Fiberoptic monitoring of central venous oxygen saturation (PediaSat) in small children undergoing cardiac surgery: continuous is not continuous [version 2; referees: 2 approved]

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Abstract

Background: Monitoring of superior vena cava saturation (ScvO₂) has become routine in the management of pediatric patients undergoing cardiac surgery. The objective of our study was to evaluate the correlation between continuous ScvO₂ by the application of a fiber-optic oximetry catheter (PediaSat) and intermittent ScvO₂ by using standard blood gas measurements. These results were compared to those obtained by cerebral near infrared spectroscopy (cNIRS).

Setting: Tertiary pediatric cardiac intensive care unit (PCICU).

Methods and main results: A retrospective study was conducted in consecutive patients who were monitored with a 4.5 or 5.5 F PediaSat catheter into the right internal jugular vein. An in vivo calibration was performed once the patient was transferred to the PCICU and re-calibration took place every 24 hours thereafter. Each patient had a NIRS placed on the forehead. Saturations were collected every 4 hours until extubation. Ten patients with a median age of 2.2 (0.13-8.5) years and a weight of 12.4 (3.9-24) kg were enrolled. Median sampling time was 32 (19-44) hours: 64 pairs of PediaSat and ScvO₂ saturations showed a poor correlation (r=0.62, 95% CI 0.44-75; p<0.0001) and Bland Altman analysis for repeated measures showed an average difference of 0.34 with a standard deviation of 7.9 and 95% limits of agreement from -15 to 16. Thirty-six pairs of cNIRS and ScvO₂ saturations showed a fair correlation (r=0.79, 95% CI 0.60-0.89; p<0.0001) an average difference of -1.4 with a standard deviation of 6 and 95% limits of agreement from -13 to 10. Analysis of median percentage differences between PediaSat and ScvO₂ saturation over time revealed that, although not statistically significant, the change in percentage saturation differences was clinically relevant after the 8th hour from calibration (from -100 to +100%).

Conclusion: PediaSat catheters showed unreliable performance in our cohort. It should be further investigated whether repeating calibrations every 8 hours may improve the accuracy of this system. CNIRS may provide similar results with a lower invasiveness.
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Grant information: The author(s) declared that no grants were involved in supporting this work.

Competing interests: No competing interests were disclosed.

Introduction

Postoperative pediatric patients who have undergone cardiac surgery may benefit from venous saturation monitoring to assess oxygen delivery and as an indirect method of systemic perfusion. A true mixed venous sample (ScvO$_2$) is drawn from the tip of the pulmonary artery catheter and includes all of the venous blood returning from the head and arms (via superior vena cava), the gut, the kidneys and lower extremities (via the inferior vena cava) and the heart (via the coronary sinus). In recent years, however, superior vena cava oxygen venous saturation (ScvO$_2$) has replaced mixed venous saturation in many clinical settings and it is considered a reliable surrogate of SvO$_2$. In neonates and pediatric patients, the placement of a pulmonary artery catheter is not routine and may be problematic. In these patients ScvO$_2$ monitoring plays an important therapeutic role. ScvO$_2$ monitoring can be done intermittently (by the “traditional” co-oximetry method with serial blood withdrawals) or by reflectance oximetry through a fiber-optic catheter. A new dedicated multilumen (PediaSat; Edwards Lifesciences, Irvine, CA, USA) central venous catheter (CVC) with incorporated fiber-optic technology for continuous oxygen saturation monitoring has been designed for use in neonates and pediatric patients. If correctly placed with the distal tip in the superior vena cava, this catheter is able to provide a reliable on-line measurement of the ScvO$_2$. There is evidence that continuous monitoring of ScvO$_2$ may have beneficial effects in the resuscitation of septic patients and after complex congenital heart disease. According to manufacturer’s recommendations, after the first calibration the PediaSat catheter should provide consistent information for the following 24 hours. After this a new calibration is recommended in order to correct for potential drift from the true value.

Near-infrared spectroscopy (NIRS) is a noninvasive technique that measures continuous regional tissue oxygenation and is routinely used during pediatric cardiac surgery. NIRS measures the percentage oxygenated hemoglobin level in tissue beds. It is commonly used to determine cerebral tissue oxygen saturation (cerebral NIRS or cNIRS) and renal somatic tissue oxygen saturation (renal NIRS). cNIRS has been proposed to estimate adequacy of oxygen delivery due to a significant correlation existing between ScvO$_2$ and cerebral NIRS.

