	Paediatric somasensor	Neonatal Oxyalert	Neonatal cerebral sensor and somatic



The probe selected for routine use in NICU is the Oxyalert Neonatal NIRS sensor (middle above). However if there is a **suspicion of HIE the small adult probe should be used to monitor cerebral saturations.**

Probe application

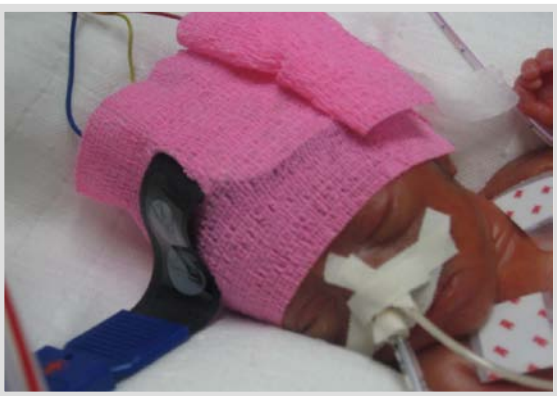
Application is simple but results may not be accurate in the following situations.

- thick hair
- tissue oedema
- conjugated hyperbilirubinaemia – no definite cut off but there needs to be awareness if utilising on a "bronzed baby"

As a neonate has reduced skin integrity, cerebral probes require frequent re-positioning with inspection of underlying skin.

Cerebral Probe

1) Cerebral probe should be positioned over the forehead, towards the right or left (frontal parietal areas)
2) Do not remove backing paper from adhesive, this allows the probe to be easily repositioned without disturbing the epidermis.
3) Secure with Co-Plus flexible bandage, making sure the ends are at the front to allow ease of position changes and skin inspection. Be careful not to over tighten/compress skin. Overlap the ends and secure with a small amount of tape - see attached pictures for application procedure
5) Inspect the skin and reposition the probe 3 hourly by moving over the region**.**
6) Position change and skin condition should be documented



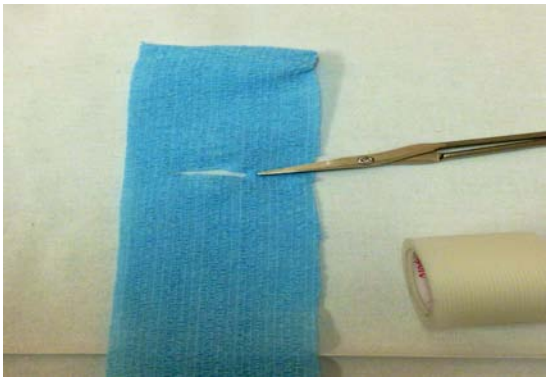
Renal Probe - Position over kidney area, T10-L2, right posterior flank – to allow access for left thoracotomy if required

1) Secure to skin as normal, removing backing paper.
2) Write date and time of application on the waterproof backing
3) Re-site 72 hourly
4) Document probe change and skin integrity

The company manual should also be referred to.

Detail of the use of Co-Plus flexible bandage to position a cerebral probe

1.



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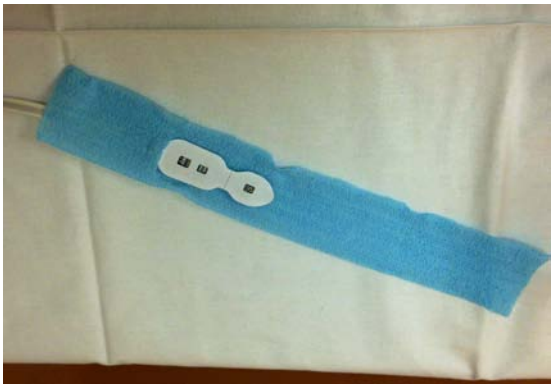

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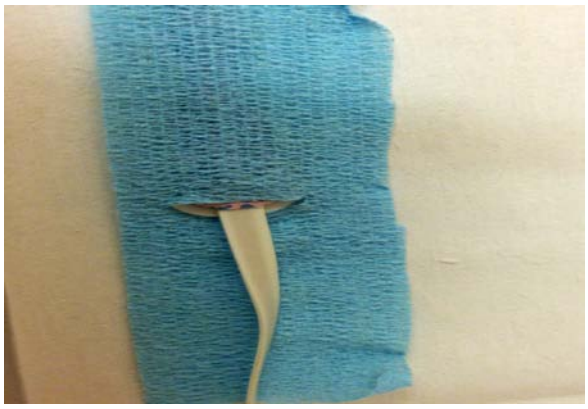

