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Methodology for Evaluating the Performance of a New Pulse Oximeter Model and Pulse Oximetry Algorithm in Neonates in a Clinical Trial (Exploratory Study)

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Summary

While evaluating a new domestically produced pulse oximeter model in clinical practice, we discovered a lack of references in Russian-language publications on clinical trial methodologies to assess device reliability and performance.

The aim of the study is to create a methodology for conducting a multicenter, prospective, cohort, non-randomized, controlled clinical trial evaluating a domestic pulse oximeter.

Methods. Measurements were performed on 20 preterm infants in the neonatal intensive care unit with a mean birth weight of 2340 [1250; 3125] g and a gestational age of 35 [30; 37] weeks using a new model pulse oximeter simultaneously with the reference monitor. Multiple oxygen saturation measurements of varying duration were taken alternately from the upper and lower limbs, and the number of false desaturation alarms was recorded. Pulse oximeter saturation data were evaluated for correlation with clinical findings.

Results. Attachment of sensors to the infant's feet was found to be optimal in terms of ease of use, minimal artifact generation, and minimal interference with routine medical procedures and neonatal care. To reduce motion-induced artifacts and false alarms, the optimal period of SpO_2 monitoring to detect desaturations and bradycardia was determined to be 120 min. Due to the high variability of pulse rate (PR) and saturation in neonates, two-second intervals were determined to be optimal for comparing records from the two monitors. Matching of ECG HR and pulse oximeter PR was required to eliminate artifacts. A mathematical software model required for accelerated analysis of data collected from all sensors during the study was approved.

Conclusion. The data analysis supported the proposed methodology for conducting a clinical trial to evaluate the performance and reliability of new pulse oximetry devices.

Keywords: pulse oximetry; neonates; neonatal pulse oximetry algorithm; Sensorex oximeter

Conflict of interest. The authors declare no conflict of interest.

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Introduction

Monitoring of vital signs, including pulse oximetry, is the foundation of the diagnostic process in the intensive care unit (ICU). The search for more advanced monitoring methods enables modernization and adaptation of treatment strategies, as well as shorter hospital stays and improved patient quality of life [1]. The timeliness of medical care depends largely on the reliability of medical equipment.

Pulse oximetry is a method of assessing arterial blood oxygen saturation (SpO_2) using photoplethysmography (PPG), which measures the increase in light absorption caused by an increase in arterial blood volume during myocardial systole [2]. Pulse oximetry is one of the most commonly used methods for continuous monitoring of vital signs in the ICU because of its ease of use and high data accuracy. Although some aspects of pulse oximeter performance can be evaluated using simulation, the pulse oximetry process involves numerous physical and optical interactions (light absorption by tissues, venous blood, etc.), so the pulse oximeter is classified as a device that requires empirical clinical studies for development, calibration, and validation [3, 4].

While preparing a protocol for clinical validation and testing of a new model of the Russian pulse oximeter «Sensorex», developed by the Ural Optical and Mechanical Company named after E. S. Yalamov, our Laboratory of Industrial Design and Re-engineering of Medical Equipment (LIDRME) faced the challenge of finding a methodology suitable for evaluating and comparing the performance of pulse oximetry devices in neonatal care in the Russian-language literature. Such a methodology was needed to list the advantages and shortcomings of a tested device in an understandable way.

As a result, it was decided to conduct an exploratory clinical trial to develop a methodology for future studies. The study determined basic parameters such as:

1. The scheme for connecting the control and tested pulse oximetry devices to the patient
2. The duration of each episode in the measurement
3. Recorded parameters
4. Automated workstation (AWS) scheme.

After reviewing the literature, we decided to use the Masimo SET® pulse oximetry monitor as the reference monitor. This decision was supported by the available studies, which provided compelling evidence of the clinical effectiveness advantage of this algorithm.

