# Dynamic Light Scattering

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# Dynamic Light Scattering: A New Noninvasive Technology for Neonatal Heart Rate Monitoring

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**Keywords**
Noninvasive measurement · Dynamic light scattering · Neonate · Heart rate · Sensor

**Abstract**
***Background:*** Heart rate (HR) detection in premature infants using electrocardiography (ECG) is challenging due to a low signal amplitude and the fragility of the premature skin. Recently, the dynamic light scattering (DLS) technique has been miniaturized, allowing noninvasive HR measurements with a single sensor. ***Objective:*** The aim was to determine the accuracy of DLS for HR measurement in infants, compared to ECG-derived HR. ***Methods:*** Stable infants with a gestational age of ≥26 weeks, monitored with ECG, were eligible for inclusion. HR was measured with the DLS sensor at 5 different sites for 15 min each. We recorded every 10th second of the DLS-derived HR and the DLS signal-to-noise ratio (SNR), and the ECG-derived HR was extracted for analysis. Patients were randomly divided into 2 groups. In the first group, the optimal SNR cut-off value was determined and then applied to the second group to assess agreement. ***Results:*** HR measurements from 31 infants were analyzed. ECG-DLS paired data points were collected at the forehead, an upper extremity, the thorax, a lower extremity, and the abdomen. When applying the international accuracy standard for HR detection, DLS accuracy in the first group ($n = 15$) was optimal at the forehead (SNR cut-off 1.66). Application of this cut-off to the second group ($n = 16$) showed good agreement between DLS-derived HR and ECG-derived HR (bias –0.73 bpm; 95% limits of agreement –15.46 and 14.00 bpm) at the forehead with approximately 80% (i.e., 1,066/1,310) of all data pairs remaining. ***Conclusion:*** The investigated DLS sensor was sensitive to movement, overall providing less accurate HR measurements than ECG and pulse oximetry. In this study population, specific measurement sites provided excellent signal quality and good agreement with ECG-derived HR.



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## Introduction

Premature infants are known to experience frequent episodes of bradycardia and apnea [1]. Drops in heart rate (HR) cause a potentially harmful decrease in cardiac output and related hypoxia, requiring timely intervention [2]. To prevent serious complications, adequate and accurate monitoring is mandatory. In infants, HR is closely correlated to cardiac output because their physiology permits only limited stroke volume variation [3], emphasizing the importance of neonatal HR monitoring.

Electrocardiography (ECG), the current gold standard, and pulse oximetry are widely used for noninvasive HR monitoring in the neonatal intensive care unit (NICU). However, both technologies have their limitations. Movement and the small size of the infant, together with a low or small signal amplitude, electrical interference, and the need for limiting the number of adhesives applied to the infant to prevent skin lesions [4–9], offer opportunities for new technologies [10].

Recently, a new miniaturized sensor has been developed, allowing noninvasive monitoring of hemodynamic parameters through dynamic light scattering (DLS). Hemoglobin motion is detected with a laser diode which emits a narrow light beam. Light scatters off moving hemoglobin, creating a time-varying speckle pattern. The speckle pattern is analyzed in real time and provides information about, for example, the speed and size of hemoglobin particles, and translates this to a pulsatile flow waveform. This enables the DLS technique to measure multiple hemodynamic parameters such as HR and, potentially, blood flow. The DLS HR is calculated from the spectrum analysis of the velocity wave. In previous studies, various DLS parameters were evaluated in animals and adult patients [11–14]. This is the first study to evaluate the potential of HR detection with DLS. As the signal quality of the DLS technique depends entirely on hemoglobin motion, the pulsatile signal is high even in small premature infants. Furthermore, DLS is an optical measurement technique, minimizing the effects of electrical interference. This study aimed to assess the potential of DLS for HR detection in infants, by evaluating the signal quality of the DLS measurements and determining agreement with ECG.

