How to Administer Near-Infrared Spectroscopy in Critically ill Neonates, Infants, and Children

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Abstract

Near infrared spectroscopy (NIRS) calculates regional tissue oxygenation (rSO_2) using the different absorption spectra of oxygenated and deoxygenated hemoglobin molecules. A probe placed on the skin emits light that is absorbed, scattered, and reflected by the underlying tissue. Detectors in the probe sense the amount of reflected light: this reflects the organ-specific ratio of oxygen supply and consumption - independent of pulsatile flow. Modern devices enable the simultaneous monitoring at different body sites. A rise or dip in the rSO_2 curve visualizes changes in oxygen supply or demand before vital signs indicate them. The evolution of rSO_2 values in relation to the starting point is more important for interpretation than are absolute values.

A routine clinical application of NIRS is the surveillance of somatic and cerebral oxygenation during and after cardiac surgery. It is also administered in preterm infants at risk for necrotizing enterocolitis, newborns with hypoxic ischemic encephalopathy and a potential risk of impaired tissue oxygenation. In the future, NIRS could be increasingly used in multimodal neuromonitoring, or applied to monitor patients with other conditions (e.g., after resuscitation or traumatic brain injury).

Introduction

Near-infrared spectroscopy (NIRS) noninvasively measures the regional tissue oxygen saturation (rSO_2) in brain, muscle, kidneys, liver or intestines[1,2,3,4,5,6,7,8,9]. It is applied in intensive care and cardiac surgery to monitor "real-time" oxygen consumption and somatic tissue saturation[10].

A probe on the skin emits near-infrared light (700 - 1000 nm)[11] that penetrates tissue and bone up to a depth of approximately 1-3 cm, thereby being scattered, absorbed

and reflected[12]. Detectors in the probe sense the amount of reflected light – representing the relative amount of deoxygenated haemoglobin – and calculate a numerical value that indicates the regional oxygenation saturation in percent (%)[2]. Unlike pulse oximetry (which reflects systemic oxygen supply and requires pulsatile flow), NIRS reflects venous oxygen saturation and does not require pulsatile flow, thus making it suitable for low-flow situations such as cardiopulmonary bypass[7].

The rSO_2 reflects the balance between oxygen supply and consumption in the tissue – changes in either become visible even before alterations become otherwise clinically evident. Changes relative to the baseline are more important than the absolute measured values themselves[10,13,14,15,16]. Measuring rSO_2 helps clinicians monitor patients during heart surgery, cardiopulmonary bypass, and in the intensive care unit; it can also assist in guiding oxygen therapy in preterm infants and monitor kidney, splanchnic, and systemic perfusion[12,17,18,19,20,21].

NIRS is a safe, feasible[22], and simple way to monitor tissue oxygenation continuously. Combined with other cerebral biomarkers and neuromonitoring techniques (e.g., continuous or amplitude-integrated EEG), NIRS will likely play a role in future (multimodal) monitoring in neonates and children[23,24]. In this article, we show clinicians how to set up NIRS monitoring for different organ systems, explain how rSO_2 values evolve corresponding to changes in physiology, and present typical results from different clinical settings.

Protocol

NIRS is conducted as part of the hospital's clinical routine. It is recommended in pediatric cardiac surgery interventions within the scope of quality assurance from the Competence Network for Congenital Heart Defects (http://www.kompetenznetz-ahf.de), the Pediatric Cardio Anesthetic Working Group and the German Society for Cardiovascular Engineering[25]. The protocol follows the guidelines of the institution's human research ethics committee. We obtained written informed consent regarding filming and publication of the material from both parents of each infant appearing in the video. The protocol we present corresponds to the clinical practice in the hospital and applies to infants and children of any age. If there are special concerns for a specific age group, we indicate this in a note in the protocol.

1. Preparation

1. Plug in and turn on the NIRS device. Enter the patient's data according to the device's setup.

2. Select the proper probe according to the patient's weight and intended site of use. The weight range is given on the probe's packaging and depends on the manufacturer (see **Table 1** for an overview of the weight ranges in common manufacturers).

3. Make sure the patient's skin is clean and dry for optimum adhesion. Dry the skin with a swab if necessary. Be very careful or omit cleaning if the skin is vulnerable.

2. Place the probe

1. After identifying the correct probe position, carefully bend the center of the probe toward the side of the white cover until it starts to come off. Gently peel off the cover without touching the probe's sticky surface.

2. Place the sensor on the skin from the center of the probe to the sides. Make sure the edges of the probe are firmly connected to the skin. If the probe disconnects, wrong NIRS values will be obtained. Disconnection in a bright

environment causes false high values; disconnection in a dark environment causes false low values.

