

# Journal of Biomedical Optics

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## **Regional tissue oxygen saturation: comparability and reproducibility of different devices**

Mirjam Pocivalnik  
Gerhard Pichler  
Heinz Zotter  
Nina Tax  
Wilhelm Müller  
Berndt Urlesberger

# Regional tissue oxygen saturation: comparability and reproducibility of different devices

Mirjam Pocivalnik, Gerhard Pichler,\* Heinz Zotter, Nina Tax, Wilhelm Müller, and Berndt Urlesberger

Medical University of Graz, Division of Neonatology, Department of Pediatrics, Research Unit for Cerebral Development and Oximetry Research, Auenbruggerplatz 30, Styria, 8036 Austria

**Abstract.** Comparability and reproducibility of different near-infrared spectroscopy devices measuring regional tissue oxygen saturation remain poor. Aim of the present study was to compare values and reproducibility of cerebral/peripheral “tissue-oxygenation-index” (TOI; NIRO 300, Hamamatsu®, Japan) with cerebral/peripheral “regional-oxygen-saturation” (rSO<sub>2</sub>; INVOS5100, Somanetics®, USA), and to analyze the influence of quality criteria. Methods: cTOI and crSO<sub>2</sub> were measured on the left forehead, pTOI and prSO<sub>2</sub> were measured on the left calf. To analyse reproducibility, optodes were reapplied five times. A quality criterion was introduced for cTOI, crSO<sub>2</sub> and prSO<sub>2</sub>. For pTOI quality criteria were introduced in combination with a venous occlusion technique. Results: Cerebral measurements were performed in 37 neonates. cTOI (72.7 ± 6.2%) was lower than crSO<sub>2</sub> (83.3 ± 5.8%) ( $p < 0.001$ ). The mean difference between cTOI and crSO<sub>2</sub> was 10%. Mean standard deviations of cTOI and crSO<sub>2</sub> were similar (cTOI: 4.9 ± 3.6; crSO<sub>2</sub>: 4.5 ± 2.6). Peripheral measurements were performed in 39 neonates. pTOI (66.0 ± 7.9%) was lower than prSO<sub>2</sub> (82.0 ± 7.0%) ( $p < 0.001$ ). The mean difference between pTOI and prSO<sub>2</sub> was 15%. Mean standard deviations of pTOI (3.7 ± 2.6%) were lower than of prSO<sub>2</sub> (5.0 ± 3.0%) ( $p = 0.047$ ). Conclusion: TOI values were significantly lower than rSO<sub>2</sub> values, in cerebral and peripheral measurements. Reproducibility was higher for pTOI than for prSO<sub>2</sub>. © 2011 Society of Photo-Optical Instrumentation Engineers (SPIE). [DOI: 10.1117/1.3575647]

Keywords: tissue oxygenation index; rSO<sub>2</sub>; NIRO300; INVOS5100; comparability; reproducibility.

Paper 10519RR received Sep. 21, 2010; revised manuscript received Mar. 18, 2011; accepted for publication Mar. 21, 2011; published online May 23, 2011.

## 1 Introduction

Near-infrared spectroscopy (NIRS), first described by Jöbsis<sup>1</sup> in 1977, enables non-invasive and continuous measurement of regional tissue oxygenation in regions of interest. Different devices measuring regional tissue oxygen saturation are available and are used in clinical settings.<sup>2</sup>

Most studies in neonates were done with either the NIRO (Hamamatsu®, Japan)<sup>3</sup> or the INVOS (Somanetics®, USA)<sup>4</sup> or both.<sup>5,6</sup> The comparison of studies using these different devices remains difficult.<sup>7</sup> These devices have already been compared in regard to cerebral oxygenation<sup>8</sup> and the interpretation of different results remains very difficult too.<sup>3,8–10</sup> One study found more agreement<sup>9</sup> and two found less agreement<sup>3,11</sup> between the two devices. Until now no data have been published comparing the reproducibility of measurements of these two devices.