## Materials and Methods

*Study Setup*

This prospective observational cohort study was conducted at a level III NICU at Erasmus MC - Sophia Children's Hospital, Rotterdam, The Netherlands.

*Study Population*

Stable infants with a gestational age (GA) of ≥26 weeks, monitored with ECG and pulse oximetry in the NICU, were eligible for inclusion. Infants with skin disorders, for which the double-sided skin adhesives used (LEA Medizintechnik GmbH, Giessen, Germany) were contraindicated, were excluded. A stable condition was defined as the absence of sepsis, fever, severe desaturation, severe apnea, or severe incidents during nursing and feeding. Patients' characteristics at birth and during the measurement period were documented. Patients were randomly divided into 2 groups. In the first group, the optimal cut-off for signal quality was calculated based on the norm for accuracy of HR detection. This cut-off was applied to the second group to compare agreement of DLS with ECG.

*Equipment*

Dynamic Light Scattering

Hemodynamic parameters were measured with an mDLS™ sensor (Elfi-Tech Ltd., Rehovot, Israel) which was connected to a computer for data collection and real-time display. The sensor contains a class I, continuous wave, vertical-cavity-surface-emitting laser (VCSEL, wavelength 852.4 ± 2 nm, and peak energy 0.85 mW) and an optoelectronic detection system (Fig. 1a). No real-time (interbeat) analysis or averaging was applied. HR was measured at 5 different sites with the mDLS™ sensor, for 15 min each. Measurements were performed at the forehead, upper and lower extremities, thorax, and abdomen, in a random order. The measured signal-to-noise ratio (SNR) parameter indicated the signal quality. A Biliband® (Natus Medical Inc., San Carlos, CA, USA) was used to protect the neonatal retina from laser exposure.

ECG and Pulse Oximetry

As part of standard care monitoring, ECG (Dräger M540, Dräger Medical GmbH, Lübeck, Germany) and pulse oximetry (Masimo SET Radical pulse oximeter, Masimo Corp., Irvine, CA, USA; POX-S) were available, with an averaging interval of 10 and 12 s, respectively. An additional pulse oximeter (Masimo SET Radical-7; POX-A) was attached to the infant during the measurement period and acquired HR data with an averaging interval of 2 s at normal sensitivity. Based on the location of the POX-S, the POX-A was placed such that both an upper and lower extremity were provided with pulse oximetry for assessing the pulsatile signal.

*Data Logging*

Vital parameters monitored as standard of care, as well as all data from all study devices, were logged at a rate of 1 Hz. The logged parameters included ECG-derived HR, pulse oximetry parameters, DLS-derived HR, and DLS SNR.

*Devices and Software*

Measurements were performed using the mDLS™ sensor, software v3.81, and the data collection system PC GUI v1.0.9.5 (Elfi-Tech Ltd., Rehovot, Israel). The Dräger Infinity M540 monitor had software vVG3.

*Statistical Analyses*

Patient characteristics are presented as median (interquartile range [IQR]) or *n* (%). Significance of differences between the 2 groups was tested with the Mann-Whitney U test for continuous data and Fisher's exact test for categorical variables. Results were considered significant with a two-sided $p$ value <0.05.