NOTE: To avoid skin lesions, do not place the probe on very immature or vulnerable skin. If the probe must be placed on vulnerable skin, use a layer of cellophane between the skin and the probe, or leave the cover on. When fixing the probe, avoid putting pressure on it (e.g., via an infant flow cap or headband) as this can impair skin perfusion and cause an erroneous measurement.

3. Select the probe position

1. Cerebral: Place the NIRS probe in the supra-orbital region on the forehead below the hairline to obtain values from the frontal cortex. Do not place the probe above hair, the frontal sinus, the temporal muscle, nevi, the superior sagittal sinus, intracranial hemorrhages or other anomalies, as that can alter the measurement and the values obtained will not represent regional tissue oxygenation. Placement of two probes, one on each forehead allows selective analysis of both hemispheres if the clinical setting requires this. Neighboring probes emit and measure signals alternately to avoid interference.

   NOTE: The rSO_2 value only reflects the oxygenation status of the tissue underneath the probe – for a large organ like the brain, obtained values do not reflect the entire organ's oxygenation status.

2. Somatic: Select a position above the region of interest. Avoid fat deposits, hair, and bones. Do not place the probe above nevi, hematoma, and injured skin. Always remember that the depth of the NIRS signal is approximately 2.5 cm - if the organ of interest is farther away from the probe, it cannot be analyzed. For renal or hepatic NIRS, use ultrasound to ensure correct placement.

1. Kidneys: Locate the kidney via dorsal sagittal sonogram before placing the probe. Make sure that the skin-to-organ-distance does not exceed the maximum depth of the probe.

   NOTE: The use of ultrasound may interfere with the minimal-handling principle (e.g., in very preterm infants).

2. Intestines: Place the probe in the region of interest (e.g., below the umbilicus or in the right or left lower quadrant).

   NOTE: Free air or liquid in the abdomen can make measuring the desired organ's tissue oxygenation impossible.

3. Liver: Place the probe exactly above the liver. If possible, confirm its position by ultrasound. To avoid measuring the wrong organ, make sure the liver tissue underneath the probe is at least as deep as the emitted light penetrates (1-3 cm, according to the probe selected).

4. Foot: Place the probe on the plantar portion of the foot. Measuring NIRS in the most distant part of the body gives information about peripheral perfusion during hypothermia, in patients with shock or in any situation where pulse oximetry does not work.

5. Muscle: Place the probe over the muscle of interest.

4. Set the baseline

1. 1-2 minutes after placing the probe, set the baseline by pushing the corresponding button on the device. The baseline reflects the starting point of the measurement. The evolution of tissue perfusion in each monitored area can be observed and interpreted individually by relying on the change from the baseline value.

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5. Check for problems with the device or clinical complications

1. If the device indicates bad recording quality or values are implausible, confirm that all the aforementioned steps have been taken correctly. If necessary, replace the probe and preamplifer, and check all electrical plug contacts.

2. Check for external light sources that might affect the sensor and contact. Cover the probe light-tight if disturbing light sources cannot be eliminated.

3. After ruling out technical problems, check the patient for clinical complications.

Representative Results

The measured rSO_2 value results from the ratio between oxygen supply and consumption (**Figure 1A**); differing metabolic characteristics lead to slightly different normal values depending on age and organ (**Table 2**). Note that - except for the brain – scientifically evaluated reference values exist only for preterm infants and newborns[26, 27, 28, 29, 30, 31] and most of the protocol steps rely on manufacturers' recommendations, personal experience, and expert opinion (**Table 3**). This is due to the fact the values depend on the device and sensors used and reveal high inter-individual variability[30, 32]. Critically low values and critical changes relative to the baseline originate from experience and expert opinion.

If the oxygen supply and demand are balanced at physiological values, tissue oxygenation is within normal range. Changes in either oxygen supply or consumption cause the rSO_2 value to fall or rise (**Figure 1B,1C**). A typical curve revealing normal cerebral and renal NIRS values is displayed in **Figure 2** from the beginning until 14:25 pm.

In the following, we provide examples to show how changes in underlying physiologic conditions affect rSO_2. During heart surgery, doctors manipulate circulation in a controlled manner - therefore the effects on rSO_2 are easy to observe. For example, clamping the descending aorta causes cerebral perfusion and the corresponding rSO_2 to rise; perfusion of the lower body results in an rSO_2 decrease (**Figure 2**). Another – non-surgical - cause of increased cerebral blood flow and elevated cerebral rSO_2 is hyperdynamic shock in conjunction with high cardiac output (**Figure 3**).

In cold shock, a dropping renal rSO_2 together with stable cerebral rSO_2 can be the first sign; a decrease in both renal and cerebral rSO_2 can occur later in the course[23]. Combined cerebral and renal NIRS can help identify early stages of shock in which cerebral perfusion is maintained at a normal level, but somatic perfusion is already impaired[23].