The objective of our study was to evaluate the correlation between continuous ScvO$_2$ and intermittent SvO$_2$ by using standard blood gas measurements during specific time points in postoperative pediatric cardiac patients. In particular, we aimed to verify if calibration of a continuous ScvO$_2$ catheter should be repeated in order to optimize the detection of potentially significant differences between continuous ScvO$_2$ and intermittent ScvO$_2$. Furthermore we also evaluated the correlation between cNIRS and intermittent SvO$_2$.

Materials and methods

A retrospective observational study was conducted in a tertiary pediatric cardiac intensive care unit from January 2013 until May 2013. Children undergoing elective cardiac surgery for congenital heart disease, and who had a PediaSat catheter placed (the indication was given by the attending anesthesiologist) at the Bambino Gesù Children’s Hospital, Rome, Italy, were enrolled in the study. Inclusion criteria were: 1) patient had been scheduled for elective cardiac surgery with cardiopulmonary bypass; 2) the patient was clinically indicated for central venous catheter placement with a size of 4.5 to 5.5 F; 3) the patient’s age was within the selected range: newborn >38 weeks gestation to child <10 years old; 4) the patient’s weight was >3.0 kg. Exclusion criteria were: 1) emergency operation; 2) need for or decision to position a femoral central venous catheter.

The INVOS 5100C Cerebral Oximeter (Somanetics, Troy, MI, USA) was used in all patients undergoing pediatric cardiac procedures with cardiopulmonary bypass according to the institutional protocol.

After induction of anesthesia, tracheal intubation, and radial or femoral artery cannulation, a central venous PediaSat catheter was inserted into the superior vena cava through the right internal jugular vein. The catheter was inserted using ultrasound guidance. Correct positioning was confirmed via transesophageal echocardiography and by a post-operative chest x-ray. The size and length of the catheters were decided on the basis of the patients’ weight. After catheter insertion an in vivo calibration was performed and repeated once the patient was transferred to the cardiac intensive care unit (CICU). The catheter was re-calibrated every 24 hours thereafter. Following induction of anesthesia, a NIRS sensor was placed on the patient’s forehead after adequate scrubbing of the skin.

Data collection

Data were retrieved from the institutional database and missing data were acquired from patients’ clinical charts. Demographics, surgical procedure, cardiac bypass time and cross clamp time were recorded. In order to obtain ScvO$_2$, blood was withdrawn from the distal port of the PediaSat catheter. Blood gases were analyzed in heparinized 1 ml syringes, within 60 seconds from withdrawal, with the GEM4000 blood gas analyzer (Brennan & Company, Dublin, Ireland). For each ScvO$_2$ value, a PediaSat and cNIRS saturation was collected. According to the institutional protocol, patients’ oxygen saturations are reported into clinical chart every 4 hours until extubation (the first value being reported 1 hour after calibration). After patient extubation, data collection was terminated.

Statistical analysis

A Spearman test was chosen for correlation estimation, and a Bland Altman analysis for repeated measures was used to verify bias and
agreement of correlated variables. Results are expressed as median (interquartile range). Wilcoxon signed rank test was used for paired group comparison. One-way analysis of variance (Kruskal-Wallis non parametric test) was applied in order to evaluate difference of saturations as measured by the PediaSat and ScvO2 over time. Agreement between the two methods for tracking changes in SvO2 was quantified using polar plots: acceptable calibration was defined as an angular mean bias of less than ±5° and the percentage of data points lying within radial limits of ±30° from the polar axis was assessed. A P value <0.05 was considered significant. Statistical analysis was performed with the GRAPHPAD PRISM 5.0 software package (GraphPad Software, San Diego, CA, USA).

Table 1. Demographic data of enrolled patients. BSA: body surface area. LOMV: length of mechanical ventilation. CPB: cardiopulmonary bypass. Xclamp: cross clamp.