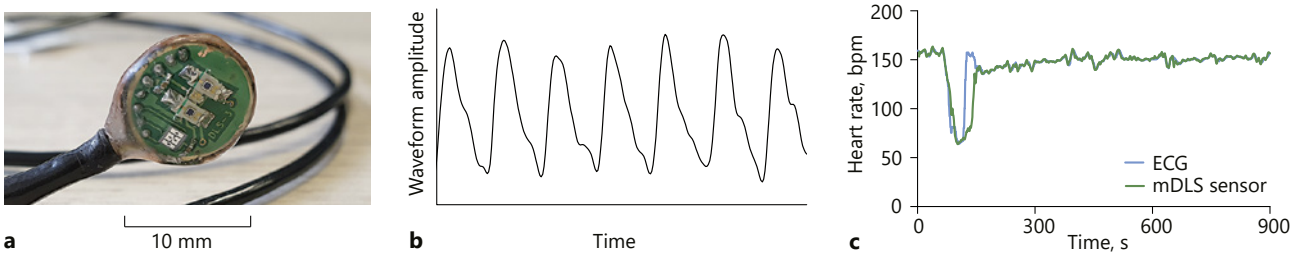



**Fig. 1. a** mDLS™ sensor. **b** Waveform example of the DLS measurement, illustrating the sphygmogram in an infant. **c** An example of the measured heart rate trend of ECG and DLS at the abdomen.

**Table 1.** Patient characteristics of all infants for each group at birth and at the time of measurement

| | Group 1 | Group 2 | *p* value |
|---|---|---|---|
| *N* | 15 | 16 | |
| *At birth* | | | |
| GA, weeks | 28[6/7] (27[1/7]–31[5/7]) | 30[4/7] (28[4/7]–31[5/7]) | 0.44 |
| Birth weight, g | 1,190 (942–2,080) | 1,330 (1,040–1,577.5) | 0.92 |
| SGA | 5 (33.3) | 8 (50.0) | 0.57 |
| Male gender | 10 (66.7) | 5 (31.2) | 0.11 |
| Cesarean section | 8 (53.3) | 12 (75.0) | 0.38 |
| APGAR score at 1 min | 6 (5–8) | 6.5 (3.75–8) | 0.69 |
| APGAR score at 5 min | 8 (7–8.5) | 8.5 (7–9) | 0.40 |
| Umbilical cord pH | 7.31 (7.26–7.35) | 7.29 (7.23–7.31) | 0.22 |
| Multiples | 4 (26.7) | 7 (43.8) | 0.54 |
| *At the time of measurement* | | | |
| Time since birth, days | 8 (6–18) | 5 (3–15) | 0.64 |
| Weight, g | 1,720 (1,160–1,930) | 1,392 (1,164–1,628) | 0.51 |
| Admission survival | 14 (93.3) | 15 (93.8) | >0.99 |
| Ventilation | | | 0.45 |
| Noninvasive | 13 (86.7) | 11 (68.8) | |
| None | 2 (13.3) | 5 (31.2) | |
| Initial number of DLS-ECG data pairs | 1,260 | 1,344 | |

Values are expressed as median (IQR) or *n* (%), unless otherwise indicated. The Mann-Whitney U test for continuous variables and Fisher's exact test for categorical variables were used to test significance with a two-sided *p* value <0.05. GA, gestational age; SGA, small for gestational age; DLS, dynamic light scattering; ECG, electrocardiogram.

The first minute of measurement was excluded because of sensor stabilization time and potential initial unrest of the infant. In order to adjust for the time-averaged ECG data, only every 10th second of the DLS-derived HR, the DLS SNR, and the pulse oximetry parameters was included for analysis.

In the first group, accuracy of HR measured with the mDLS™ sensor was evaluated for compliance to the IEC 60601-2-27:2011 standard [15], with the ECG value as a reference. The percentage deviation of DLS relative to the ECG reference value was calculated and the measurement was classified as accurate or inaccurate based on the norm criteria for accuracy. The sensitivity and specificity of the SNR for selecting norm-compliant DLS HR measurements were determined with an area under the receiver operating characteristic (ROC) curve according to the method of Obuchowski [16], adjusting for clustered data. The optimal SNR at each measurement location was calculated with Youden's Index (*J*) [17]. To visualize the effect of the signal quality or SNR on agreement between DLS and ECG, Bland-Altman analysis of agreement, corrected for repeated measurements, was performed [18]. Agreement was assessed by calculating the mean difference (bias) between DLS-derived HR and ECG-derived HR, with ±1.96 SD around the mean difference as upper and lower limits of agreement (LoA). Bias, upper LoA, and lower LoA were calculated and plotted (A-B plot) for every SNR value in steps of 0.01 at all measurement locations.