When using two cerebral NIRS probes, values from the right and left sides should be similar - dissonance between the right and left channel NIRS can be caused by the NIRS sensor's incomplete adhesion (**Figure 4**, red star) or indicate a complication: During some heart surgeries, the brain is perfused selectively via one carotid artery, making use of intracerebral collaterals (the circle of Willis) to supply the opposite side. Throughout this procedure, dissonance between the two cerebral NIRS channels can help diagnose a dysfunctional circle of Willis (**Figure 5**).

Another example of a complication discovered by NIRS is a dislocated vena cava superior cannula during cardiopulmonary bypass leading to venous stasis and lowered cerebral oxygen supply (**Figure 6**). The use of NIRS can help to identify impaired cerebral perfusion that

would otherwise remain undetected and result in severe brain damage.

Besides heart surgery and cardiac intensive care, rSO$_2$ measurements can also facilitate "standard" pediatric intensive care – complications and changes in therapy can be accompanied by changes in cerebral rSO$_2$ (**Figure 7**).
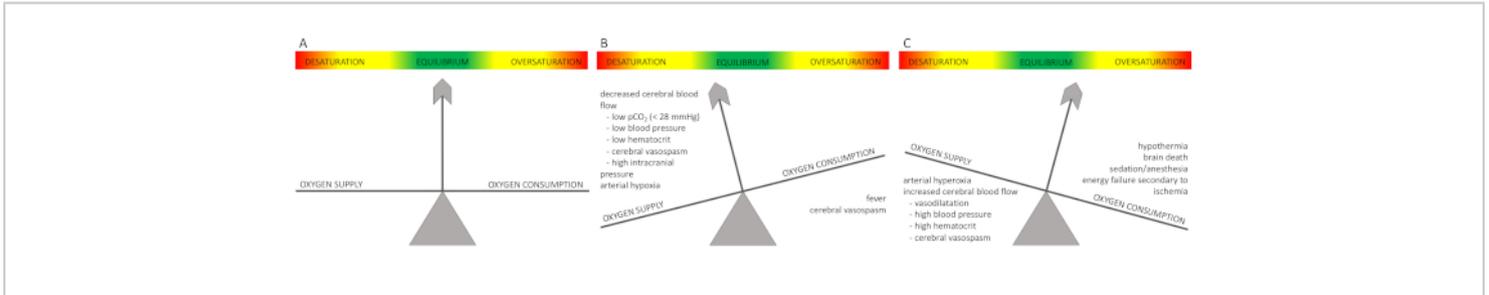
Figure 1: Balancing the ratio between oxygen supply and demand.

(**A**) Under physiologic conditions, oxygen supply and consumption are balanced, and regional tissue oxygenation is within normal range. (**B**) A decreasing cerebral rSO$_2$ results from either increased oxygen consumption or decreased oxygen supply. Reasons for low or decreasing cerebral NIRS values are illustrated in the figure. For example, fever increases cerebral oxygen consumption by 10-13% per 1 °C increase in body temperature. Cerebral spasms can increase oxygen consumption by up to 150-250%. (**C**) An increase in cerebral rSO$_2$ results from reduced oxygen consumption or increased oxygen supply. Reasons for high or rising cerebral NIRS values are provided in the figure. A cerebral rSO$_2$ above 80%, caused by high cerebral blood flow after the loss of cerebral vascular autoregulation, is also called "luxury perfusion". Please click here to view a larger version of this figure.

Figure 2: Evolution of cerebral and renal rSO$_2$ during clamp out of the descending aorta.

