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Title Page

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- Running title: Bilirubin and regional tissue oxygen saturation
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Mona Momeni: This author helped conceptualize the study, perform the study design, design the analysis plan, perform statistical analysis, interpret the results, and write the manuscript.

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Abstract

Background: Tissue oximetry devices use wavelengths in the 680-870 nm range to separate between oxygenated/deoxygenated hemoglobin (Hb). Conjugated bilirubin has an absorption peak at 730 nm.

Aims: We hypothesized that ForeSight Elite using 5 wavelengths reduces interference from bilirubin and shows higher regional tissue oxygen saturation (rSO_2) than INVOS 5100C incorporating 2 wavelengths.

Methods: Infants and children undergoing living donor liver transplantation were included between March 2019 and September 2020. Cerebral and somatic rSO_2 were measured and real-time simultaneous data were collected. Additionally, measurements were collected at 1) Baseline 2) Beginning of dissection phase 3) Beginning of anhepatic phase 4) Reperfusion phase 5) Skin closure. Bilirubin level was available at baseline and at reperfusion. Hyperbilirubinemia was defined as bilirubin level $\geq$1.0 mg/dl.

Results: Thirty-three patients with median age of 27 months and median weight of 12 kg were included. Baseline bilirubin levels were higher compared to values at reperfusion (*P*=0.021). A linear mixed effects model considering bilirubin as fixed and patient as random effect showed that there was a statistically significant difference in cerebral rSO_2 readings in function of time (*P*=0.031), device (*P*< 0.001) and bilirubin concentrations (*P*=0.007) but not for Hb (*P*=0.347), SpO_2 (*P*=0.882) and arterial partial pressure of CO_2 ($PaCO_2$) (*P*=0.146). The model showed that there was a statistically significant difference in somatic rSO_2 readings in function of device (*P*< 0.001) and bilirubin concentrations (*P*=0.023) but not for time (*P*=0.074), Hb (*P*=0.954), SpO_2 (*P*=0.108) and $PaCO_2$ (P=0.775). Bland-Altman plot analyzing cerebral and somatic rSO_2 between both devices showed respectively a mean absolute Bias and 95% limits of agreement of 21.73% (-10.21 to 53.67) and 19.52% (-29.51 to 68.54).

Conclusions: Oximetry devices emitting light at > 2 wavelengths may overcome interference from hyperbilirubinemia providing higher rSO_2 readings.

Key words: Bilirubin; Near-infrared spectroscopy; Regional tissue oxygen saturation; Liver transplantation

a. What is already known about the topic? Oximetry devices using Near-infrared spectroscopy (NIRS) technology may be influenced by external factors and provide different rSO_2 readings.

b. What new information this study adds: In children with hyperbilirubinemia undergoing living donor liver transplantation, rSO_2 measured with ForeSight Elite is higher than with INVOS 5100 C. NIRS devices emitting light at > 2 wavelengths may overcome interference from bilirubin.

Body

Introduction:

Pediatric living donor liver transplantation (LDLT) alleviates organ shortage and has been shown to be a safe and efficient therapy for end-stage liver failure in children.[1] It is nevertheless a high-risk surgery and may be associated with severe hemodynamic instability.[2] In addition to the classical invasive monitoring methods, continuous and non-invasive measurement of regional tissue oxygen saturation (rSO_2) based on near-infrared spectroscopy (NIRS) technology may help in intraoperative hemodynamic management of children undergoing LDLT.

The NIRS technology is based on the transmission of light in the near-infrared spectrum across tissue and its absorption by several biologic molecules, called chromophores. In clinical practice the concentration of most chromophores is assumed to be constant. Cytochrome oxidase C and hemoglobin (Hb) are the only chromophores reflecting respectively intracellular and blood oxygenation and thus tissue oxygen saturation. In clinical applications aimed at measuring the oxygen saturation of Hb, the concentration of oxygenated Hb is measured as the ratio of light absorbed for oxygenated Hb compared with light absorbed for total Hb. Commercial NIRS devices currently utilize wavelengths in the 680-870 nm range to be sensitive to Hb and to maximize separation between oxygenated and deoxygenated Hb. Conjugated bilirubin has an absorption peak at 730 nm.[3] In theory NIRS devices using two wavelengths of light source are sufficient to measure the relative concentration of oxygenated and deoxygenated Hb but the absolute NIRS values are decreased in case of increased conjugated bilirubin concentration.[4-6] This is the case for the INVOS 5100 C device. The INVOS 5100 C device emits light at 730 and 810 nm wavelengths. We hypothesized that ForeSight Elite NIRS device emitting light at 5 wavelengths (685, 730, 770, 810 and 870 nm) reduces interference from bilirubin and shows higher cerebral and somatic rSO_2 in children undergoing LDLT as compared to INVOS 5100 C device emitting light at 2 wavelengths. We additionally assessed agreement between two devices as pediatric LDLT entails significant hemodynamic instability due to patient-related and surgery-related aspects.

Materials and methods

This study was approved by the Comité d'Ethique Hospitalo-Facultaire Saint-Luc, Université Catholique de Louvain (Chairperson Prof. J-M Maloteaux) on November 07, 2018 (2018/07NOV/413) and registered by Principal Investigator at ClinicalTrials.gov (NCT03945942) on May 10, 2019. The study adheres to the appropriate enhancing the quality and transparency of health research (EQUATOR) guidelines. Parental written informed consent was obtained for all children. Infants and children (<18 y) undergoing elective LDLT were enrolled. Exclusion criteria were parental refusal to participate and subjects with congenital heart disease or known neurological disorders.