**Table 2.** Agreement between heart rate measured with DLS and POX with ECG

| | DLS-ECG | | | | |
|---|---|---|---|---|---|
| SNR filter | No | | Yes | | |
| Location | bias (lower LoA – upper LoA), bpm | data pairs, $n$[a] | bias (lower LoA – upper LoA), bpm | data pairs, $n$[a] | SNR cut-off value, $J$ |
| Forehead | −4.61 (−40.14 to 30.93) | 1,310 | −0.73 (−15.46 to 14.00) | 1,066 | 1.66 |
| Upper extremity | −9.26 (−60.64 to 42.13) | 1,322 | −1.26 (−21.70 to 19.19) | 1,009 | 2.25 |
| Thorax | −12.50 (−71.18 to 46.17) | 1,307 | −2.62 (−36.39 to 31.15) | 788 | 4.29 |
| Lower extremity | −18.99 (−88.85 to 50.86) | 1,312 | −1.82 (−27.32 to 23.68) | 693 | 3.63 |
| Abdomen | −37.55 (−116.34 to 41.25) | 1,230 | −16.25 (−78.73 to 46.23) | 646 | 0.81 |
| | POX-ECG | | Data pairs upper/lower extremity, $n$ | | |
| Standard of care POX | 0.18 (−6.14 to 6.51) | 6,476 | 414/6,062 | | |
| Additional POX | −0.06 (−5.23 to 5.36) | 6,467 | 6,062/414 | | |

DLS, dynamic light scattering; ECG, electrocardiogram; POX, pulse oximetry; SNR, signal-to-noise ratio; LoA, limit of agreement; bpm, beats per minute.

[a] After exclusion of incomplete data pairs (initially $n$ = 1,344 for DLS-ECG and $n$ = 6,720 for POX-ECG)

The optimal SNR was applied to the second dataset to determine agreement between DLS and ECG at every location. Agreement between HR measured with both pulse oximetry and ECG was also analyzed. Incomplete data pairs were excluded from the analyses. Data pairs were excluded when non-DLS measurements failed. Data were analyzed in *R* v3.5.3 (The *R* Foundation for Statistical Computing, Vienna, Austria).

## Results

A total of 34 infants were included between October 2017 and August 2018. Three patients were excluded from the analyses: 1 case of data logging failure and 2 cases with a postinclusion diagnosis of sepsis. Infants were randomly divided into 2 groups, with 15 infants in group 1 and 16 infants in group 2. There were no significant differences in basic patient characteristics between the 2 groups at birth and at the time of measurement (Table 1). Groups 1 and 2 consisted of 1,260 and 1,344 initial DLS and ECG HR data pairs per measurement site, respectively, after which incomplete data pairs were removed. At every measurement site, the mDLS™ sensor (Fig. 1a) was able to provide a signal in which characteristics of an arterial blood flow waveform could be identified (Fig. 1b). The DLS HR measurements were able to follow the trend of ECG during rapid HR changes (Fig. 1c).

The discriminative ability of the DLS SNR varied greatly between measurement sites. The highest ROC AUC was 0.94 ($n$ = 1,180, 95% CI 0.90–0.99) when DLS HR was measured at the forehead, with a sensitivity and specificity of 87 and 90%, respectively (Fig. 2). At this measurement site, the optimal cut-off value ($J$) for the DLS SNR was 1.66 (Table 2). Measurements performed