Initially, cerebral (blue) rSO$_2$ is lower than renal rSO$_2$ (yellow), as in physiological conditions. During clamp-out of the descending aorta, cerebral blood flow increases while the lower half of the body is undersupplied. Thus, cerebral rSO$_2$ rises and renal rSO$_2$ drops. The red area indicates that renal rSO$_2$ values are critically low because they decreased more than 25% below the baseline. After removing the aortic clamp and establishing reconstruction of the aorta and establishing normal circulation, both rSO$_2$ curves normalize. Please click here to view a larger version of this figure.
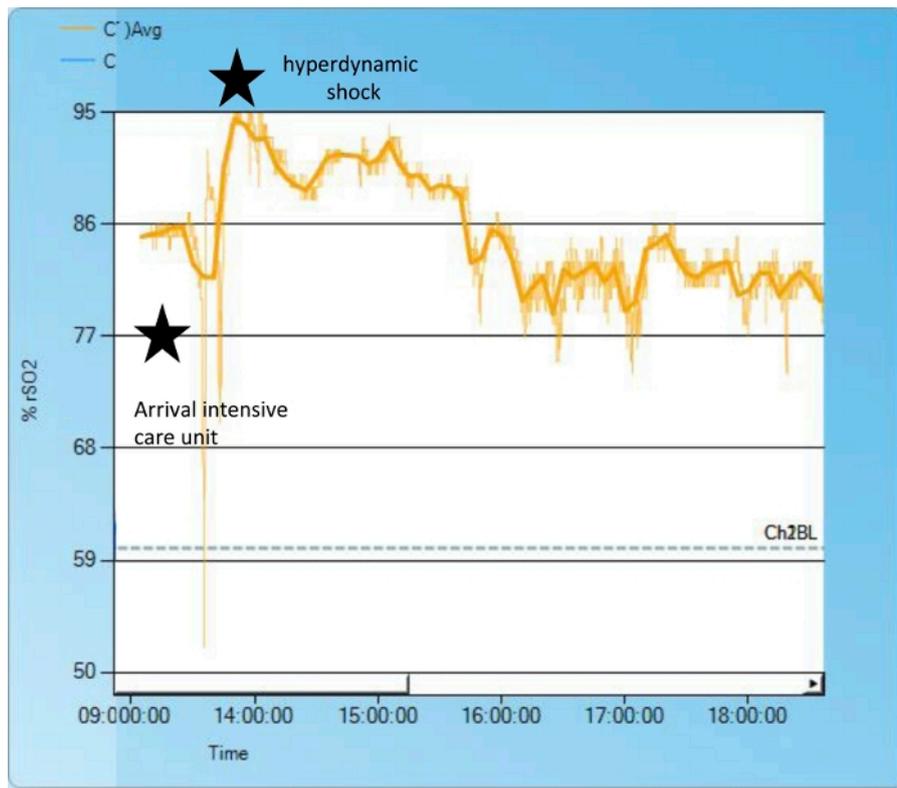
Figure 3: Hyperdynamic shock.

After arriving at the intensive care unit after cardiac surgery and changing respirator tubes, we experienced severe problems with mechanical ventilation (reaching only low tidal volumes at high ventilation pressures due to a defective filter). The patient developed hyperdynamic shock and respiratory acidosis with increased central venous saturation of 90% and increasing cerebral rSO_2 up to 92%. After changing the filter, fluid resuscitation, and vasopressor treatment, the patient stabilized quickly and cerebral rSO_2 normalized. Please click here to view a larger version of this figure.
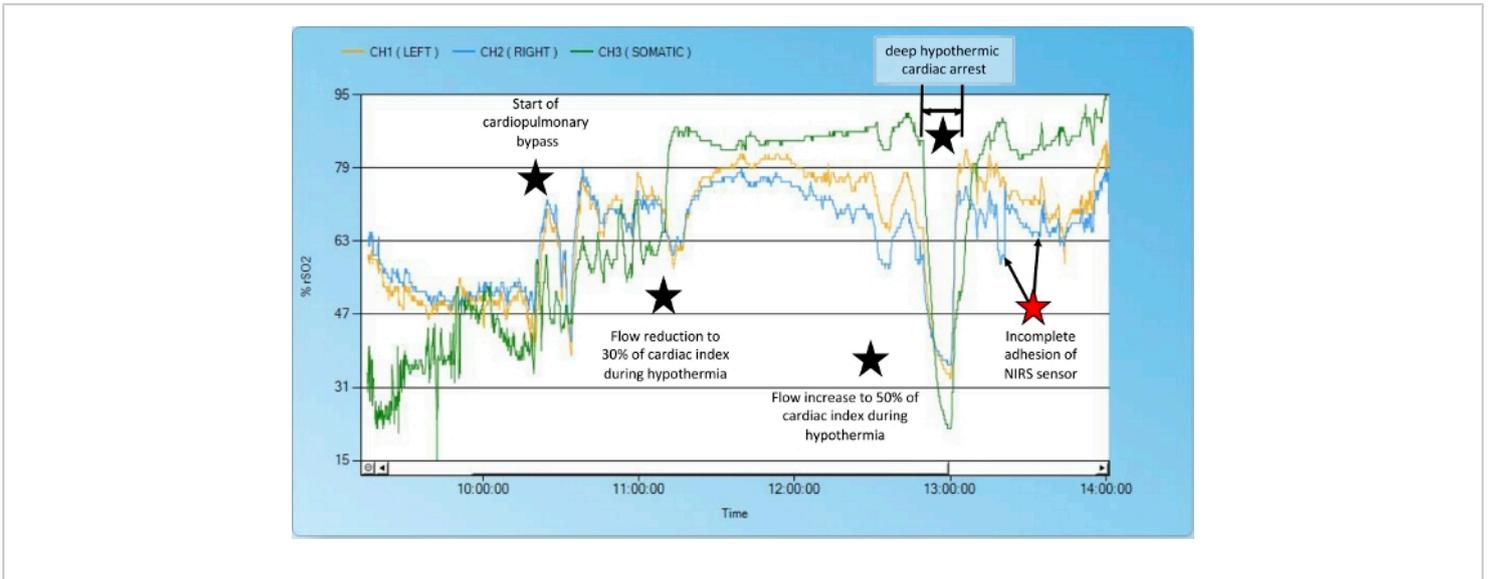
Figure 4: Evolution of NIRS values during hypothermia and deep hypothermic cardiac arrest.