<table>
<thead>
<tr>
<th>Number of patients=10</th>
<th>Weight (Kg)</th>
<th>Height (cm)</th>
<th>BSA</th>
<th>Age (years)</th>
<th>LOMV (days)</th>
<th>CPB (min)</th>
<th>Xclamp (min)</th>
<th>Sampling time (hours)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minimum</td>
<td>3,100</td>
<td>50,00</td>
<td>0,2119</td>
<td>0,03288</td>
<td>1,000</td>
<td>54,00</td>
<td>64,00</td>
<td>16,00</td>
</tr>
<tr>
<td>25% Percentile</td>
<td>3,950</td>
<td>52,50</td>
<td>0,2435</td>
<td>0,1295</td>
<td>1,750</td>
<td>89,00</td>
<td>79,00</td>
<td>19,00</td>
</tr>
<tr>
<td>Median</td>
<td>12,40</td>
<td>82,50</td>
<td>0,5364</td>
<td>2,242</td>
<td>2,000</td>
<td>149,0</td>
<td>114,0</td>
<td>32,00</td>
</tr>
<tr>
<td>75% Percentile</td>
<td>24,25</td>
<td>123,3</td>
<td>0,8932</td>
<td>8,481</td>
<td>3,000</td>
<td>185,5</td>
<td>130,0</td>
<td>44,00</td>
</tr>
<tr>
<td>Maximum</td>
<td>30,00</td>
<td>133,0</td>
<td>1,050</td>
<td>11,48</td>
<td>3,000</td>
<td>295,0</td>
<td>195,0</td>
<td>44,00</td>
</tr>
<tr>
<td>Diagnosis</td>
<td>Mitral regurgitation</td>
<td>Pulmonary atresia with ventricular septal defect</td>
<td>2 × Transposition of the great arteries</td>
<td>Aortic arch interruption</td>
<td>2 × Truncus arteriosus</td>
<td>Tetralogy of Fallot</td>
<td>Mitral stenosis and subaortic stenosis</td>
<td>Univentricular heart with aortic arch hypoplasia</td>
</tr>
<tr>
<td>Surgery</td>
<td>correction</td>
<td>correction</td>
<td>correction</td>
<td>correction</td>
<td>correction</td>
<td>correction</td>
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<td>correction</td>
</tr>
</tbody>
</table>

Ten patients with a median age of 2.2 (0.13–8.5) years and a weight of 12.4 (3.9–24) kg were enrolled. Median mechanical ventilation duration was 36 hours (12–48). Cardiologic diagnoses and surgical procedures with cardiopulmonary bypass (CPB) details are reported in Table 1. Median sampling time was 32 (19–44) hours: at 48 hours all patients were extubated and the data collection never lasted longer than this. Sixty-four pairs of PediaSat and ScvO2 saturations were available (Figure 1A): 5 missing pairs are acknowledged (on the clinical chart, once was ScvO2 value alone reported and 4 times no value was reported). Median PediaSat venous saturation was 71 (64–81)% whereas the median ScvO2 value was 74 (64–82) (p=0.347). Correlation between these two methods was poor (r=0.62, 95% CI 44–75; p<0.0001). Bland Altman analysis for repeated measures revealed a bias of 0.34 with a standard deviation of 0.89; p<0.0001). Analysis of median percentage differences between PediaSat and ScvO2 saturation over time showed that there was not a significant modification over the different timeframes (p=0.28) (Figure 2A). However, although not statistically significant, the change of percentage saturation differences was clinically relevant especially after the 8th hour after calibration when errors from -100% to +100% were noted both as under and overestimation by the PediaSat method (Table 2). Similar results were found when percentage cNIRS-ScvO2 differences were evaluated (p=0.86) (Figure 2B) although the error never exceeded 20% at any time point and cNIRS showed a slight tendency to systematic underestimation of true values (Table 2). Trending ability of PediaSat as assessed by a Polar plot showed a mean angular deviation from the polar axis of 90°, with 50% of the data points lying outside the radial limits of ±30° from the polar axis. Trending ability of cNIRS assessed by Polar plot showed a mean angular deviation from the polar axis of 42° with 30% of the data points lying outside the radial limits of ±30° from the polar axis.
**Figure 1. Saturation pairs.** Simultaneous SvO2 values provided by intermittent blood gas analysis (BGA), the PediaSat catheter (A) and cerebral Near Infrared Spectroscopy (cNIRS) (B) for each patient.