Both devices are based on “spatially resolved spectroscopy” (SRS),<sup>12,13</sup> but with differences in the mode of light absorption and in the number of used wavelengths. The NIRO 300 works with laser diodes using four different wave lengths and the INVOS 5100 is based on light emitting diodes and two different wave lengths.<sup>8</sup>

The aim of the present study was to compare the values and the reproducibility of measurements of cerebral and peripheral muscle “tissue oxygenation index” (cTOI and pTOI; measured with the NIRO 300) with the cerebral and peripheral muscle

“regional oxygen saturation” (crSO and prSO; measured with the INVOS 5100) before and after introduction of certain quality criteria.

## 2 Methods

### 2.1 Patients

In a prospective observational study, 22 term and 60 preterm newborn infants weighing over 2 kg who were admitted to the Neonatal Unit of the Department of Paediatrics, Medical University of Graz, were considered for inclusion in the study.

Two neonates with abnormal cerebral ultrasound scans or congenital malformations were excluded from the study. Four neonates were excluded because of agitation.

Nine infants were admitted because of IRDS (II-III), 17 because of infection, 21 because of TRDN and 29 infants because of preterm birth.

The study was approved by the local ethical committee.

Neonates were allocated to either cerebral measurements or peripheral muscle measurements.

Cerebral measurements were performed in 8 term and 29 preterm neonates with a male/female ratio of 20:17. Peripheral muscle measurements were performed in 11 term and 28 preterm neonates with a male/female ratio of 25:14.

### 2.2 Cerebral Measurements

Measurements were performed during undisturbed daytime sleep after feeding. The infants were in a supine position with the

Address all correspondence to: Pichler Gerhard, MD, Div. of Neonatology, Dep. of Pediatrics, Medical University Graz; Auenbruggerplatz 30, 8036 Graz; Tel: +43 316 385 2605; Fax: +43 316 385 3300; E-mail: pichler.gerhard@klinikum-graz.at.

head tilted up (10 degrees). Heart rate and SaO<sub>2</sub> were measured by pulse oxymetry on the right forearm. Capillary refill time was measured centrally over the sternum and peripherally over the left calf. A pneumatic cuff was placed on the right upper arm and a pulse-oxymetry sensor on the right wrist. A rectal temperature sensor and a skin sensor, placed on the right upper arm, continuously measured central and peripheral temperatures. After a five-minute resting period arterial blood pressure was measured by oscillometer.

### 2.2.1 NIRO 300 (Hamamatsu Photonics® 82, Japan)

The spatially resolved method enables non-invasive continuous measurement of tissue-oxygenation-index (TOI). The NIRS optodes were applied to the left side of the forehead. The inter-optode distance was 4 cm, and the sampling rate was 2 per sec. After a resting period of at least one minute, cerebral NIRS data were recorded for 20 sec. The NIRS optodes were reapplied five times<sup>14</sup> with a calm-down period of at least 30 sec between measurements.

### 2.2.2 INVOS 5100 (Somanetics® 91, USA)

The spatially resolved method enables non-invasive continuous measurement of regional oxygen saturation (rSO<sub>2</sub>). The NIRS optodes were applied on the same area on the left side of the forehead. As recommended by Somanetics® we used the neonatal sensor. The inter-optode distance was 4 cm, and the sampling rate was 1 per 8 sec. After a resting period of at least one minute, cerebral NIRS data were recorded for 20 sec. The NIRS optodes were reapplied five times<sup>14</sup> with a calm-down period of at least 30 sec between measurements.

## 2.3 Quality Criteria

Regional tissue oxygenation is a measure of tissue oxygen saturation made up of venous, capillary and arterial oxygen saturation (venous:arterial = 84:16).<sup>15</sup> Thus, cTOI and crSO<sub>2</sub> have to be lower than productal SaO<sub>2</sub>. All cTOI and crSO<sub>2</sub> values, which were higher or equal SaO<sub>2</sub>, were excluded from further analysis.

## 2.4 Peripheral Muscle Measurements

Measurements were performed under standardized conditions<sup>7</sup> during undisturbed daytime sleep after feeding. A pneumatic cuff was placed on the left thigh and a pulse-oxymetry sensor on the left foot. A rectal temperature sensor and a skin sensor, placed on the left thigh continuously measured central and peripheral temperatures. Furthermore, the circumference of the left thigh and calf were measured. After a five-minute resting period non invasive blood pressure was measured by oscillometer.