This figure illustrates how cerebral and renal NIRS values change under hypothermia, adjustment of cardiopulmonary bypass flow and in deep hypothermic cardiac arrest (arterial switch surgery in a patient with transposition of the great arteries and ventricular septal defect). The patient's baselines rSO$_2$ values are 59% (left, yellow) and 64% (right, blue) for the brain and 32% (green) for the left kidney. The blood supply to the lower half of the body depends on the ductus arteriosus. Intraoperatively-induced hypothermia reduces oxygen consumption, which leads to rising NIRS values, especially in the kidney. With increasing NIRS values we reduced the flow rate of cardiopulmonary bypass. Due to falling NIRS values caused by an altered metabolic situation (e.g., due to insufficiently deep anesthesia), the flow was adjusted again. During deep hypothermic cardiac arrest, renal and cerebral rSO$_2$ fell to critically low values and rose again immediately after reestablishing physiological circulation. The red star with arrows shows two dips in the right cerebral NIRS curve due to incomplete probe adhesion. After gently remolding the sensor onto the skin, the values again run parallel to the left side's. Please click here to view a larger version of this figure.
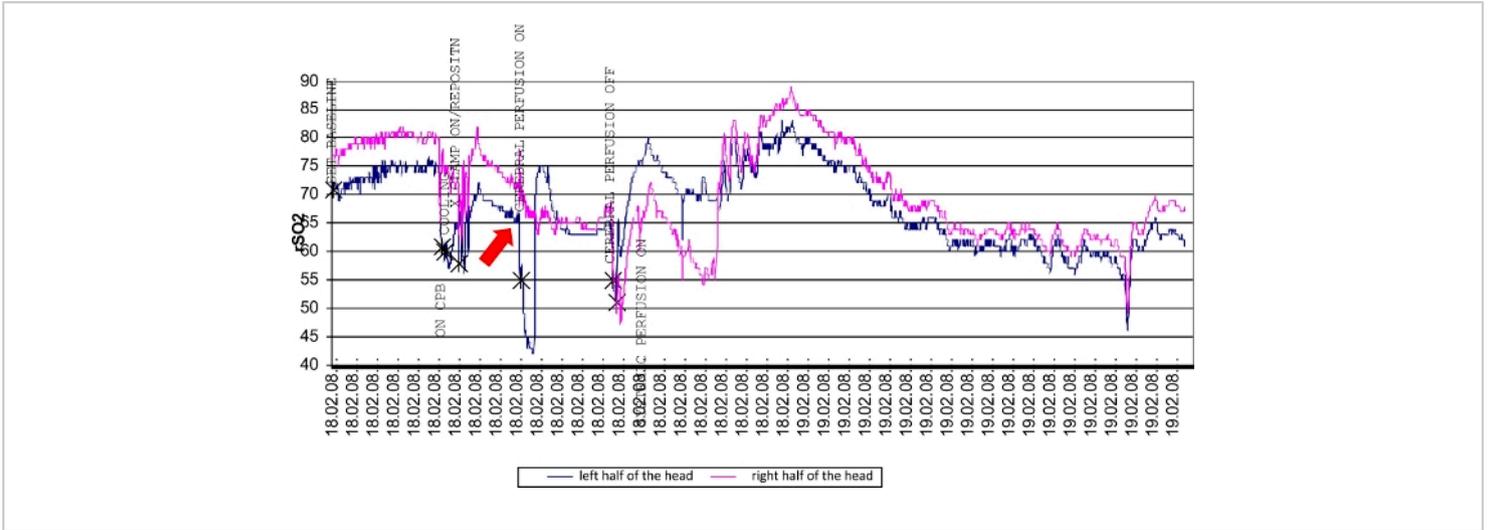
Figure 5: Dysfunctional circle of Willis during aortic arch surgery.