**Figure 2. Saturation differences over time.** Coupling of SvO2 values obtained by blood analysis (BGA) and PediaSat (A), and BGA and cerebral near infrared spectroscopy (cNIRS) (B), expressed over time for each patient.
### Table 2. Median and range percentage differences between ScvO2 reference values (achieved by catheter withdrawn blood gas analysis) and PediaSat/cerebral Near Infrared Spectroscopy (cNIRS).

<table>
<thead>
<tr>
<th></th>
<th>PediaSat</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Time points</td>
<td>Calibration + 1h</td>
<td>4 hours</td>
<td>8 hours</td>
<td>12 hours</td>
<td>16 hours</td>
<td>20 hours</td>
</tr>
<tr>
<td>Median</td>
<td>-1.809</td>
<td>1.086</td>
<td>-1.220</td>
<td>-2.564</td>
<td>2.103</td>
<td>6.542</td>
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<tr>
<td>75% Percentile</td>
<td>1.022</td>
<td>4.727</td>
<td>3.374</td>
<td>2.599</td>
<td>20.70</td>
<td>24.91</td>
<td></td>
</tr>
<tr>
<td>Maximum</td>
<td>11.59</td>
<td>13.46</td>
<td>7.046</td>
<td>7.500</td>
<td>100.0</td>
<td>57.32</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>cNIRS</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Time points</td>
<td>0 hour + 1h</td>
<td>4 hours</td>
<td>8 hours</td>
<td>12 hours</td>
<td>16 hours</td>
<td>20 hours</td>
</tr>
<tr>
<td>Median</td>
<td>-1.299</td>
<td>-5.857</td>
<td>-4.435</td>
<td>-5.852</td>
<td>1.587</td>
<td>-8.451</td>
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<tr>
<td>75% Percentile</td>
<td>3.603</td>
<td>4.224</td>
<td>9.798</td>
<td>2.096</td>
<td>7.500</td>
<td>-8.451</td>
<td></td>
</tr>
<tr>
<td>Maximum</td>
<td>15.38</td>
<td>18.57</td>
<td>14.54</td>
<td>20.55</td>
<td>7.500</td>
<td>-8.451</td>
<td></td>
</tr>
</tbody>
</table>

**Discussion**

Evaluation of oxygen delivery is optimized by measurement of continuous superior vena cava oxygen saturation. This is due to the fact that unexpected/sudden low cardiac output events may occur in the timeframe between serial ScvO2 evaluations; of note, the trigger for occasional venous samplings (hypotension, need for increasing vasoactive drugs dose, etc.) may also be prompted untimely with respect to cardiac decompensation. The ideal device to perform this continuous monitoring should be accurate and minimally invasive, it should provide at least two saturation values per minute, it should be applicable to smaller patients and, finally, it should be cost-effective. To date, such a device is not yet available in routine clinical practices. The PediaSat catheter does certainly have some of these features and several initial reports seemed to provide encouraging results in clinical practice. Unfortunately, the application of PediaSat to our small cohort of patients below 10 kg of body weight provided unsatisfactory results: the PediaSat catheter provided unacceptable saturation differences, with respect to the reference ScvO2 values (-26 to 25%). Furthermore, such deviation from actual values did not show a systematic error on the device and the PediaSat did not display a consistent over- or under-estimation of true ScvO2 values: hence adjustments did not seem possible in order to correct the measures. In terms of trend estimation, PediaSat provided fair results, although still far from being adequate in terms of reliable routine utilization. The reasons for its lack of accuracy are not completely clear, but they could be caused by imperfect functioning of the miniaturized technology. It is also possible that more frequent calibrations should be performed: in our cohort, precision of PediaSat started to decrease, in a clinically significant way, after the 8th hour after calibration and this trend was similar after each calibration (as seen in the subgroup of patients who passed the 24th monitoring hour and whose PediaSat catheter was therefore re-calibrated). On the other hand, cNIRS, whose application is favored due to its low invasiveness, showed similar results, if not slightly better, in terms of coupling with ScvO2 values, limits of agreement at Bland Altman analysis, drift from actual values over time and trending ability. It must be remarked, however, that cNIRS values may be significantly affected by ventilation, sedation, cardiac anatomy and temporal distance from the surgical procedure.

Our results conflict with some reports and agree with others. However, this is one of the first studies evaluating PediaSat in routine practice, and not during a specifically designed study. Furthermore, we hypothesize that PediaSat catheter might improve its performance with the calibration repeated every 8 hours.