### 2.4.1 NIRO 300 (Hamamatsu Photonics® 118, Japan)

The NIRS optodes were applied to the left lateral calf. The inter-optode distance was 3 cm, and the sampling rate was 2 per sec. We avoided circular fixation of optodes to prevent compromisation of venous circulation.<sup>7</sup> A differential path length factor of 5.51 was used.<sup>16</sup> In addition to TOI the NIRO 300 measures changes in the concentration of oxygenated

haemoglobin (HbO<sub>2</sub>) and deoxygenated haemoglobin (Hb). Changes in the concentration of total haemoglobin (Hbtot) can be calculated from the sum of changing HbO<sub>2</sub> and, Hb levels. HbO<sub>2</sub>, Hb, and Hbtot were measured in micro-mol units. All measurements were combined with venous occlusion. Venous occlusion<sup>17,18</sup> was performed using a pneumatic cuff around the left thigh. Venous occlusion causes an increase in calf blood volume by undisturbed arterial flow and interrupted venous flow. Thus, changes in HbO<sub>2</sub>, Hb, and Hbtot during venous occlusion are caused only by arterial flow and oxygen consumption. After a resting period of at least one minute, the pneumatic cuff was inflated within 0.5–1 sec to a pressure below the diastolic arterial pressure and above the venous pressure (20 mmHg). The cuff remained inflated for 20 sec and NIRS data were recorded. The optodes were reapplied five consecutive times with venous occlusion performed each time after a resting period of at least one minute.<sup>14</sup>

### 2.4.2 INVOS 5100 (Somanetics®, USA)

The NIRS optodes were applied on the same area on the left lateral calf. The neonatal sensor as recommended by Somanetics® was used. The inter-optode distance was 4 cm, and the sampling rate was 1 per 8 sec. After a resting period of at least one minute, NIRS data were recorded for 20 sec. The NIRS optodes were reapplied five times<sup>14</sup> with a calm-down period of at least 30 sec between measurements.

## 2.5 Quality Criteria

NIRO 300: Two recently published quality criteria were applied during the measurements<sup>18</sup> (1. quality criterion: exclusion of data with non-linear changes of Hbtot with  $R^2 > 0.95$  during venous occlusion; 2. quality criterion: exclusion of data which do not fulfill the following requirement:  $0 \leq \text{TOI} - \text{SvO}_2 \leq (\text{SaO}_2 - \text{SvO}_2) \times 0.2$ ; SvO<sub>2</sub>: mixed venous oxygenation). Therefore only pTOI values are presented after introduction of quality criteria, and only comparison of pTOI values fulfilling the quality criteria were performed.

INVOS 5100: same as for cerebral measurements

## 2.6 Statistics/Analysis

Descriptive analysis of demographic, clinical and NIRS data are given as mean with standard deviations.

In each neonate, the mean of values and the mean of standard deviations of NIRS data were calculated before and after introduction of quality criteria. Data of TOI and rSO<sub>2</sub> were compared using students-t-Test. Data of cTOI, crSO<sub>2</sub>, and prSO<sub>2</sub> before and after introduction of quality criteria were compared using students-t-Test.

# 3 Results

## 3.1 Cerebral Measurements

Cerebral measurements were performed in 8 term and 29 preterm neonates with a male/female ratio of 20:17. Demographic data are presented in Table 1.

cTOI was always significantly lower than crSO<sub>2</sub> (Table 2), before and after the introduction of quality criteria. The mean

**Table 1** Demographic data of neonates.

	Peripheral muscle measurement	Cerebral measurement
Neonates, n	39	37
Gestational age (weeks of gestation)	35.2 +/- 3.2	35.2 +/- 3.0
Age (days)	9.9 +/- 15.3	3.9 +/- 4.8
Birth weight (g)	2380.5 +/- 816.4	2270.1 +/- 731.6
Actual weight (g)	2479.5 +/- 747.6	2262.3 +/- 766.3
Oxygen saturation (%)	97.1 +/- 2.4	95.1 +/- 1.9
Heart rate (ppm)	134.6 +/- 15.4	128.3 +/- 10.3
Thigh-circumference (cm)	12.6 +/- 2.2	
Calf-circumference (cm)	9.6 +/- 1.4	
Capillary refill time, central (sec)	2.7 +/- 0.7	2.8 +/- 0.52
Capillary refill time, peripheral (sec)	2.8 +/- 0.7	3.0 +/- 0.6
Mean blood pressure (mmHg)	42.5 +/- 8.8	43.0 +/- 5.2
Central temperature (°C)	36.8 +/- 0.4	36.9 +/- 0.3
Peripheral temperature (°C)	35.2 +/- 0.8	35.9 +/- 0.6