In one study, Masimo SET® pulse oximetry detected 86% fewer false alarms of SpO_2 and heart rate in neonates and detected more true episodes of hypoxia and bradycardia than pulse oximetry monitors with other algorithms (Nellcor N-200, Nellcor N-395, Novametrix MARS, Philips Viridia 24C). [5]. Because neonatal ICU patients typically have active limb movements, it was critical to maintain pulse oximetry accuracy during motor activity. Laboratory testing of pulse oximetry accuracy during active patient arm movement showed that the Masimo SET® pulse oximeter outperformed 20 other devices tested, including the Agilent Viridia 24C, Agilent CMS, Datex-Ohmeda 3740, Nellcor N-395, Criticare 5040, and others [6].

In addition, pulse oximetry using the Masimo SET® algorithm resulted in significantly faster acquisition of a steady signal after the sensor was placed on the body in neonates requiring resuscitation. Comparing Radical-7 (Masimo) and Biox 3700, the mean time to a stable reading was 20.2±7 and 74.2±12 seconds, respectively (P=0.02). When comparing Radical-7 and Nellcor N-395, the time to stable measurements from the start of monitoring was 20.9±4 and 67.3±12 seconds, respectively (P=0.03) [7].

Recent studies of the characteristics of pulse oximetry during extremity motion have shown a continuing trend of decreasing accuracy of data acquisition [8, 9]. Several studies have shown that virtually all pulse oximeters studied during movement tests showed an increase in mean square error to values above the recommended threshold of 3% [8, 9]. In this context, we also decided to match the episodes of sensor measurements to the clinical presentation, since the use of even a reference pulse oximetry monitor could lead to measurement errors in the presence of increased motor activity.

The growing need to create a consortium of domestic medical equipment manufacturers to replace foreign equipment that is difficult to import due to sanctions or disruptions in logistics chains [10] is of strategic importance and requires the development of validated testing methods. This will allow medical organizations to optimize their supply of equipment, as well as identify defects and flaws in tested equipment more quickly.

Aim of the study was to develop the methodology of the upcoming clinical study under the R&D program «Clinical testing of Sensorex pulse oximeter and developing algorithms for newborns».

The objectives of the study were:

- to determine the patient population according to the inclusion and exclusion criteria;
- to obtain informed consent from each patient's legal representative to test a new medical device (Sensorex pulse oximeter);
- to evaluate the safety of the Sensorex pulse oximeter during a single 180-minute test measurement;
- to perform a series of measurements with the Sensorex pulse oximeter;
- to determine the parameters necessary for measurement in a full-scale, multicenter clinical trial;
- to determine the optimal connection scheme of the pulse oximetry sensors of the Sensorex device under study and the reference control monitor;
- to determine the optimal duration of measurements;
- to design the automated workstation based on the data obtained;
- to formulate technical specifications for the development of software to process the array of data obtained.

Materials and Methods

This article is a publication of the study protocol.

Study design. Prospective, cohort, non-randomized, controlled study.

Allocation of patients to groups. Study (main) group. There was no control group.

Inclusion criteria. Neonatal intensive care unit patients (newborns).

Exclusion criteria.

- Participation in the study would interfere with diagnostic and therapeutic measures or routine patient care.
- Refusal of the legal representative of the child to participate in the clinical trial.

Location and period of the study. Ekaterinburg Perinatal Clinical Center from 01.10.2023 to 30.10.2023.

Study participants. Intensive care physicians of the neonatal intensive care unit.

General study principles. During the study, measurements were made using a Sensorex heart rate monitor and a reference monitor with a built-in Masimo SET® algorithm that is used daily in the newborn intensive care unit (NICU).

In the NICU, patients received routine interval care every three hours, which included repositioning, feeding and hygiene procedures. These activities took 30 to 50 minutes. We chose a study time of no more than 120 minutes between care procedures,

which has been shown in practice to influence the number of artifacts in pulse oximetry and thus the accuracy of the results obtained.

Transmission-type pulse oximetry sensors (control and study monitor) were placed on the child's extremities.

The start time of the study was confirmed using the control and study monitors. Values were manually recorded on a trend chart every 10 seconds.

At the end of the study, the investigator manually transferred each patient's data from the trend chart to an Excel spreadsheet. The time interval for data recording was set to 10 seconds.