Our study is certainly limited by the small subgroup of patients that may have potentially caused a bias in the statistical analysis: as a matter of fact, correlation and ANOVA should be calculated, in a larger population, for repeated measures (as done for Bland Altman). For this reasons it has been decided to present Figure 1 and Figure 2 in order to graphically depict the overall group tendency, although visualized per single patient and per single time point. Finally, we acknowledge that the comparison between PediaSat and cNIRS...
monitor may be biased by the fact that cNIRS values were fewer in number and this may have randomly reduced the possibility for cNIRS errors. For these reasons we cannot definitely state which of the two monitoring techniques performs better.

In conclusion, 4.5 and 5.5 F PediaSat catheters showed unreliable performance during the early post operative course of children below 10 kg, who underwent cardiac surgery with CPB. It should be further investigated if repeating calibrations every 8 hours instead of every 24 hours may improve the accuracy of this system. At the moment cNIRS provides similar results with a lower invasiveness.

Data availability
figshare: Post-operative clinical data of children enrolled for comparison of ScvO2% with PediaSat and with cerebral NIRS values. doi: http://dx.doi.org/10.6084/m9.figshare.900915

Author contributions
FG Iodice and Z Ricci conceived and drafted the paper, R Haiberger and I Favia collected the data. P Cogo supervised the final version of the manuscript. All the authors agreed with the final content.

Competing interests
No competing interests were disclosed.

Grant information
The author(s) declared that no grants were involved in supporting this work.

Acknowledgements
The PediaSat catheters and the cNIRS sensors used in this data collection were provided by the Bambino Gesù Hospital.

References

9. Edwards PediaSat catheter online brochure. Reference Source
Open Peer Review

Current Referee Status: ✔ ✔

Version 2

Referee Report 22 May 2014
doi:10.5256/f1000research.4216.r4505

Mirela Bojan
Department of Anesthesia and Critical Care, Necker Sick Children's Hospital, Paris, France

I thank the authors for considering all of the remarks, it was a pleasure to read the revised manuscript which, I believe, is improved. Albeit I believe this is a valuable report, I am unsure that the figures highlight the message. My (last) suggestion is use a trellis chart: if time is on the abscissa axis, and the three individual measurements (BGA, Pediasat, cNIRS) on the ordinate axis, than this should result in 10 boxes, each box showing all measurements per patient along time. I believe it will become obvious to the reader that the Pediasat measurement becomes unreliable after 8 hours, and requires calibration.

I have read this submission. I believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Competing Interests: No competing interests were disclosed.

Referee Report 09 May 2014
doi:10.5256/f1000research.4216.r3313

Sabino Scolletta
Department of Anesthesiology and Intensive Care, University of Siena, Siena, Italy

The authors have improved their manuscript. The statistical analysis is correct. The results are well presented and the discussion is focused.

I thank the authors for having followed my suggestions.

Sincerely,

Sabino Scolletta

I have read this submission. I believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Competing Interests: No competing interests were disclosed.
Mirela Bojan  
Department of Anesthesia and Critical Care, Necker Sick Children's Hospital, Paris, France

I have read with pleasure the article by Dr Ricci and colleagues. The topic is of high interest, since SvO₂ measurements represent standard monitoring in the postoperative management of several pediatric cardiac procedures. Also, ScvO₂ is nowadays an accepted surrogate measurement of SvO₂. Significant differences have been reported between continuous fiberoptic measurements and intermittent measurements in adults with cardiac surgery (Baulig et al., 2008), requiring repeated calibration of the continuous measurement instrument. The findings here suggest a requirement for calibration every 8hrs, albeit the population is too small to allow for conclusions.

I believe there is a bias in the statistical analysis, since correlations have been estimated between repeated measurements – as a matter of fact, there is a temporal autocorrelation between the results of a same patient at different time points. However, this bias should result in overestimation of the relationship. The negative result concerning ScvO₂-BGA correlation is somewhat “reinforced” by this bias. But one can question about the positive NIRS-BGA correlation. I understand that the population is too small to calculate correlations at each time point, or to analyse data using a mixed model for repeated measurement. Therefore, I suggest presenting the results in Figure 1 and Figure 3 separately for each patient, showing on the same graph the BGA, ScvO₂ and NIRS measurements, and allow for visual assessment of the relationship in each patient at each time point. This should reassure the reader about the potential bias due to temporal autocorrelation. Since the correlation between ScvO₂-BGA is negative, and since the authors do not demonstrate but only suggest a positive correlation between NIRS-BGA, this should be acceptable.