Tissue oximetry analysis

Cerebral and somatic rSO_2 were simultaneously measured with the INVOS 5100 C (Somanetics Corporation, Troy, MI) and the ForeSight Elite (CASMED, Branford, CT) tissue oximetry. Due to lack of space only one sensor was used for each device. The INVOS 5100 C and ForeSight Elite cerebral sensors were positioned as such to avoid interfering the emitting light of one sensor with the detecting light of the other sensor. Supplemental Fig. 1 illustrates how the sensors were positioned at the cerebral site. The somatic sensors were each positioned at each deltoid muscle. We avoided the flank as a somatic side to overcome any possible artifact from the overflowing abdominal liquid. In addition, no blood pressure cuff was used at the arm level where the somatic probes were placed. The medium-size pediatric sensors allowing a depth of penetration of 20 mm were used with the ForeSight Elite for somatic and cerebral measures in infants and children weighing <40 kg. For children weighing ≥40 kg the large-size ForeSight Elite sensors were used allowing a depth of penetration of 25 mm. Neonatal/infant INVOS cerebral and somatic sensor was used in infants ≤15 kg. Pediatric INVOS sensors were applied for infants and children weighing >15 kg. Both INVOS sensors have a depth of penetration of 20 mm.
All sensors were placed after proper cleaning of the skin surface and before the induction of anesthesia. Proper functioning of the monitors was checked before establishing baseline values.
Real-time simultaneous data from both devices were collected on an USB key in Excel table and were classified by exactly matching time using the VLOOKUP

function in Microsoft Excel™ software. Simultaneous NIRS data were recorded during the entire intraoperative period and analyzed at intervals between 4 and 40 seconds in order to compare exact simultaneous measurements.

In addition, hemodynamic parameters [mean arterial blood pressure, heart rate, pulse oximetry oxygen saturation (SpO_2)] and simultaneous cerebral and somatic rSO_2 were recorded at the following time points: 1) Baseline (breathing room air) 2) Beginning of dissection phase (surgical skin incision) 3) Beginning of anhepatic phase (clamping of inferior vena cava) 4) Reperfusion phase and 5) Skin closure.

Study protocol

General anesthesia was performed according to institutional's clinical practice. An arterial catheter was placed in the radial artery and a central venous catheter in the subclavian vein under ultrasound guidance. Anesthesia was only conducted by three pediatric anesthesiologists (TP, NMA, CST) with experience in LDLT. Total bilirubin level at baseline was available at routine laboratory analysis performed the day before surgery. At reperfusion the total bilirubin concentration was measured according to the protocol. Arterial blood gas analyses including Hb concentrations and arterial partial pressure of CO_2 ($PaCO_2$) were performed at dissection phase, anhepatic phase, reperfusion phase, at skin closure and whenever deemed necessary by the anesthesiologist in charge of the patient. Hyperbilirubinemia was defined as total bilirubin level $\geq$1.0 mg/dl. The hemodynamic management of the patients was based on the information provided by the invasive hemodynamic monitoring and the blood gas analyses.

Statistical analysis:

The main objective of this study was to evaluate whether the rSO_2 values measured with the ForeSight Elite device were significantly higher compared to those measured by INVOS 5100 C when considering the total bilirubin concentrations at baseline and at reperfusion. A linear mixed effects model was used to answer the question. The primary outcome variable was the rSO_2 readings. The bilirubin concentration was considered as a fixed effect, and patients as random effect. As tissue oximetry values are influenced by total Hb concentration, SpO_2 and $PaCO_2$, the latter variables were included as confounders in the model.[7]

We further evaluated agreement between both devices. A modified Bland-Altman analysis, taking into consideration random effects model for repeated measures data

within the same subject was used.[8] Bland-Altman plots were performed for cerebral as well as somatic rSO_2.

Data are presented as numbers (%) for categorical data and as median (IQR) for continuous variables that did not show a normal distribution. A *P*-value <0.05 was considered significant. A Mann-Whitney U test was performed to compare continuous variables. A Wilcoxon signed rank test was used to compare paired data. Receiver operating characteristic (ROC) curves were constructed to determine the optimal cutoff values of bilirubin for cerebral and somatic rSO_2 measured by INVOS 5100 C < 55%, with the optimal cutoff defined as that with the highest product of sensitivity and specificity.

The sample size calculation was as follows: as the primary objective of the study was to detect a difference between the rSO_2 measured by INVOS 5100 C and ForeSight Elite, using a paired t-test a minimum of 27 subjects were required to detect a 10% mean difference, assuming a 17% standard deviation for the difference with 80% power based on a two-tailed paired t-test and an α-level of 0.05. More patients were included to consider any eventual dropouts. This sample size calculation was based on previously collected data and our clinical experience with both NIRS devices.

Statistical analysis was performed using IBM SPSS 27. Data management was performed by means of Microsoft Excel™ software and SAS 9.4.

Results

In total 33 patients were included in the study between March 2019 and September 2020. Fig. 1 illustrates the flowchart of the study. Among the 33 included patients, simultaneous rSO_2 for both devices could not be obtained for 9 patients during the entire intraoperative period. In these 9 patients simultaneous oximetry readings were only obtained at the previously mentioned 5 time points of the study protocol. Table 1 shows the patients' data. Two patients weighted >40 kg. Median total bilirubin values at reperfusion were significantly lower compared to values at baseline (P=0.021; effect size=-0.28). Hyperbilirubinemia at baseline was present in 28 (84.8%) subjects. At reperfusion 31 (93.0%) of the subjects presented hyperbilirubinemia.

Fig. 2A and Fig. 2B show respectively the cerebral and the somatic rSO_2 for both devices at different time points. There was a statistically significant difference between rSO_2 readings by both devices at all time points. Supplemental Table 1 reports cerebral and somatic rSO_2 values for both devices at baseline and at reperfusion phase and illustrates the percentage of the values for each device that were outside of the normal 55 – 85% tissue oxygen saturation range.

We further analyzed whether there was a significant difference in rSO_2 within each monitor between those patients with a normal total bilirubin versus those with hyperbilirubinemia at the two timepoints (baseline and reperfusion phase) when total bilirubin was measured (Table 2). At baseline the cerebral and somatic rSO_2 as measured by INVOS 5100 C monitor were statistically significantly different between patients with or without hyperbilirubinemia (respectively P=0.009 and P=0.009). However, at baseline this difference was not statistically different for the ForeSight Elite monitor (P=0.801 for cerebral rSO_2 and P=0.488 for somatic rSO_2). At reperfusion there was no statistically significant difference in cerebral and somatic rSO_2 readings by INVOS 5100 C (respectively P=0.403 and P=0.273) and ForeSight Elite (respectively P=0.581 and P=0.970) for patients with or without hyperbilirubinemia. Furthermore, the degree of change in rSO_2 between baseline and reperfusion was analyzed for each monitor. This difference was statistically significantly different for the INVOS 5100 C but not for the ForeSight Elite device.