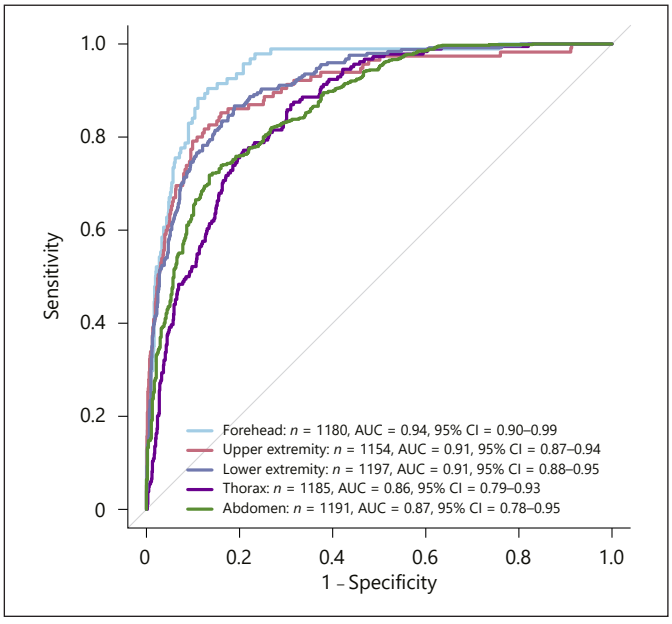



**Fig. 2.** Receiver operating characteristic curves for detection of DLS heart rate signal using the DLS signal-to-noise ratio with the mDLS™ sensor at all measurement sites. Number of data pairs ($n$) after exclusion of incomplete data pairs (initially $n$ = 1,260), area under the curve (AUC) with the 95% CI are presented.