As soon as the brain is selectively perfused via the right carotid artery (red arrow), the rSO$_2$ measured on the left side (dark blue) decreases because the intracerebral collaterals via the circle of Willis are insufficient. After placing an additional cannula in the left carotid artery, sufficient perfusion of both hemispheres and thus normal NIRS values are achieved. Please click here to view a larger version of this figure.
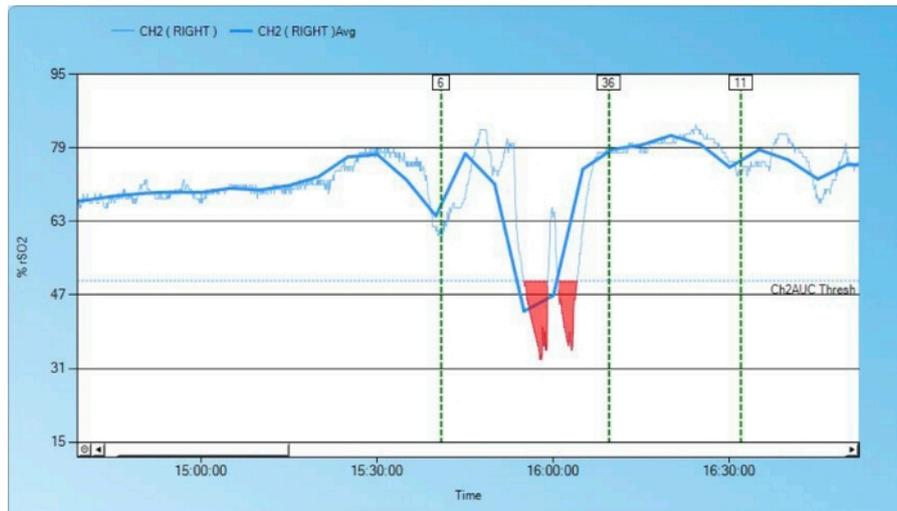
Figure 6: Detection of upper vena cava obstruction caused by a dislocated cardiopulmonary bypass cannula.

Shortly after the start of cardiopulmonary bypass (for closure of an atrial septal defect), cerebral NIRS values dropped. Troubleshooting showed that the venous cardiopulmonary bypass cannula had become dislocated, leading to occlusion of the superior vena cava and obstructed cerebral venous drainage. This caused a cerebral undersupply of oxygen, which was only detected through the low rSO$_2$ value. After repositioning the superior vena cava cannula, venous flow was restored and NIRS values normalized. No. 6: start cardiopulmonary bypass; No. 36 aorta clamped; No. 11 end of ischemia. Please click here to view a larger version of this figure.
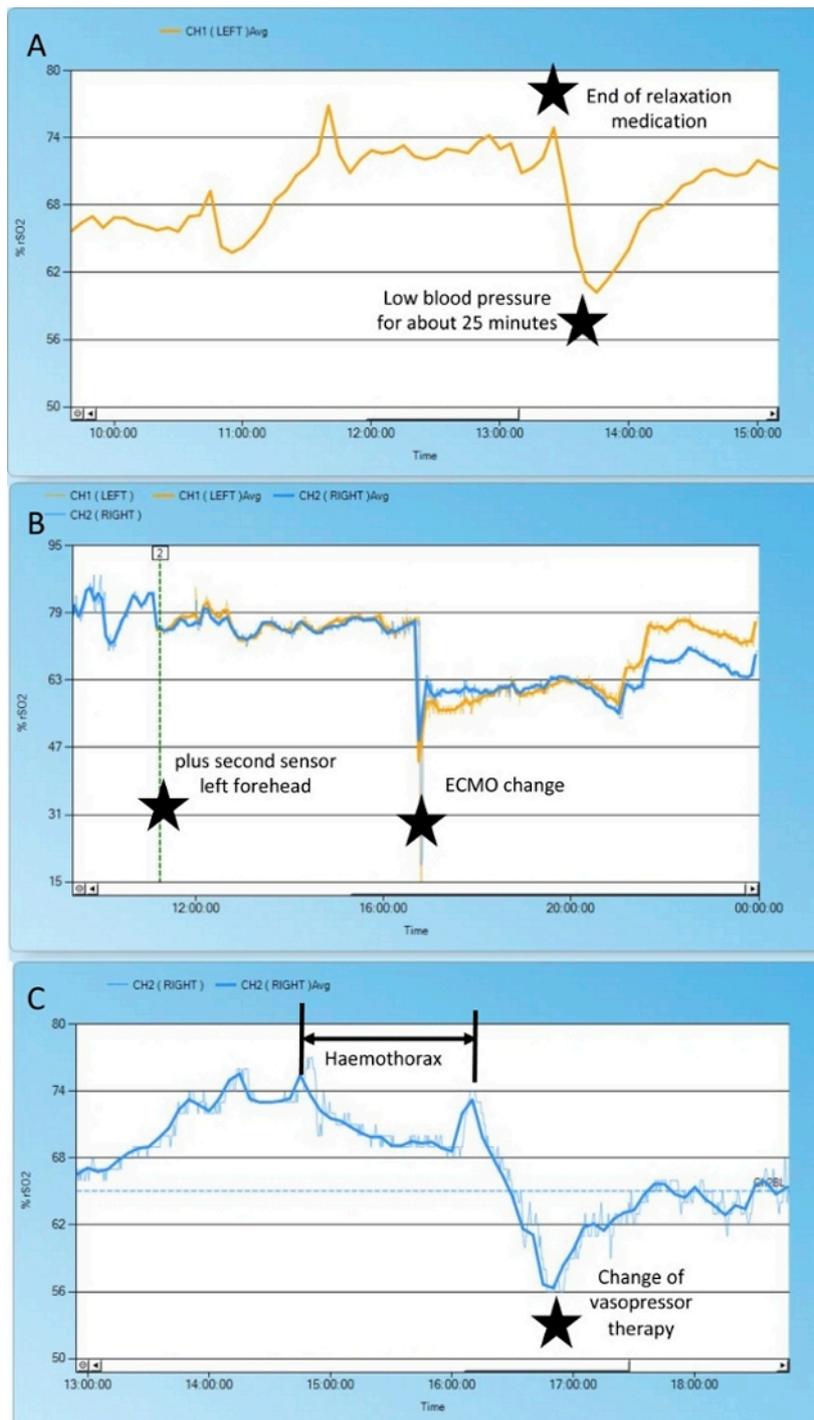
Figure 7: Changes in cerebral rSO$_2$ in a pediatric patient.