I have read this submission. I believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

**Competing Interests:** No competing interests were disclosed.

Zaccaria Ricci, Department of Pediatric Cardiosurgery, Bambino Gesú Hospital, Italy

We wish to thank Dr Bojan for her valued suggestions; these are in line with the comments of Sabino Scolletta. As recommended, we will change the figures as per improved visualization of data and leave the remaining results unchanged. As remarked by the reviewer, the new figures will reassure the reader, in order to cope for repeated measure analysis, although confirming the results presented in the text.

**Competing Interests:** I declare I have no conflict of interest
Sabino Scolletta  
Department of Anesthesiology and Intensive Care, University of Siena, Siena, Italy

In this article, Dr. Iodice and associates presented the results on the correlation between continuous and intermittent ScvO\textsubscript{2} values, obtained with a fiber-optic oximetry catheter (PediaSat) and standard blood gas measurements, respectively. In addition, ScvO\textsubscript{2} values were compared to those obtained by cerebral near infrared spectroscopy (cNIRS). The study was conducted on ten children undergoing cardiac surgery.

Although this is a retrospective observational study, it has been well described. Also, the article is clear, and the results are well presented. The discussion is very concise but highlights sufficiently some positive and negative aspects of the devices under study. Furthermore, it makes comparisons with other studies showing similar or opposite results on this field.

My major criticism is about statistical analysis. Indeed, as the measurements of oxygen saturation have been performed at different times, the adjustment for the effects of repeated measurements in the Bland-Altman analysis had to be used. Conversely, the authors have used standard Bland-Altman and correlation analyses.

Despite the aforementioned criticism, I think the topic of this article is of interest. Indeed, monitoring tissue oxygenation in critically ill patients is crucial during cardiac surgery. In particular, children undergoing cardiac operations may benefit from assessing the adequacy of their oxygen delivery (DO\textsubscript{2}) with respect to their oxygen requirements. To this purpose, an indirect index of tissue perfusion is the mixed venous oxygen saturation (SvO\textsubscript{2}). However, to measure this parameter a pulmonary artery catheter (PAC) is required. Unfortunately, PAC is invasive and usually not practicable in children. Over the past years, the central venous oxygen saturation (ScvO\textsubscript{2}) has been used in many clinical settings as a surrogate of SvO\textsubscript{2}. Thus, ScvO\textsubscript{2} can be measured continuously (fiber-optic catheter) or intermittently (blood withdrawals) and it is currently considered a possible alternative to SvO\textsubscript{2}. Besides, the measure of ScvO\textsubscript{2} requires a less invasive technique, as for its measurement a central venous catheter is needed instead of a PAC.

In this study, the main result was that the fiber-optic catheter PediaSat showed unreliable performance. However, the authors had repeated measures from a small cohort of children with <10 kg of body weight. This may have biased their findings. Further studies are warranted, as conflicting results on this issue still remain in the current literature.

Of note, a key message from this investigation is that monitoring brain function with cNIRS is safe, continuous and easy to achieve in children undergoing cardiac surgery. In addition, this method has the main advantage of providing useful information on brain function, which can be considered a subtle marker of systemic hypoperfusion in case of low cerebral oxygen saturation. Monitoring cerebral function with cNIRS may avoid potential neurological complications, which are associated with increased morbidity and mortality, and poor quality of life.

I have read this submission. I believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

**Competing Interests:** No competing interests were disclosed.
We are thankful to the reviewer for the precious suggestions and kind comments. We agree that the topic of assessing the adequacy of children's oxygen delivery (DO$_2$) with respect to their oxygen requirements is crucial in pediatric intensive care and we are convinced that this topic has not been addressed effectively, so far. Indeed he is right: Bland Altman analysis for repeated measures should have been performed for our data analysis. This will be certainly modified in the revised version of the manuscript. Of note we already performed the corrected analysis and did not found significantly different results. In light of this we think that the overall message of the study has not been affected by our methodological mistake.

**Competing Interests:** I have no competing interest to declare