difference between cTOI and crSO<sub>2</sub> was 10%, there was no difference before and after introduction of quality criteria. The mean standard deviations of cTOI and crSO<sub>2</sub> showed no differences, neither before nor after the introduction of quality criteria. 10% of crSO<sub>2</sub> measurements and 3% of cTOI measurements had to be eliminated because of quality criteria, this difference was significant ( $p = 0.015$ ). With the introduction of quality criteria crSO<sub>2</sub> values changed significantly ( $p = 0.01$ ), cTOI values did not change. Mean standard deviations of cTOI and crSO<sub>2</sub> did not change significantly.

### 3.2 Peripheral Measurements

Peripheral muscle measurements were performed in 11 term and 28 preterm neonates with a male/female ratio of 25:14. Demographic data are presented in Table 1.

As quality criteria were applied during pTOI measurements according to recent recommendations,<sup>18</sup> there are only pTOI values after introduction of quality criteria. pTOI values and mean standard deviations of pTOI were significantly lower than prSO<sub>2</sub> values and mean standard deviations ( $p < 0.001$ ;  $p = 0.047$ ) (Table 3). The mean difference of pTOI and prSO<sub>2</sub> was 15%. prSO<sub>2</sub> values and mean standard deviations did not change significantly with introduction of quality criteria.

## 4 Discussion

To our knowledge this is the first study to compare absolute values and reproducibility of cerebral and peripheral oxygenation saturation using different NIRS devices.

**Table 2** Tissue oxygenation index (cTOI; NIRO 300, Hamamatsu) and regional oxygen saturation (crSO<sub>2</sub>) of cerebral tissue in neonates.

Mean values	cTOI	crSO <sub>2</sub>	p-value
Before quality criteria	73.1 +/- 6.9 (n = 177)	84.1 +/- 6.4 (n = 184)	<0.001
After quality criteria	72.7 +/- 6.2 (n = 171)	83.3 +/- 5.8 (n = 166)	<0.001
Mean of SD			
Before quality criteria	5.3 +/- 3.9	4.7 +/- 2.2	0,47
After quality criteria	4.9 +/- 3.6	4.5 +/- 2.6	0,6

**Table 3** Tissue oxygenation index (pTOI; NIRO 300, Hamamatsu) and regional oxygen saturation (prSO<sub>2</sub>) of peripheral muscle in neonates.

Mean values	pTOI	prSO <sub>2</sub>	p-value
Before quality criteria	—	82.7 +/- 7.6 (n = 185)	
After quality criteria	66.0 +/- 7.9 (n = 126)	82.0 +/- 7.0 (n = 168)	<0,001
Mean of SD			
Before quality criteria	—	5.4 +/- 3.4	
After quality criteria	3.7 +/- 2.6	5.0 +/- 3.0	0,047

There was a significant difference in the measured values for regional oxygen saturation between the two devices (NIRO 300 vs. INVOS 5100). Cerebral as well as peripheral values for TOI were significantly lower than rSO<sub>2</sub> values. For cerebral measurements the reproducibility was similar. In peripheral muscle measurements higher reproducibility with a significantly lower mean standard deviation for TOI was observed, compared to rSO<sub>2</sub> measurements.

The comparability of cerebral measurements has been analyzed in different studies leading to different results<sup>5,9,11</sup> (see Table 4). In children, Dullenkopf et al.<sup>5</sup> observed significantly lower TOI values (measured with the NIRO 300) compared to rSO<sub>2</sub> values (measured with the INVOS 5100) and described a very large range in cerebral oxygenation values in children (rSO<sub>2</sub>: 59–95%; TOI: 48–85%). These results are consistent with our cerebral measurements in neonates.