After near drowning, this patient was put on extracorporeal membrane oxygenation. Due to side differences in arterial

blood gas analyses, we put a second cerebral NIRS sensor in place (yellow). The end of muscle relaxation (**A**), change of

extracorporeal membrane oxygenation system (**B**), blood pressure fluctuations (**A, C**), and the effect of a hemothorax (**C**) are reflected by changes in the NIRS curves. Please click here to view a larger version of this figure.

Figure 8: Placing the NIRS probe over hair.

(**A**) This patient has a lot of hair on the forehead. (**B**) The NIRS probe was still put in place. (**C**) The device indicates that the signal intensity is suboptimal. (**D**) The NIRS curve values and the course of the curve follow the actions during the surgical procedure (reconstruction surgery in Ebstein's anomaly). Please note that the absolute values cannot be interpreted, even if they seem normal. Please click here to view a larger version of this figure.

Manufacturer	Device	Age group		
		Neonates	**Infants/Children**	**Adult**
Casmed	Fore-Sight Elite	< 8 kg	≥ 3 kg	≥ 40 kg
Masimo	Root with O3 Oximetry	< 40 kg	< 40 kg	≥ 40 kg
Medtronic	INVOS 5100C	< 5kg	5-40 kg	> 40 kg
Medtronic	INVOS 7100C	-	-	> 40 kg
Nonin	SenSmart Model X-100	< 40 kg	< 40 kg	> 40 kg

Table 1: NIRS probes by manufacturer and weight range.

Organ	Age group	Approximate values under physiologic conditions [%]	Critically low values [%] [E]	Critically high values [%][E]	Critical relative change to baseline [%][E]
Brain	Preterm infants	60 – 90[26,27,30]	< 45	> 90	> 25
	Newborns	60 – 90[26,29,E]	< 45	> 80	> 25
	Infants/Children	60 – 80[26,E]	< 45	> 80	> 25
Kidneys	Preterm infants	70 – 90[28,30]	< 40	Not defined	> 25
	Newborns	80 – 95[26,29]	< 40		> 25
	Infants/Children	Not defined, tend to be 5-15 % higher than cerebral values[26,31,E]	< 40		> 25
Intestines	Preterm infants	18 – 80[26,30]	Not defined	Not defined	Not defined
	Newborns	55 – 80[26,29]			
	Infants/Children	Not defined, tend to be 5-15 % higher than cerebral values[26,E]			
Liver		Not defined	Not defined	Not defined	Not defined
Muscle		Not defined	Not defined	Not defined	Not defined
[E] Experience/expert opinion					
Absolute values depend on the device and the sensors used, on the metabolic state, and show high interindividual variability. They should be interpreted with caution – if in doubt, the change relative to the baseline is more meaningful.					

Table 2: Typical rSO$_2$ values by organs and age group.

Step	Level of evidence*
Cleaning the skin before placing the NIRS probe	5
Use of NIRS in neonates, infants and children of different ages	1-5
Use of two NIRS sensors on the forehead	5
Use of ultrasound to ensure correct placement of NIRS probes	5
Placing NIRS probe in different positions (brain, liver, intestine, kidney, foot, muscles)	(1-)2-5
Interpreting NIRS values with respect to reference values	2-5
*According to the Oxford Center of Evidence Based Medicine Evidence Levels: 1 – Systematic reviews of randomized controlled trials/randomized controlled trials with narrow confidence interval; 2 – Systematic reviews of cohort studies/ individual cohort study or low quality randomized controlled trials; 3 – Systematic review of case-control studies/ individual case-control studies; 4 – Case series and poor quality cohort and case-control studies; 5 – Expert opinion.	

Table 3: Levels of evidence of the protocol steps.