If episodes of SpO_2 reduction of less than 85% and episodes of more than 20 min^{-1} difference between the device heart rate readings were recorded within the specified intervals, the clinical concordance of heart rate (HR) and SpO_2 reduction was recorded by marking «+» for concordance and «–» for discordance on the trend chart.

Depending on the study group, the extremities for the pulse oximetry sensors were changed at the specified interval.

If treatment interference occurred, the study was stopped early and not marked as completed.

The study was divided into three phases: determining the best location for the sensors on the patient, the best time to perform the study, and the use of the reference ECG channel.

Statistical analysis. The study materials were analyzed using both parametric and nonparametric analysis methods. The original data were collected, corrected, and organized, and the results were visualized using the developed trend chart and Microsoft Office Excel 2016 software. IBM SPSS Statistics v.26 software (developed by IBM Corporation) was used for statistical analysis. The Kolmogorov-Smirnov test was used to determine the normality of the distribution of quantitative parameters. The distribution of most parameters was not normal. Numerical parameters were described by median *(Me)* and lower and upper quartiles *[Q1; Q3]*. Categorical data were described by absolute values and percentages. The Mann–Whitney *U* test was used to compare the different conditions. Pearson's χ^2 test was used to compare categorical data. When analyzing four-way tables with an expected phenomenon and a value in at least one cell less than 10, the χ^2test was calculated using Yates' correction. A two-tailed value of $P<0.05$ was used to determine the statistical significance of differences.

Results

The study yielded a total sample of patients distributed over several phases (total *N*=20). The median body weight was 2340 [1250; 3125] g, the median gestational age was 35 [30; 37] weeks, and the median number of days after birth was 4 [2; 5].

Phase 1: Determination of optimal sensor placement on the patient. Two-hour measurements were performed on four patients.

During the first hour of the measurement, the pulse oximeter sensors were placed on the feet, and 30 minutes after the start of pulse oximetry, the location of the sensors was changed from one foot to the other. Sixty minutes after the start of the measurement, the sensors were moved to the wrists, and after 30 minutes, the sensors were moved to a different wrist. A total of 16 measurements of 30 min each were performed — 8 on the feet and 8 on the wrists.

The target parameter of the first phase of the study was the ratio of the number of measurements with artifacts (false bradycardia and hypoxemia in the absence of clinical manifestations) to the number of measurements without artifacts, and the correlation between this ratio and the location of the sensor (wrist or foot).

During the 30-minute foot and wrist measurements, the number of measurement with artifacts differed significantly for both the Sensorex pulse oximeter (7 vs. 3, *P*=0.039) and the reference monitor (6 vs. 2, *P*=0.046), as did the total number of artifacts for the two pulse oximetry monitors (13 vs. 5, *P*=0.005). The results are shown in Table 1.

Phase 2: Determination of the optimal study period. Before the study, the patients were divided into 3 subgroups according to the planned study time:

1. Subgroup with total study time of 30 minutes, with limb change after 15 minutes (5 patients);
2. Subgroup with total study time of 60 minutes, with limb change after 30 minutes (5 patients);
3. Subgroup with total study time of 120 minutes, with limb change after 60 minutes (5 subjects).

The target parameter of the second phase of the study was the number of patients who did not have any episodes of deviation from reference values during the study period.

Thus, in the 30-minute subgroup of the study, 3 (60%) patients had no abnormal episodes, and in the 60-minute subgroup of the study, 2 (40%) patients

Table 1. Comparative analysis of the number of measurements with artifact when pulse oximetry was performed at the wrists of the hands and feet for 30 minutes.

Monitor	Number of measurements with artifacts		*P*-value
	Wrists	Feet	
Sensorex, *N*=8	7	3	0.039*
Reference, *N*=8	6	2	0.046*
Total, *N*=16	13	5	0.005*

Note. Here and in the Table 3: * — significant differences.

had no abnormal episodes. In the 120-minute subgroup, at least one abnormal episode was observed in every patient.

The results are presented in Table 2.