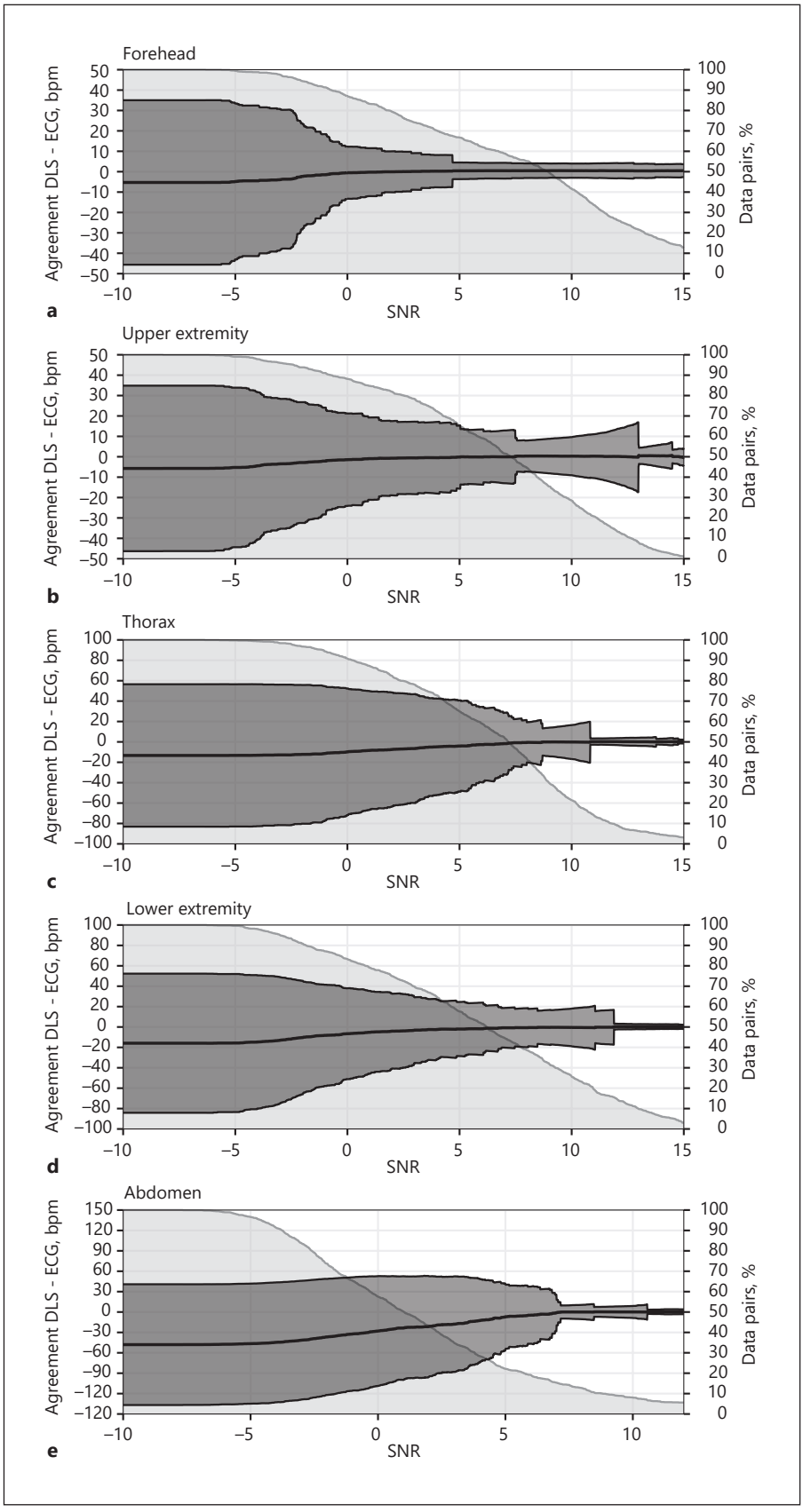
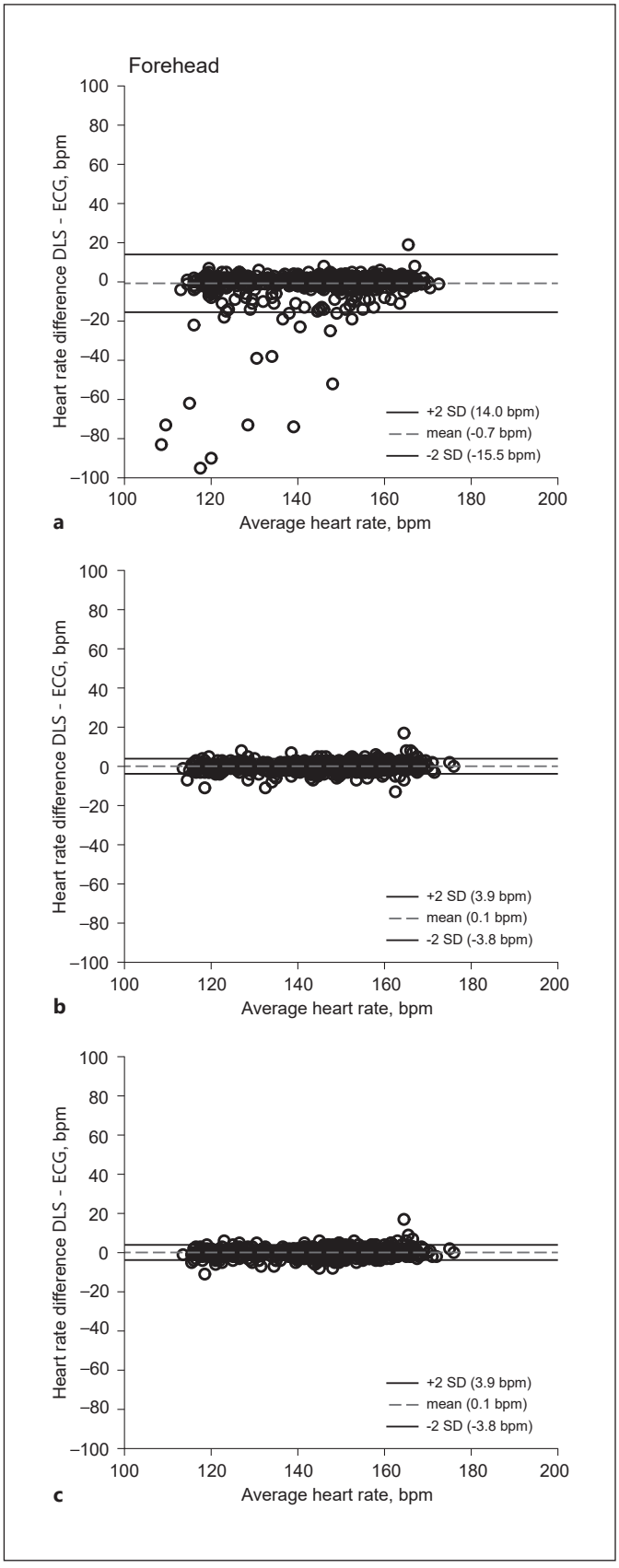