Discussion

This article illustrates how cerebral and somatic NIRS is set up in infants and children. Cerebral NIRS is used for monitoring purposes during procedures such as patent ductus arteriosus closure, surfactant administration, heart surgery and cardiopulmonary bypass; it is also used to monitor critically ill patients in intensive care, to predict necrotizing enterocolitis in preterm infants, and to predict outcome after hypoxic ischemic encephalopathy[2,5,6,33,34,35,36,37,38,39,40]. Further, NIRS can assist in guiding oxygen therapy in preterm infants[17,18,19]. Somatic NIRS helps to monitor kidney, splanchnic, and systemic perfusion[12,20,21] and may also be valuable to detect complications during or after liver transplantation[8,41,42]. The simultaneous use of multiple probes (multisite NIRS) facilitates the detection of systemic hypoperfusion[23,43].

For the NIRS measurement to function accurately, selecting the appropriate probe and position is crucial. Vulnerable skin may require the use of non-adhesive probes (for example by leaving the cover or attaching a layer of cellophane to the sticky side). However, the entire probe must be in firm contact with the skin; otherwise, the sensors will not provide reliable values (**Figure 4** and **Figure 8**). A bright environment causes false high and dark environment false low values if the probe is not firmly attached to the skin. In case of poor recording quality (indicated by the device) or implausible values, troubleshooting starts by checking whether the above-mentioned essential steps have been carried out. If the problem persists, the probe and preamplifier should be replaced and all electrical plug contacts checked. External light sources acting on the sensor can also trigger incorrect values; covering the probes with a light-impermeable cover will remedy this. If abnormal NIRS values persist, the patient must be examined to rule out

complications. The following parameters should be assessed and optimized: arterial blood pressure, systemic oxygenation, pH, hemoglobin, cerebral oxygen return (when the patient is on cardiopulmonary bypass)[44].

To modify the standard use, there is no limit to the possible applications. It is possible to place a NIRS probe on any site of interest provided the skin is intact. Deriving values simultaneously from several sites enables a great variety of setups according to each specific clinical or scientific question. For example, NIRS and multisite NIRS can be used outside of critical care and even during exercise[12].

Despite its ease of application and use, measuring rSO_2 has some limitations that must be considered when interpreting values and curves. The values measured depend on the device and sensors used[32]. Absolute values should therefore be interpreted with caution - reference values cannot be transferred easily between devices and setups[32]. rSO_2 values for organs other than the brain vary highly between individuals[30]. But even within one recording, values can fluctuate by up to 6% if a probe becomes detached and is then reattached[45]. Additionally, NIRS values depend on the individual's metabolic state, which is altered by interventions such as therapeutic hypothermia and medication[24].

Changes in tissue boundary conditions – for example the entry of blood or air due to surgery – also yield incorrect NIRS values[46]. In preterm infants' first days of life, the transition from meconium to regular stool alters the fecal absorption spectra and can affect the measured intestinal rSO_2 values[47]. Placing a NIRS probe over tissue other than the intended location produces inaccuracies in absolute values, but may still be helpful for monitoring trends[7].

Despite its limitations, NIRS is a good means of noninvasively and continuously monitoring the oxygenation of a specific region in real time. Alternative methods for assessing global tissue perfusion are invasive and discontinuous: arterial blood draws, serum lactate concentration, central venous saturation or oxygen saturation of the jugular bulb. These can be particularly problematic in preterm infants, who frequently develop iatrogenic anemia due to repeated blood draws and whose cerebral rSO_2 is impaired during arterial blood drawing[48]. In cases of low cardiac output, during extracorporeal membrane oxygenation or when non-pulsatile cardiac assist devices are in use, NIRS still functions – in contrast to pulse oximetry – as it does not require pulsatile flow and can even selectively monitor areas at risk for hypoxia[7, 49]. rSO_2 changes in these regions can serve as early signs of reduced cardiac output[7]. By these features, NIRS provides essential clinical information that currently cannot be obtained from other measures of tissue saturation.

The scope of applying rSO_2 monitoring in neonatal and pediatric intensive care is likely to expand in the future. One potential application is monitoring cerebral hemodynamics after traumatic brain injury, which is already being investigated in adults[50, 51, 52, 53, 54, 55]. In preterm infants, goal-directed oxygen supplementation may lead to better neurodevelopmental outcomes by reducing cerebral hypoxemia[17, 18, 19]. The combination of cerebral NIRS with other cerebral biomarkers may also be promising. For example, combining amplitude-integrated EEG and NIRS can help to determine prognosis in moderate hypoxic ischemic encephalopathy[56]. Possible further applications for this combination include compromised hemodynamics or seizures[23].

In summary, NIRS is a promising technology with the potential for even broader application. Correctly applied and interpreted, rSO$_2$ measurements help to detect complications or deteriorated clinical conditions at an early stage and guide therapy in various clinical settings. This protocol provides clinicians with the tools to set up and interpret rSO$_2$ measurements at different body sites, and to interpret those results.

Disclosures

The authors have nothing to disclose.

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