The linear mixed effects model was performed for the entire study group (n=33) for whom simultaneous rSO_2 was available for INVOS 5100 C and ForeSight Elite at the 5 predefined time points. The model showed that there was a statistically significant

difference in cerebral rSO_2 readings in function of time (P=0.031), device (P<0.001) and total bilirubin concentrations (P=0.007) but not for Hb values (P=0.347), SpO_2 (P=0.882) and $PaCO_2$ (P=0.146). The linear mixed effects model demonstrated similar results for the somatic rSO_2. The model showed that there was a statistically significant difference in somatic rSO_2 readings in function of device (P<0.001) and total bilirubin concentrations (P=0.023) but not for time (P=0.074), Hb values (P=0.954), SpO_2 (P=0.108) and $PaCO_2$ (P=0.775). The validity of the model was confirmed as the residuals followed a normal distribution.

A Bland-Altman analysis for agreement between cerebral rSO_2 measured by INVOS 5100 C and ForeSight Elite while considering repeated time and total bilirubin value as continuous variable was performed on the 24 patients for whom simultaneous rSO_2 was available for both monitors during the entire intraoperative period.

Fig. 3 illustrates the Bland-Altman analysis for the cerebral rSO_2 measured by both devices for the entire 24 patients and for patients with and without hyperbilirubinemia. The Bland-Altman plot analyzing cerebral rSO_2 for the entire cohort showed a mean absolute Bias of 21.73% (95% CI: 21.62% to 21.84%) with 95% limits of agreement: -10.21 to 53.67. Patients with hyperbilirubinemia had a mean Bias of 24.63% (95% CI: 24.52% to 24.75%) with 95% limits of agreement: - 6.42 to 55.69 and those without hyperbilirubinemia had a mean Bias of 5.96 % (95% CI: 5.84% to 6.08%) with 95% limits of agreement: - 7.91 to 19.82. Fig. 4 shows this Bland-Altman plot for the somatic rSO_2. The Bland-Altman plot analyzing somatic rSO_2 for the entire cohort showed a mean absolute Bias of 19.52% (95% CI: 19.35% to 19.68%) and 95% limits of agreement: -29.51 to 68.54. Patients with hyperbilirubinemia had a mean Bias of 23.30% (95% CI: 23.12% to 23.49%) and 95% limits of agreement: - 26.41 to 73.00 and those without hyperbilirubinemia had a mean Bias of -1.04% (95% CI: 1.13% to - 0.95%) and 95% limits of agreement: - 11.77 to 9.69. We found that the optimal cutoff for observing cerebral and somatic rSO_2 < 55% as measured by INVOS 5100 C was a total bilirubin level of 3.45 mg/dl (sensitivity 96% and specificity 56% for the cerebral values; sensitivity 96% and specificity 48% for the somatic values).

Hemodynamic parameters at five study time points are represented in Supplemental Fig. 2. Although dark skin color may affect tissue oximetry readings,[9] the small number (n=2) of dark-skinned children in this study precluded any meaningful statistical analysis.

Discussion

The results of this prospective study in children undergoing LDLT show that medical conditions inducing hyperbilirubinemia significantly reduce rSO_2 values measured by the INVOS 5100 C that only uses 2 wavelengths (of which one corresponds to the absorption peak of conjugated bilirubin) as compared to the ForeSight Elite monitor using 5 wavelengths. This finding was demonstrated by different statistical analyses. The Bland-Altman plots for repeated measures showed a large mean bias and limits of agreement for all patients but specifically for those with hyperbilirubinemia. Previous studies have demonstrated a difference between these two devices in adult population.[10] In addition, the linear mixed effects model showed that the cerebral as well as somatic rSO_2 were statistically different between both devices and that total bilirubin concentration significantly influenced this effect. We also demonstrated that there was a significant difference in rSO_2 INVOS 5100 C between those patients with a normal total bilirubin concentration versus those with increased bilirubin concentrations at baseline but not at the reperfusion phase when the average bilirubin concentrations were low. This difference was not observed for the ForeSight Elite at any moment. Moreover, there was a statistically significant difference with respect to the degree of change between baseline and reperfusion for the INVOS 5100 C. This difference was not observed for the ForeSight Elite. Indeed, as there was a significant decrease in total bilirubin concentration between baseline and reperfusion phase the cerebral and somatic rSO_2 measured by the INVOS 5100C device showed a significant increase over the time. This increase was not observed for the ForeSight Elite. Our linear mixed effects model showed that direct changes in cerebral rSO_2 were observed over time, indicating that there is an association between bilirubin levels and cerebral rSO_2 but that both devices could be used as a trend monitor for the hemodynamic management of children undergoing LDLT. This effect of time was less obvious for the somatic rSO_2.

To be noted, cerebral and somatic rSO_2 values as measured by INVOS 5100 C showed high variability all over the entire intraoperative period. This “intra-device” variability of the INVOS 5100 C may be a confounder in our comparisons. It may moreover make the interpretation of the oximetry readings by INVOS 5100 C difficult for this kind of procedure. Nevertheless, these devices should be rather used as a trend monitor.

Considering that rSO_2 as measured by NIRS is influenced by Hb concentrations, $PaCO_2$ and SpO_2,[7,11-13] we included these variables measured at specific time points of the study in the linear mixed effects model. Indeed, LDLT in children is a surgery at high risk of bleeding and these variables may show important fluctuations. However, our results showed that only the bilirubin concentrations and the type of device were associated with the rSO_2 readings. To be noted the important perioperative volume loss and fluid administration in pediatric LDLT resulted in a significant decrease in total bilirubin concentrations from baseline to reperfusion phase which resulted in different observations at baseline compared to the reperfusion phase.

The results of this study confirm that NIRS devices emitting light at different wavelengths may reflect higher rSO_2 readings in patients with high bilirubin levels and associated jaundice. These results may have an impact in other medical conditions i.e. neonates undergoing congenital heart surgery where the use of tissue oximetry is often part of the routine monitoring.