**Fig. 3.** Agreement (A-B plot) between heart rate measurements obtained with the mDLS™ sensor and ECG, plotted for every measured DLS SNR value at the forehead (**a**), an upper extremity (**b**), the thorax (**c**), a lower extremity (**d**), and the abdomen (**e**). Agreement is presented as bias with upper and lower limits of agreement (dark grey). The percentage of remaining data pairs (DLS-ECG) used for the Bland-Altman analyses are illustrated against the SNR (light grey).




at the thorax and abdomen had the lowest AUC (Fig. 2). Moreover, respiratory motion created waveforms that were detected as heartbeats, resulting in high DLS SNR values at incorrectly measured DLS HR values. The Bland-Altman analysis performed for every DLS SNR value showed improvement of the agreement between DLS and ECG as the SNR increased, together with an extreme decrease in the remaining data pairs (DLS-ECG; Fig. 3).

After application of the SNR cut-off value in the second group, agreement between HR measured with DLS and ECG improved significantly for each site (Table 2). When HR measurements were obtained at the forehead, agreement (bias [lower LoA – upper LoA]) improved from –4.61 (–40.14 to 30.93) to –0.73 (–15.46 to 14.00) bpm (Fig. 4) while retaining approximately 81% (i.e., 1,066/1,310) of all data pairs (Table 2). HR measured with the POX-S and POX-A during this period showed a bias (lower LoA – upper LoA) of 0.1 (–3.8 to 3.9) bpm in both when compared with ECG HR measurements (Fig. 4). Agreement at other sites also improved markedly, but the LoAs remained wide even after exclusion of approximately half of all the included data pairs (Table 2). The overall agreement between HR measured with the 2 pulse oximeters and ECG was comparable to or better than in previous studies (Table 2) [19–21].

## Discussion

This study is the first to evaluate the performance of a miniaturized DLS sensor for HR monitoring, showing good agreement with ECG-derived HR when not distorted by movement. DLS technology has several potential advantages over current neonatal HR monitoring. Sensors with this technology can be smaller than any current HR sensor, and also have the potential for measuring other hemodynamic parameters such as blood flow. The key strength of DLS is, however, the excellent signal strength due to the exclusive detection of hemoglobin motion, provided that breathing and movement artifacts can be adequately filtered out.

**Fig. 4.** Bland-Altman plots (A-B plot) of the heart rate (HR) difference against the average HR during measurements performed at the forehead. **a** Agreement between DLS and ECG HR of data pairs with a DLS SNR above the calculated cut-off value (1.66). **b** Agreement between the standard of care POX (POX-S) and ECG HR. **c** Agreement between the additional POX (POX-A) and ECG HR.