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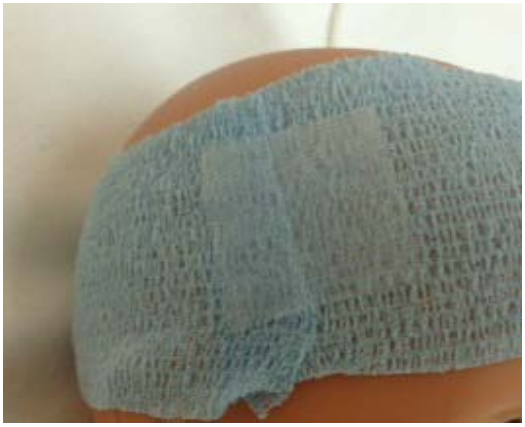

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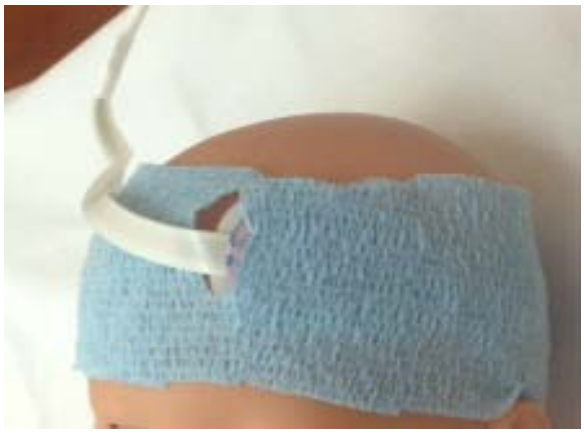
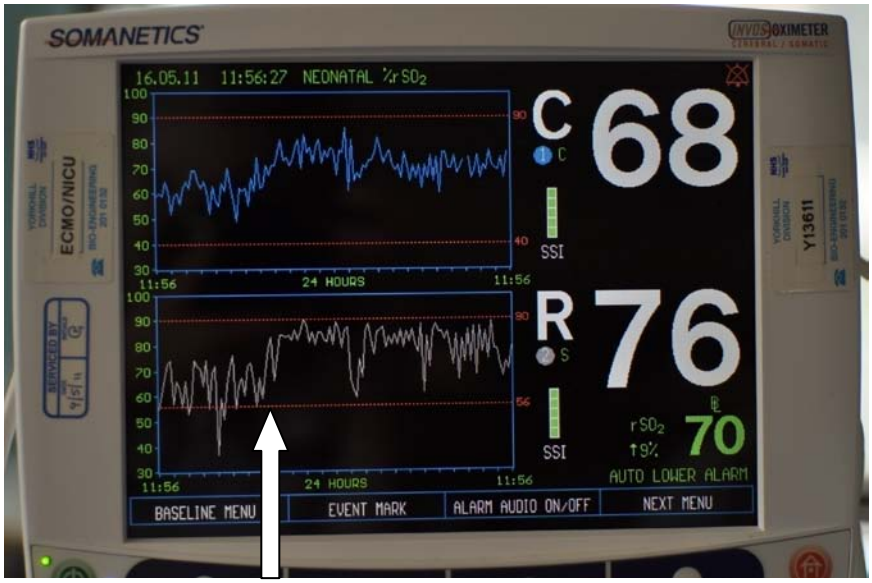


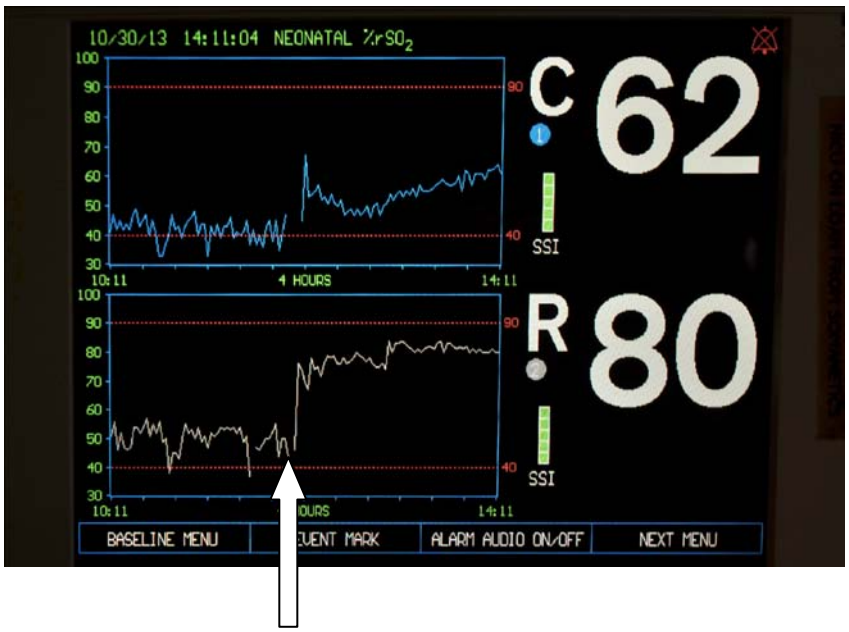
Clinical examples

Case 1. Effect of blood transfusion in univentricular circulation



Demonstrates Invos monitor with Cerebral and Renal trace in infant with hypoplastic right heart on PGE2 . Treatment with inodilator considered because of low regional saturations and poor perfusion. Decision to transfuse with RBC (arrow) initially resulted in rapid improvement in NIRS. No other pre operative interventions required.