To the best of our knowledge this is the first study in children undergoing LDLT analyzing cerebral as well as somatic rSO_2 with different NIRS technologies. Song et al. using the INVOS 5100 B oximeter showed that in adult patients with end-stage liver failure, elevated bilirubin levels were independently related to cerebral rSO_2 <50%. The optimum cutoff for observing cerebral rSO_2 <50% in their study was total bilirubin >7.2 mg/dl.[6] This value was considerably lower in our population. This decrease in cerebral rSO_2 was also observed in a study using INVOS 3100 in adults undergoing orthotopic liver transplantation.[5] These observations could however not be reproduced by Plachky et al.[14] The bilirubin levels in the latter study were rather constant and ranged between 2.7 - 3.4 mg/dl.

In addition to the different number of wavelengths used to maximize separation between the oxygenated and the deoxygenated Hb, the INVOS 5100 C and the ForeSight Elite tissue oximeter use different technologies to measure the rSO_2 and have shown a bias in different situations in adults.[7,10] It is therefore not surprising that even in the absence of hyperbilirubinemia wide differences exist between rSO_2 readings with both monitors. Although the INVOS 5100 C and the ForeSight Elite tissue oximeter both use the principle of spatial resolution to distinguish contribution of the superficial vs deeper layers of tissues, there are important differences regarding this aspect that should be borne in mind. Each monitor incorporates a light source and two light detectors, one shallow and one deep localized at a specific

distance from the light source, to eliminate signal contamination from superficial layers. The depth of penetration of light is a function of the distance between the light emitter and the light detectors. This distance is different between both monitors, and it varies for the ForeSight Elite tissue oximeter depending on the type of sensor used. However, the depth of penetration for the INVOS 5100 C monitor is 20 mm whatever sensor is used (adult, pediatric, neonatal) (Fig. 5). The INVOS 5100 C monitor uses, based on the probe size, an internal subtraction algorithm and removes most of the transmitted shallow signal. It is nevertheless understandable that this difference in depth of penetration between both devices results in a non-insignificant difference in rSO_2 readings with both monitors. Another difference between the two devices is the assumed fixed ratio of venous/arterial blood content which is somehow higher for the INVOS 5100 C monitor.[10] Volume shifts during LDLT are not negligeable and can thus theoretically influence rSO_2 readings as well as the bias between both devices, regardless of the number of wavelengths used by both monitors.

This study shows several limitations. First, although baseline rSO_2 values were recorded before induction of anesthesia, baseline bilirubin levels and rSO_2 values were performed under likely different physiologic conditions. Second, due to lack of space on the children's forehead and the forearm, we did not apply the cerebral and the somatic sensors of both devices on the ipsilateral side. Sequential measurement over the same hemisphere under the same hemodynamic conditions and bilirubin level would have helped to measure how much of the bias at any given time point was due to measurement algorithm differences inherent to the device.[15] Indeed, right-left differentials exist for the same device but have not been accounted for here. Any subtle discrepancy due to the normal anatomical differences can therefore not be excluded. Third, the depth of penetration between the sensors used for larger patients was not the same between sensors due to difference in the technology. Finally, we only compared both monitors during the intraoperative period. Postoperative course of children undergoing LDLT can be challenging, and total bilirubin levels may further decrease in the postoperative period. Continuous comparison of both devices in the postoperative period would have provided more data.

In conclusion, hyperbilirubinemia in infants and children undergoing LDLT significantly reduces cerebral and somatic rSO_2 readings by INVOS 5100 C through "competitive" absorbance of transmitted light. These observations are more important

at baseline when the total bilirubin concentrations are higher. The decrease in bilirubin levels occurring during LDLT, due to reperfusion of the transplanted liver and the intraoperative volume replacement, results in a milder reduction of rSO_2 values measured by INVOS 5100 C. NIRS devices emitting light at > 2 wavelengths overcome interference from hyperbilirubinemia and may provide higher rSO_2 readings.

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Tables

Table 1: Patients‘ characteristics and intraoperative data

Table 2: Cerebral and somatic rSO_2 values at baseline and reperfusion phase when total bilirubin levels were measured

Figure captations

Figure 1: Flowchart of the study

Figure 2: Comparison of the cerebral (2A) and somatic (2B) regional tissue oximetry (rSO_2) for INVOS 5100 C and the ForeSight Elite oximeters at different time points

Figure 3: Bland-Altman plot for repeated measures demonstrating the bias and the limits of agreement for cerebral regional tissue oximetry (rSO_2) measured by INVOS 5100 C and the ForeSight Elite oximeters

Figure 4: Bland-Altman plot for repeated measures demonstrating the bias and the limits of agreement for somatic regional tissue oximetry (rSO_2) measured by INVOS 5100 C and the ForeSight Elite oximeters

Figure 5: Schematic illustration of the differences between the available probes manufactured for the INVOS 5100 C and the ForeSight Elite oximeters

Table 1: Patients' characteristics and intraoperative data

Variables	**Cohort (n=33) n (%) or median [IQR]**	**min - max**
Age (months)	27 [12 to 56]	6 - 192
Weight (kg)	12.0 [8.2 to 17.0]	6.3 - 51.0
Gender (M/F)	15/18 (45.5/54.5)	
Dark skin	2 (6.1)	
Baseline Hemoglobin (g/dl)	9.4 [8.7 to 10.6]	6.9 - 12.1
Baseline total bilirubin (mg/dl)	14.1 [1.8 to 21.8]	0.2 - 34.0
Baseline direct bilirubin (mg/dl)	13.3 [5.8 to 20.2]	1.2 - 30.0
Baseline aspartate aminotransferase (U/l)	166 [66 to 238]	3 - 419
Liver pathology		
- Alagille syndrome	2 (6.1)	
- Biliary atresia	22 (66.7)	
- Budd Chiari	2 (6.1)	
- Hepatic metastases	1 (3.0)	
- Hepatoblastoma	2 (6.1)	
- Idiopathic portal hypertension	1 (3.0)	
- Hyperoxaluria	1 (3.0)	

- Progressive familial intrahepatic cholestasis	2 (6.1)	
Total bilirubin at reperfusion (mg/dl)	4.9 [2.4 to 8.9]	0.9 - 13.7

Table 2: Cerebral and somatic rSO_2 values at baseline and reperfusion phase when total bilirubin levels were measured