Phase 3: Use of Reference Electrocardiographic Channel. In Phase 3 of the study, the quality of the reference pulse oximeter signal was evaluated by the correspondence of the pulse oximeter pulse values to the electrocardiography (ECG) sensor heart rate values, rather than by clinical presentation to the observer's judgment. The signal from the reference monitor's pulse oximeter sensor was considered true if the pulse rate matched the heart rate from the ECG sensors (a difference of no more than 20 min^{-1}).

The frequency of true episodes of hypoxemia and bradycardia recorded by the pulse oximeters (when the pulse rate matched the data from the ECG sensors) was compared with the mean number of episodes of hypoxemia and bradycardia obtained from the pulse oximeters that the observers considered consistent with the clinical presentation in studies without ECG sensors (Phase 2). The results are presented in Table 3.

Table 2. Matching the number of patients without episodes of pulse oximetry abnormalities to the duration of the study.

Study subgroup	Patients without abnormalities, *N* (%)
30 minutes, *N*=5	3 (60)
60 minutes, *N*=5	2 (40)
120 minutes, *N*=5	0 (0)

Discussion

Phase 1 of the study. From a clinical point of view, it is preferable to measure capillary blood saturation on the right arm, taking into account the need to determine preductal oxygenation in newborns (with a functioning patent ductus arteriosus, blood saturation values on the right and left arms may differ) [12], including pulse oximetry in the delivery room according to the Methodological Letter of the Ministry of Health of Russia «Resuscitation and Stabilization of Newborns in the Delivery Room» dated March 4, 2020 [13], as well as screening examination of all newborns before discharge from the maternity hospital for congenital heart disease [14, 15]. Meanwhile, differences in pre- and post-ductal saturation at the right and left wrists for physiological reasons may bias the results of the data analysis of the target study. In addition, the study procedure should not interfere with routine and unscheduled medical procedures and child care activities. For example, systemic blood pressure is measured at least once every 3 hours, primarily in the upper extremities, which will affect the pulse oximeter readings when the sensor is placed on the wrist and reduce the power of the study.

During the study, fewer artifacts were detected on the feet, in part due to more intense motor activity of the upper extremities. Therefore, the feet were determined to be the optimal location for the sensors during the study in terms of reducing the impact on the neonate's medical care and reducing the frequency of artifacts.

Phase 2 of the study. A total measurement time of 2 hours is optimal for assessing the clinical performance of the pulse oximeter in an individual patient. A shorter measurement period increases the risk of missing episodes of abnormalities and measurement errors. Prolonged placement of the pulse oximeter sensor on the limb increases the likelihood of adverse effects on the child's skin (compression, pressure sores) without a significant increase in information value [16]. Also, if the duration of measurement is increased, the influence of therapeutic and hygienic measures performed every 3 hours on the recorded events is inevitable. Thus, the maximum possible duration of measurement while minimizing the impact on treatment is 120 minutes.

Phase 3 of the study. The next step was to manually enter the data into a spreadsheet for further processing. When comparing the parameters of the study and reference pulse oximeters, the lack of a mechanism to control false values and the reduced accuracy of the signal from the reference pulse oximeter became significant.

In addition, determining whether pulse oximetry data correspond to the clinical presentation to detect erroneous values is not always a reliable method in neonates, since episodes of moderate SpO_2 reduction (up to 80–85%) may occur without significant changes in the patient's clinical condition [13].

Heart rate data obtained from ECG sensor readings can be an effective criterion for determining study objectives and serve as a reference channel for comparison and analysis.

Summary of the three phases of the study. During the study it became obvious that the input of large amounts of numerical data significantly prolongs the study time, introduces a certain number of misprints and errors, which negatively affects the reliability of the calculated parameters. It is

Table 3. Frequency of events considered true with and without ECG sensors.

Study phase	Number of episodes of hypoxemia and bradycardia		*P*-value
	Based on oximetry, *N*	Recorded, *N* (%)	
2. Clinical, without ECG sensors, *N*=5	47	16 (34)	0.029*
3. Based on ECG, *N*=1	9	6 (62.5)	

technically possible to record parameters manually no more often than once every 10 seconds. In order to reduce the influence of the human factor on the results, we decided to develop a special software that allows to extract and process the trend data of the tested monitors.