In adults, Tavasothy et al.<sup>9</sup> described similar baseline values for both devices (see Table 4). Values of the NIRO were similar to the present values. Values of INVOS were lower compared to the present values. In the study of Tavasothy only a small number of patients were measured resulting in a low powered study. In juvenile swine, Gagnon et al.<sup>11</sup> observed TOI values ranging lower than rSO<sub>2</sub> values at higher levels of tissue/regional oxygenation index (Table 4). These data are again consistent with the present data.

In neonates with patent ductus arteriosus Lemmers et al.<sup>19</sup> showed that cerebral rSO<sub>2</sub> values (using the INVOS 4100, Somanetics®) achieve differences around 10% between the study and the control group. Similar differences of this level were measured in the present study only by using different devices.

By comparing the adult and the pediatric sensor of INVOS 5100, Dullenkopf et al.<sup>5</sup> observed also a difference of 10%, whereby the neonatal sensor, which is recommended in neonates, was not analyzed and compared until now.

There is also a considerable amount of controversy regarding the reproducibility of cerebral NIRS. In the present study reproducibility for cTOI and crSO<sub>2</sub> were comparable. Furthermore, a quality criterion was introduced. The quality criterion was based on physiological considerations that regional tissue oxygen saturation has to be lower than arterial oxygen saturation. The introduction of the quality criterion did not change reproducibility (expressed in mean of SD) but crSO<sub>2</sub> values decreased. Since the present quality criterion eliminates outliers only at the upper end, this will cause some bias. With this quality criterion certainly false measurements can be excluded. On the other hand we also need to consider the precision of pulse-oxymetry (2–4%),<sup>20</sup> which may also cause the inclusion or exclusion of correct or incorrect outliers. These considerations cause some limitations of the quality criterion used.

In twenty neonatal and pediatric intensive care patients Dullenkopf et al.<sup>3</sup> showed a poor reproducibility of cTOI values, using the NIRO 300. On the other hand, in neonates Menke et al.<sup>21</sup> showed a good reproducibility of cTOI, but less reproducibility of HbO<sub>2</sub>, HbD, and HbT values. Problematic remains the large intra- and especially inter-patient variance.<sup>22</sup>

Peripheral oxygen saturation has been evaluated in several studies in neonates.<sup>18,23–25</sup> The present study was the first to analyze the comparability and reproducibility of different devices. In analogy to cerebral measurements, peripheral measurements always showed significantly lower pTOI values (compared to

**Table 4** Studies comparing values of NIRO 300 and INVOS 5100 in cerebral measurements.

			NIRO (TOI)	INVOS (rSO <sub>2</sub> )	
Gagnon RE et al. (Ref. 11) n = 24	2002	Healthy	36.2%	0%	Nonlinear
		juvenile swine	56.8%	56.8%	correlation
			85.9%	100%	r = 0.62
Thavasothy et al. (Ref. 9) n = 10	2002	Healthy adult	64.9% (5.1 SD)	62.3% (6.0 SD)	
Dullenkopf A et al. (Ref. 5) n = 30	2003	Paediatric	48% – 85%	59% – 95%	p < 0.0001

prSO<sub>2</sub>). The present pTOI values were comparable to other studies.<sup>18,23,24,26,27</sup>

For prSO<sub>2</sub> measurements a similar quality criterion was introduced as for cerebral measurements.

prSO<sub>2</sub> values and mean standard deviations decreased but as discussed above this quality criterion has some limitations.

The second quality criterion including venous occlusions can only be done with the NIRO 300, which increases the reliability of measurements.<sup>18</sup>

Reproducibility of prSO<sub>2</sub> values was lower compared to pTOI values. The reproducibility for pTOI has already been analyzed in recent studies for adults as well as for neonates.<sup>18,24</sup>

One has to emphasize, that there are technical differences between both devices, which may significantly influence the measurement of peripheral oxygen saturation. The INVOS system is calibrated for cerebral measurements only. It is not possible to introduce different pathlength factors for cerebral and peripheral measurements, in contrast to the NIRO system.

In conclusion, different devices enable measurements of tissue oxygenation in regions of interest, especially in cerebral and muscle tissue, but at the moment we should be careful comparing values of different devices using different techniques.

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