		Hyperbilirubinemia median [IQR]	**No hyperbilirubinemia median [IQR]**	**P† (effect size)**	**P ‡ (effect size)**
Baseline	Cerebral rSO_2 by INVOS 5100 C	54 [40 to 65]	79 [79 to 81]	0.009 (- 0.45)	0.003 (- 0.36)
	Cerebral rSO_2 by ForeSight Elite	80 [77 to 87]	82 [73 to 83]	0.801 (- 0.05)	0.062 (- 0.23)
	Somatic rSO_2 by INVOS 5100 C	54 [39 to 73]	88 [78 to 89]	0.009 (- 0.44)	0.005 (- 0.35)
	Somatic rSO_2 by ForeSight Elite	85 [80 to 89]	88 [83 to 91]	0.448 (- 0.14)	0.114 (- 0.20)
Reperfusion	Cerebral rSO_2 by INVOS 5100 C	64 [42 to 79]	77 [66 to 88]	0.403 (- 0.17)	
	Cerebral rSO_2 by ForeSight Elite	84 [77 to 89]	86 [82 to 90]	0.581 (- 0.10)	
	Somatic rSO_2 by INVOS 5100 C	71 [46 to 91]	88 [82 to 94]	0.273 (- 0.20)	
	Somatic rSO_2 by ForeSight Elite	87 [81 to 90]	87 [85 to 89]	0.970 (-0.007)	

†: Mann-Whitney U test for comparison between patients with hyperbilirubinemia vs without hyperbilirubinemia

‡: Wilcoxon signed rank test for comparison within each monitor between baseline and reperfusion phase

Abbreviations: rSO_2: regional tissue oxygen saturation

Screened for study inclusion: n=47

Did not meet inclusion criteria: n=1

Met inclusion criteria: n=46

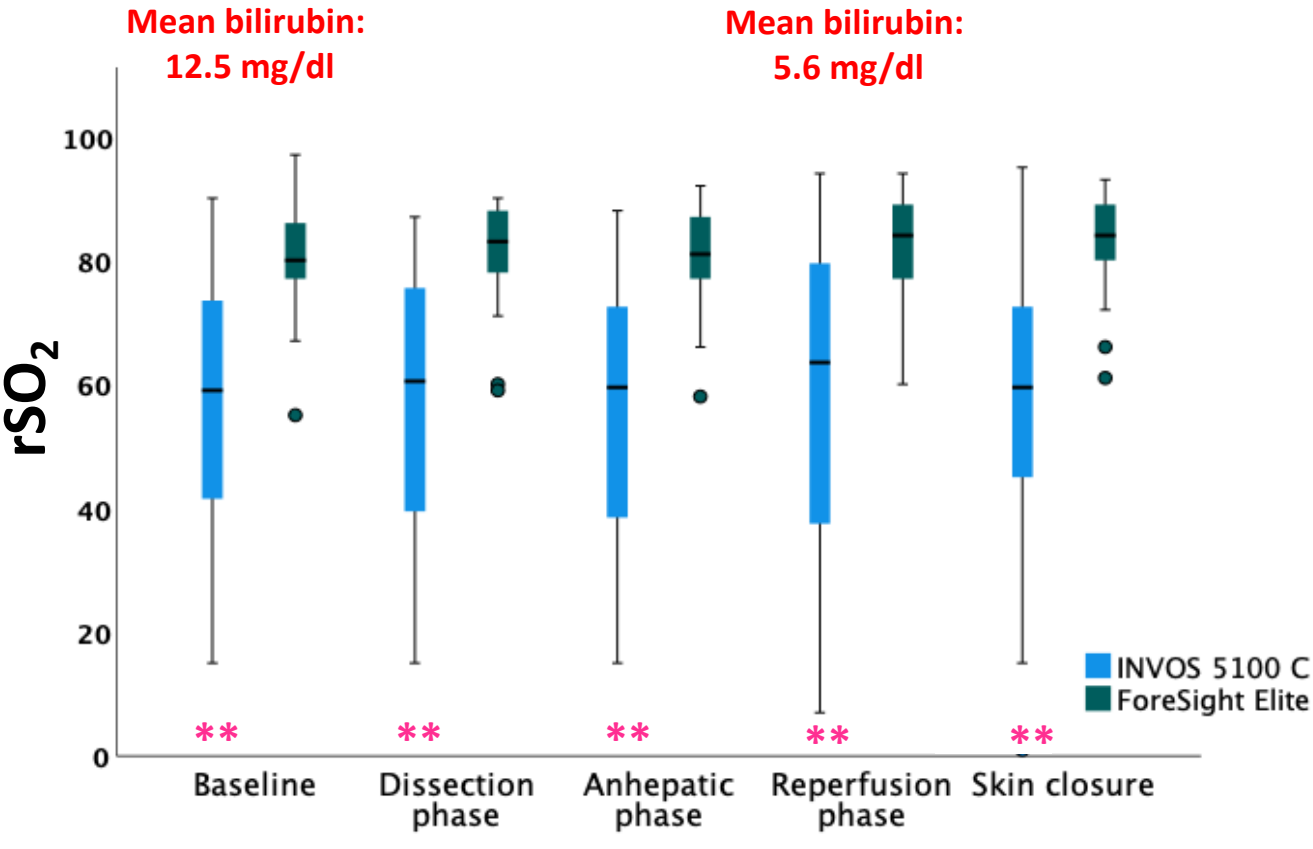
Patients not included: n=13
- study personnel not present
- study not proposed

Included in the study and analyzed: n=33

Simultaneous rSO_2 available for INVOS 5100 C & ForeSight Elite during the entire intraoperative period: n=24