Comparison of monitor data with the frequency of their recording every 10 seconds is not very meaningful because episodes of significant variation in heart rate and SpO_2 may occur in a shorter time interval and the fact of their recording is critical to determining the clinical effectiveness of the pulse oximeter.

As a result, the recommended time interval for trend recording was 2 seconds, which is the minimum possible time for averaging the values of the two monitors used in the study.

It is impossible to perform the study with a sufficient level of accuracy and statistical significance while observing the limitation of the interval of recording parameters to 2 seconds manually. Therefore, it is necessary to develop specialized software capable of extracting, recording and processing data from the tested monitors.

Simultaneous connection of pulse oximetry sensors of the control and the tested device is critical for comparing their performance and clinical effectiveness.

We decided to use the ECG sensors of the control monitor as a reference for additional control of the accuracy of the signal received from the pulse oximetry sensors and to exclude episodes of unreliable data recording due to sensor displacement on the patient's foot.

Based on the obtained data, we developed an automated workstation (AWS) scheme.

We determined the data necessary for statistical analysis, developed schemes and algorithms for evaluation of four main target parameters for the upcoming clinical trial, which include:

- frequency and duration of episodes of false bradycardia and tachycardia (deviation of heart rate according to pulse oximetry sensor data by $\geqslant$25 min^{-1} from ECG sensor readings);
- frequency and duration of episodes of false hypoxemia (decrease in SpO_2 below 85%, not correlated with reference monitor readings);
- frequency and duration of episodes of true bradycardia (according to ECG monitor data), accuracy of pulse oximeter trend correspondence with ECG monitor data;
- frequency and duration of true hypoxemia episodes (SpO_2 drops below 85%, correlated with reference monitor readings).

Based on the obtained results, we prepared technical specifications for the development of analytical software for processing trends obtained from the tested and reference monitors.

Safety assessment. Transcutaneous pulse oximetry is a standard, noninvasive and safe method of monitoring vital signs. The devices were used in accordance with the instructions for use regarding safety measures (3601.00000000 RE) and on the basis of the technical characteristics. No complications or adverse effects of pulse oximetry with the Sensorex device on the patient's body were observed.

Study limitations. A limitation of the study is the lack of sample size calculation.

Conclusion

During the exploratory study, we formulated the principles and methodology for conducting a full-scale multicenter clinical trial of a new model of pulse oximetry device and pulse oximetry algorithm.

In this case, as a result of the forthcoming study, the performance of the device will be expressed in clear numerical values, and the obtained data will help to formulate a set of proposals for improving the device and algorithm of pulse oximetry in newborns.