Case 2. Effect of intubation in TGA prior to septostomy



Neonate with transposition of the great arteries on PGE2. CPAP in air with arterial saturations drifting to 80s, increasing capillary lactate (2.8) and concerningly low cerebral saturation. Decision to intubate (arrow) and ventilate in air whilst awaiting septostomy resulted in dramatic improvement in cerebral and renal sauturations with no significant change in pulse oximetery.

Case 3. Effect of slow cardiac tamponade on ECMO

Neonate on VV ECMO with pulmonary hypertension had stable SVO2, pulse oximetery and other observations. However slowly but steadily falling NIRS (1 = cerebral, 2= renal) values prompted a cardiac echo revealing a tamponade. NIRS saturations improved dramatically with insertion of a pericardial drain (arrow)

References.

1.**Abdul-Khaliq H**, Troitzsch D, Berger F, Lange PE. Regional transcranial oximetry with near infrared spectroscopy (NIRS) in comparison with measuring oxygen saturation in the jugular bulb in infants and children for monitoring cerebral oxygenation. *Biomed Tech (Berl).* 2000 Nov;45(11):328-32

2. **Kim MB**, Ward DS, Cartwright CR, Kalona J, Chlebowski S, Henson LC,. Estimation of jugular venous O2 saturation from cerebral oximetry and arterial O2 saturation during isocapnic hypoxia. *J Clin Moni 2000*: 16:191-199

3. **Van Bel F**, Lemmers P, Naulaers G. Monitoring neonatal regional cerebral oxygen saturation in clinical practice: value and pitfalls. *Neonatology.* 2008;94(4):237-44.

4. **Hyttel-Sorensen S**, Austin T, van Bel F, Benders M, Claris O, Dempsey E, Fumagalli M, Greisen G, Grevstad B, Hagmann C, Hellström-Westas L, Lemmers P, Lindschou J, Naulaers G, van Oeveren W, Pellicer A, Pichler G, Roll C, Skoog M, Winkel P, Wolf M, Gluud C. A phase II randomized clinical trial on cerebral near-infrared spectroscopy plus a treatment guideline versus treatment as usual for extremely preterm infants during the first three days of life (SafeBoosC): study protocol for a randomized controlled trial. Trials. 2013 May 1;14:120

5. **Kurth CD,** McCann JC, Wu J. Cerebral oxygen saturation-time threshold for hypoxic-ischemic injury in piglets. *Anesth Analg 2009*; 108:1268-77.

6.**Toet MC**, Lemmers PM, van Schelven LJ, van Bel F. Cerebral oxygenation and electrical activity after birth asphyxia: their relation to outcome. Pediatrics. 2006 Feb;117(2):333-9

7. **Lemmers PM**, Toet MC, van Bel F. Impact of patent ductus arteriosus and subsequent therapy with indomethacin on cerebral oxygenation in preterm infants. Pediatrics. 2008 Jan;121(1):142-7.

8. **Thomas Alderliesten**, Petra M. A. Lemmers, Janneke J. M. Smarius, Ren_e E. van de Vosse, Willem Baerts and Frank van Bel. Cerebral Oxygenation, Extraction, and Autoregulation in Very Preterm Infants Who Develop Peri-Intraventricular Hemorrhage. *J Pediatr 2013*;162:698-704

9.**Lemmers PM,** Zwanenburg RJ, Benders MJ, de Vries LS, Groenendaal F, van Bel F, Toet MC. Cerebral oxygenation and brain activity after perinatal asphyxia: does hypothermia change their prognostic value? Pediatr Res. 2013 Aug;74(2):180-5.

10. **Johnson BA**, Hoffman GM, Tweddell JS, Cava JR, Basir M, Mitchell ME, Scanlon MC, Mussatto KA, Ghanayem NS. Near-infrared spectroscopy in neonates before palliation of hypoplastic left heart syndrome. *Ann Thorac Surg.* 2009 Feb;87(2):571-7

11. **Dix LM**, van Bel F, Baerts W, Lemmers PM. Comparing near-infrared spectroscopy devices and their sensors for monitoring regional cerebral oxygen saturation in the neonate. *Pediatr Res.* 2013 Nov;74(5):557-63.

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