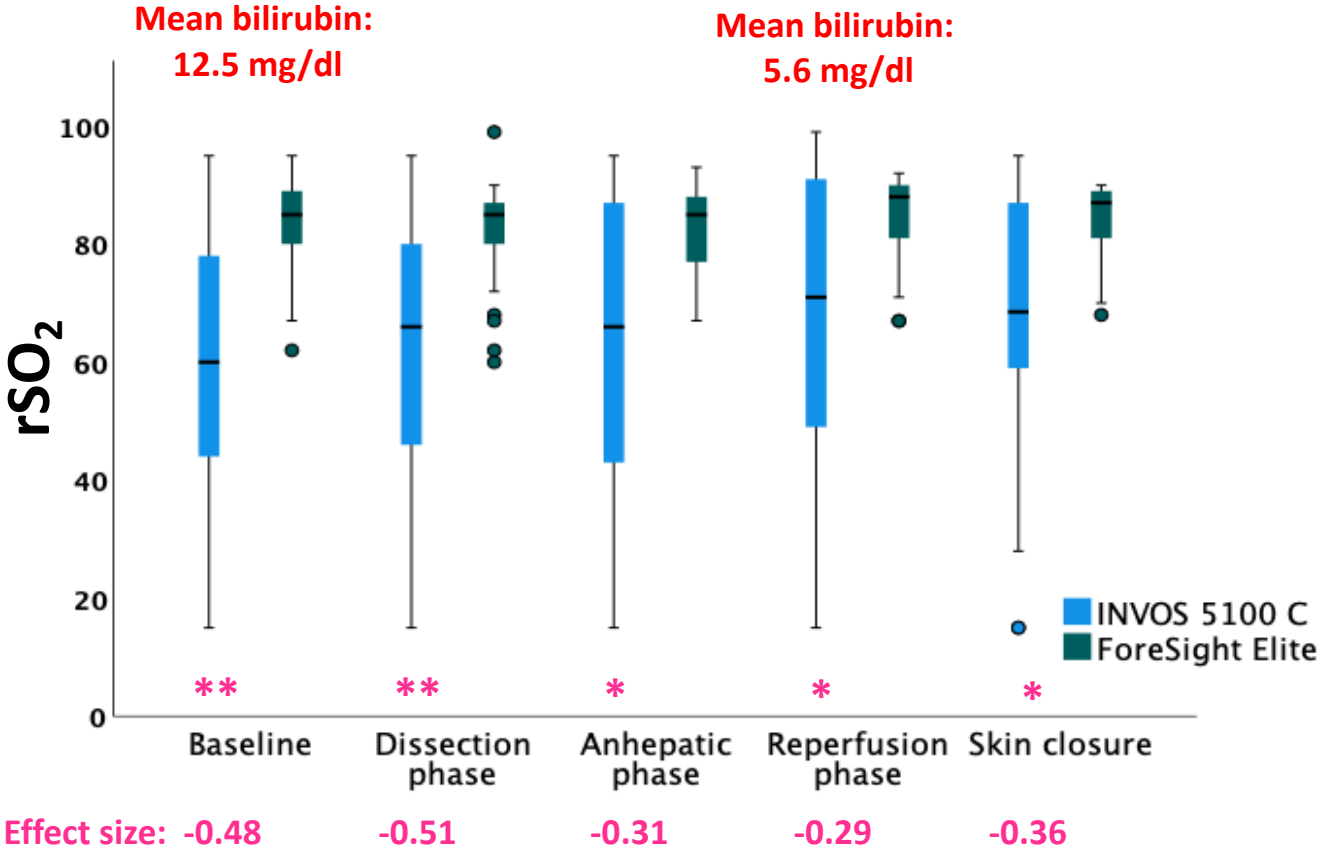
Simultaneous rSO_2 available for INVOS 5100 C & ForeSight Elite at 5 time points: n=33

Figure 2A: Cerebral rSO_2



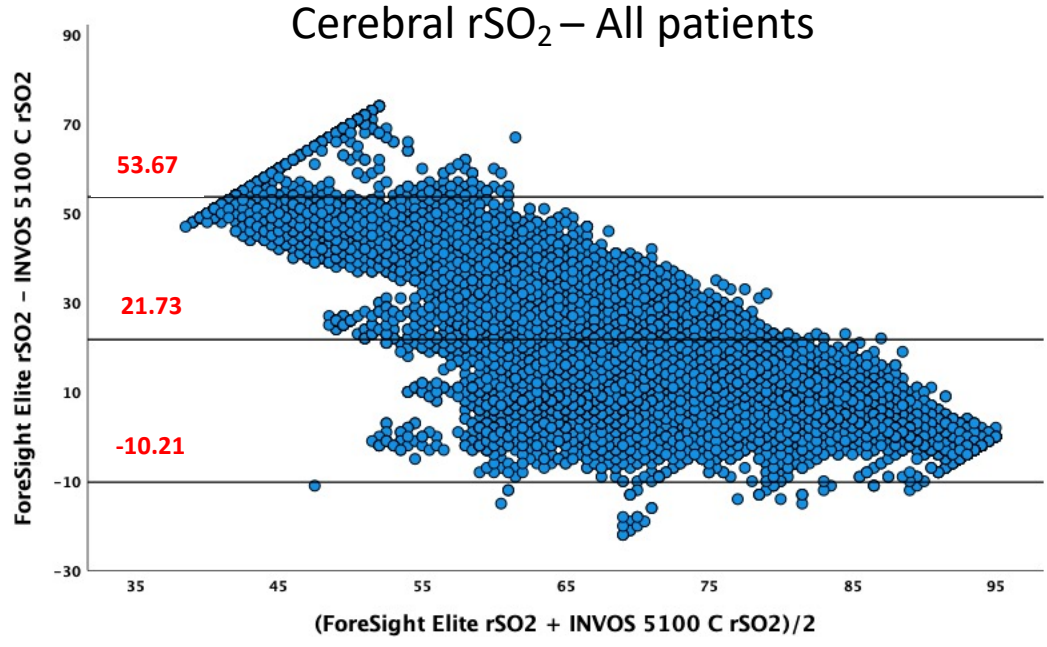
Effect size: -0.61 -0.63 -0.61 -0.52 -0.62