References

1. *Enoch A.J., English M., Shepperd S.* Does pulse oximeter use impact health outcomes? A systematic review. *Arch Dis Child*. 2016; 101 (8): 694–700. DOI: 10.1136/archdischild-2015-309638. PMID: 26699537.
2. *Nitzan M., Romem A., Koppel R.* Pulse oximetry: fundamentals and technology update. *Medical devices* (*Auckl)*. 2014; 7: 231–239. DOI: 10.2147/MDER.S47319. PMID: 25031547.
3. *Batchelder, P.B., Raley, D. M.* Maximizing the laboratory setting for testing devices and understanding statistical output in pulse oximetry. *Anesth Analg*. 2007; 105 (6 Suppl.): S85–S94. DOI: 10.1213/01.ane.0000268495.35207.ab. PMID: 18048904.
4. *Mannheimer P.D.* The physio-optics of pulse oximetry, numerical modeling and clinical experience. Doctoral Thesis. University of Luebeck: Luebeck, Germany. 2003
5. *Hay W.W. Jr, Rodden D.J., Collins S.M., Melara D.L., Hale K.A., Fashaw L.M.* Reliability of conventional and new pulse oximetry in neonatal patients. *J Perinatol*. 2002; 22 (5): 360–366. DOI: 10.1038/sj.jp.7210740. PMID: 12082469.
6. *Barker S.J.* «Motion-resistant» pulse oximetry: a comparison of new and old models. *Anesth Analg*. 2002; 95 (4): 967–972. DOI: 10.1097/00000539-200210000-00033. PMID: 12351278.
7. *Baquero H., Alviz R., Castillo A., Neira F., Sola A.* Avoiding hyperoxemia during neonatal resuscitation: time to response of different SpO_2monitors. *Acta Paediatr*. 2011; 100 (4): 515–518. DOI: 10.1111/j.1651-2227.2010.02097.x. PMID: 21091987.
8. *Giuliano K.K., Bilkovski R.N., Beard J., Lamminmaki S.* Comparative analysis of signal accuracy of three SpO_2 monitors during motion and low perfusion conditions. *J Clin Monit Comput*. 2023; 37 (6): 1451–1461. DOI: 10.1007/s10877-023-01029-x. PMID: 37266709.
9. *Louie A., Feiner J.R., Bickler P.E., Rhodes L., Bernstein M., Lucero J.* Four types of pulse oximeters accurately detect hypoxia during low perfusion and motion. *Anesthesiology*. 2018; 128 (3): 520–530. DOI: 10.1097/ALN.0000000000002002. PMID: 29200008.
10. *Болиева, М.В.* Проблема импортозамещения медицинского оборудования и его расходных материалов для проведения функциональных методов исследования в кардиологии. *Интернаука*. 2022; 46–5 (269): 56–57. *Bolieva, M.V.* The problem of import substitution of medical equipment and its consumables for carrying out functional research methods in cardiology. *Interscience=Internauka*. 2022; 46–5 (269): 56–57. (in Russ.). EDN SPOUHQ.
11. *Багаева Д.А., Мацаева Р.А.* Проблема импортозамещения в здравоохранении в условиях внешних ограничений. *Студенческий вестник*. 2023; 24 (263): 48–50. *Bagaeva D.A., Matsaeva R.A.* The problem of import substitution in healthcare under conditions of external restrictions. *Student Bulletin = Studencheskiy Vestnik*. 2023; 24 (263): 48–50. (in Russ.). EDN VVFGAR.
12. *Mariani G., Dik P.B., Ezquer A., Aguirre A., Esteban M.L., Perez C., Jonusas S.F., et al.* Preductal and post-ductal O2 saturation in healthy term neonates after birth. *J Pediatr*. 2007; 150 (4): 418–421. DOI: 10.1016/j.jpeds.2006.12.015. PMID: 17382123.
13. Методическое письмо «Реанимация и стабилизация состояния новорожденных детей в родильном зале» от 04.03.2020. Methodical instructions «Resuscitation and stabilization of newborns in the delivery room» dated 03/04/2020. (in Russ.). https://neonatology.pro/wp-content/uploads/ 2020/03/letter_resuscitation_newborn_delivery_2020.pdf.
14. *Карпова А.Л., Спивак Е.М., Пыханцева А.Н., Бокерия Е.Л., Карпов Н.Ю., Кондакова Н.Н., Третьякова Л.Н.* Пульсоксиметрия как метод раннего неонатального скрининга на наличие критических пороков сердца у детей. *Неонатология: новости, мнения, обучение*. 2015; 4: 68–72. *Karpova A.L., Spivak E.M., Pykhantseva A.N., Bokeria E.L., Karpov N.Yu., Kondakova N.N., Tretyakova L.N.* Pulse oximetry as a method of early neonatal screening for critical heart defects in children. *Neonatology: News, Opinions, Training= Neonatologiya: Novosti, Mneniya, Obucheniye*. 2015; 4: 68–72. (in Russ.).

15. *Janjua D., Singh J., Agrawal A.* Pulse oximetry as a screening test for congenital heart disease in newborns. *J Mother Child*. 2022; 26 (1): 1–9. DOI: 10.34763/jmotherandchild.20222601.d-21-00033. PMID: 35853444.

16. *Desai K., Taksande A., Meshram R.J.* Second-degree burns in neonates: a rare case report of saturation probe injury in neonates. *Cureus*. 2023; 15 (10): e47761. DOI: 10.7759/cureus.47761. PMID: 38022296.

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