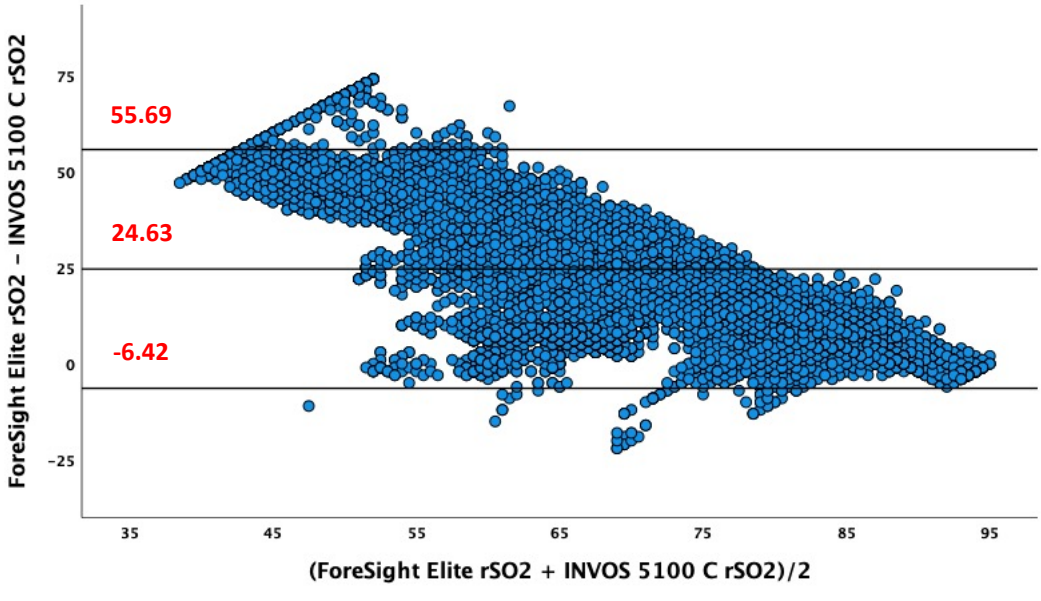
Figure 2B: Somatic rSO_2

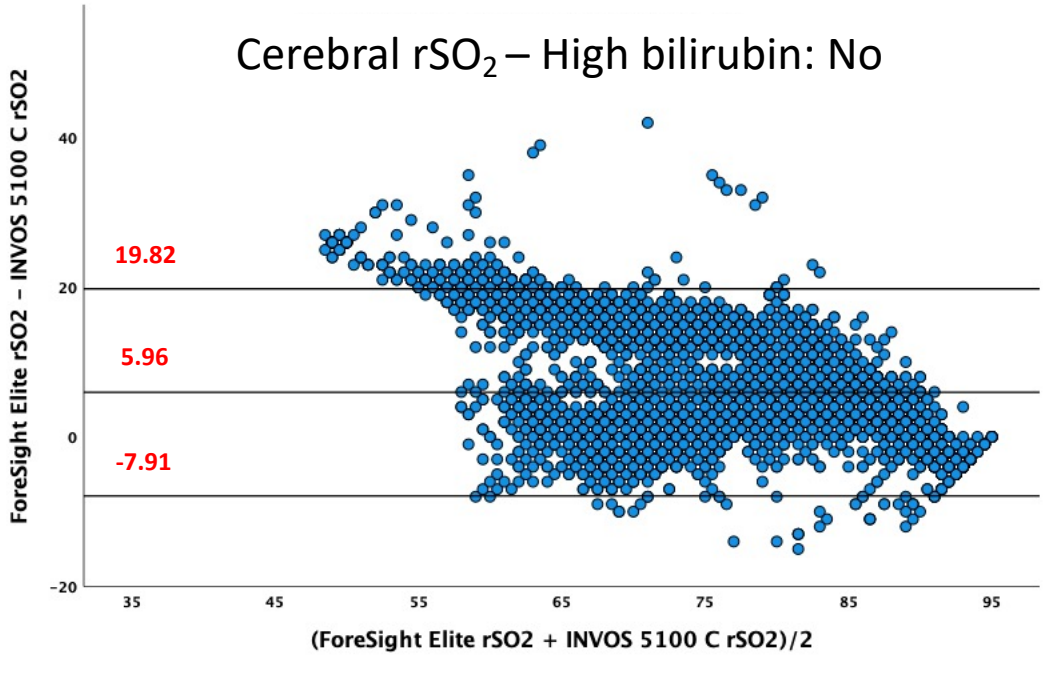


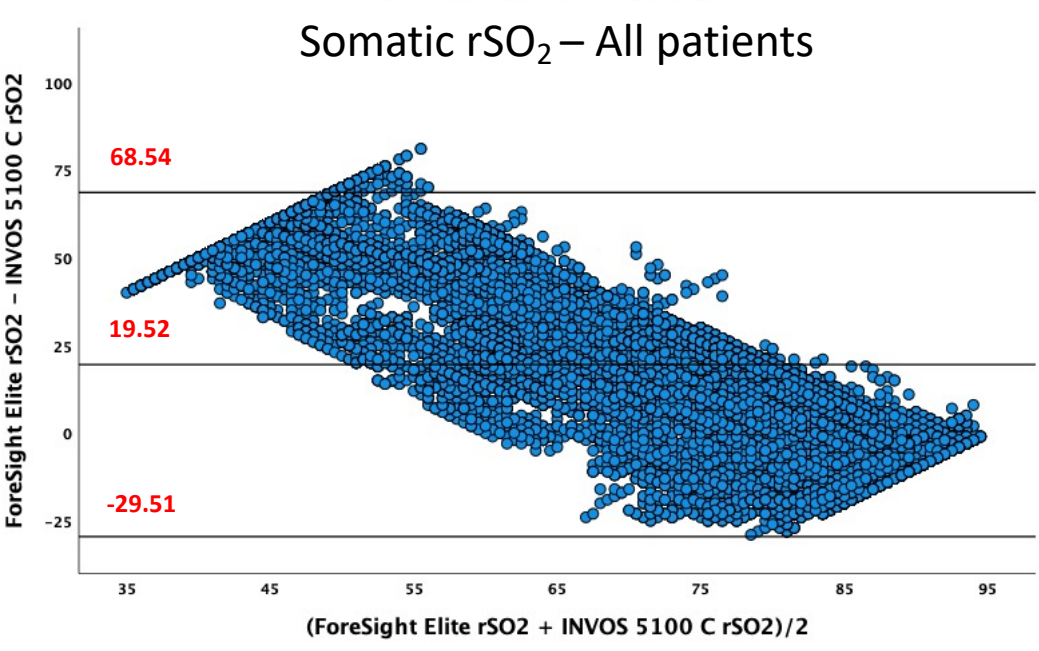
Effect size: -0.48 -0.51 -0.31 -0.29 -0.36

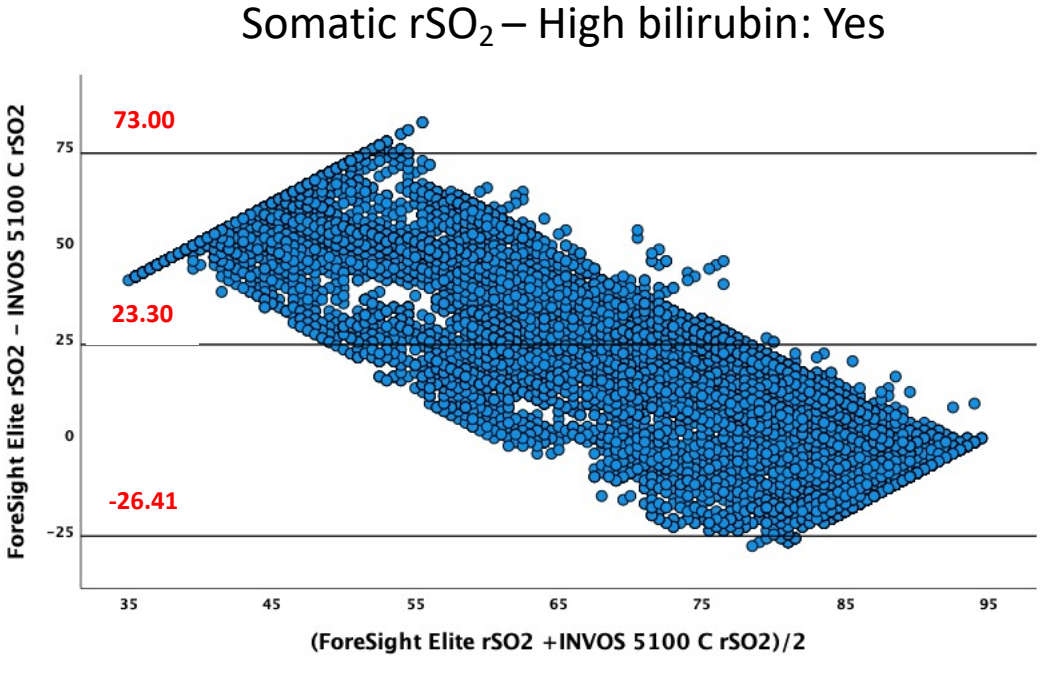
* : P < 0.05 and ** : P < 0.001 between both devices (Mann-Whitney U test)

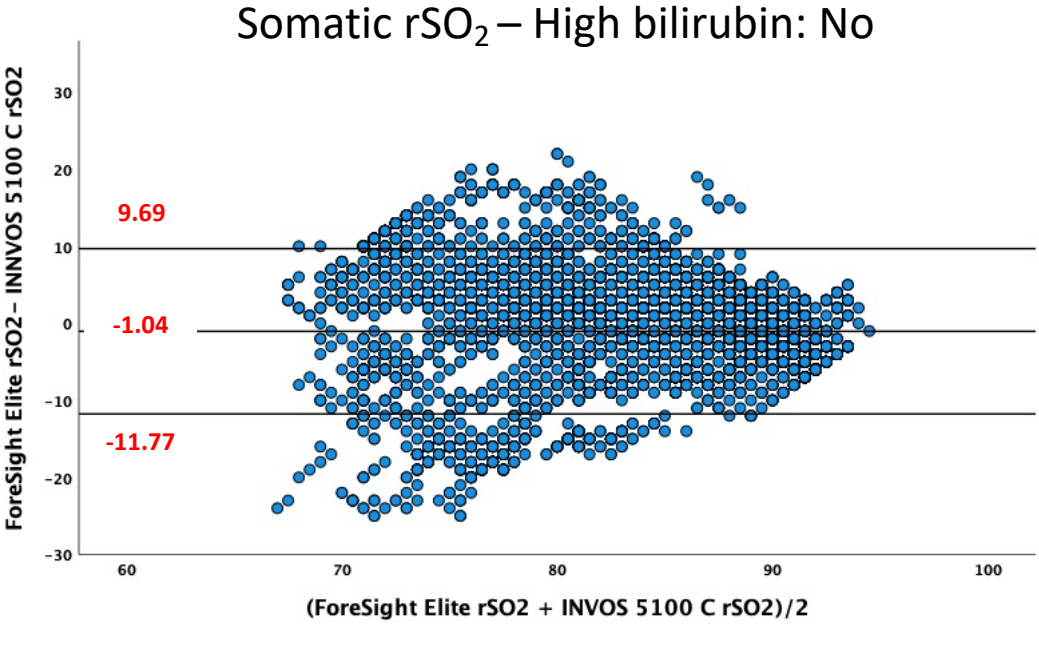


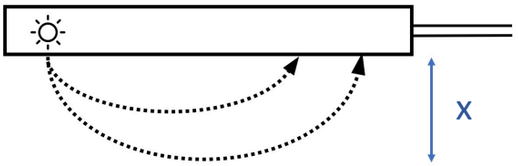
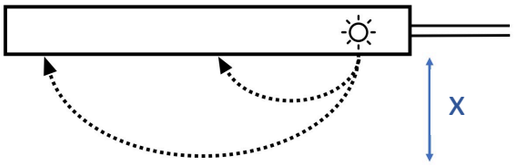










INVOS 5100 C	ForeSight Elite
	
Wavelenghts of emitted light	
730 – 810 nm	685 – 730 – 770 – 810 – 870 nm
Position of light-emitting diode	
Distal	Proximal

NIRS Sensors

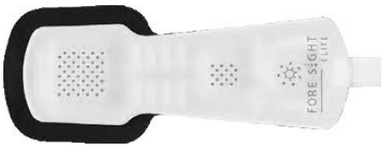
(x : depth of penetration)

<u>Adult</u>

x = 20mm

Not used in this study

<u>Adult</u>



x = 25mm

Used for children > 40 kg

<u>Pediatric</u>

x = 20mm

Used for children > 15 kg

<u>Junior Medium</u>

x = 20mm

Used for children < 40 kg

<u>Infant - Neonatal</u>

x = 20mm

Used for children < 15 kg

<u>Neonatal</u>

x = 12,5mm

Not used in this study