Accurate detection of HR depends on both a good signal quality and the adequate filtering of artifacts. Movement patterns in infants are particularly difficult to filter out compared to in adults. Movements of the extremities are abrupt, unpredictable, and of short duration, leading to a loss of HR detection. In addition, accuracy was strongly impaired when measuring at the thorax and abdomen due to respiration. Distortion of the DLS signal resulted in the registration of incorrect frequencies, amplitudes, and breathing-induced fluctuations (baseline wander), erroneously detecting the respiratory waveforms as heartbeats. As a consequence, falsely low HRs were measured with a high SNR and were therefore considered to be good-quality measurements. The most important resolution to this problem involves band-pass filtering of HRs specific to the neonatal population. In addition, the narrow light beam creates a small measurement site, amplifying the influence of movement and requiring good skin adhesion. The convex sensor surface, in combination with the applied skin adhesive, allowed rotational movement relative to the skin, influencing the accuracy of the measurements. This can potentially be resolved by a flat sensor surface. For clinical practice, the substantial loss of data due to signal distortion is the largest concern, resulting in the absence of HR measurements during an unacceptable portion of the measurement time.

Despite the main limitation of this study, the small size of the mDLS™ sensor and its noninvasiveness demonstrated excellent usability. However, regular signal failure currently provides insufficient HR information for a comparison of clinical use to ECG. Furthermore, the performance in extremely premature infants and during circulatory deterioration could not be derived from the findings in the stable patients in this study. Future studies should investigate the use of the DLS technology during more dynamic settings, such as resuscitation. The setup of this study analysis did not evaluate accuracy during bradycardia, which is of particular importance for infants. Although the DLS class I laser should be safe for the retina, this has not been proven in premature infants. In addition, the blink reflex is often absent in infants, allowing for longer exposure. Until its safety is proven, its clinical use requires the implementation of a laser power down when detached from the skin.

With the exception of the DLS signal, the output of all clinical devices (for ECG and pulse oximetry) is a HR which is averaged over several seconds. Although DLS measurements adequately followed the general HR trend, the absence of averaging might explain the earlier detection of changes in HR when compared to the ECG-derived HR. Agreement between the pulse oximeters and ECG was better than that described in the literature so far [19–21]. This might be explained by the use of precisely time-synchronized computers. Furthermore, analyses were corrected for repeated measures, resulting in an increase of the SD. When applying the demands for accuracy for clinical use on DLS HR measurements, the difficulty lies within the application of the norms for clinical HR detection, which are aimed at ECG accuracy and reliability [15]. Although accuracy could be determined as a deviation from the reference value, the norms do not specify the percentage of time in which the HR should be accurately detected. With the necessary improvements, future iterations of DLS technology will be able to provide specific advantages over currently used techniques like ECG and pulse oximetry, because of the possibility of measuring HR, blood flow, and cardiac output with a single sensor, and even contact-free up to a distance of several millimeters from the skin. Skin pigmentation is unlikely to affect the detection of hemoglobin motion as DLS depends on the scattering of light instead of light absorption.

As previous studies reported, DLS has the potential to measure various hemodynamic parameters [14]. Blood flow and cardiac output are currently unavailable parameters in neonatal intensive care but can be valuable for the assessment of infants due to infant physiology. As DLS has the potential to measure blood flow in patients of all ages, more research is required to investigate DLS blood flow measurements. Novel applications in the neonatal population could include the early detection of hypotension, the detection of microcirculatory impairment, or the replacement of functional echocardiography. The absence of an available clinical gold standard for flow measurement, however, complicates the investigation of the DLS technology for flow measurements in future studies.

## Conclusion

DLS is a new and promising miniaturized technique for noninvasive HR detection in infants, showing good agreement with ECG-derived HR when measured at the forehead under a stable condition of the infant. Movement, however, has a notable influence on accuracy. Overall, the accuracy of HR detection with DLS is currently inferior to ECG and pulse oximetry. In addition, DLS has the potential for continuously measuring other hemodynamic parameters such as blood flow, an important yet currently unavailable parameter in neonatal care.

## Acknowledgement

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## Statement of Ethics

This prospective observational cohort study was approved by the Medical Ethics Committee of Erasmus Medical Center (MEC-2017-059). Parental consent was provided both verbally and written before inclusion in the study.

## Disclosure Statement

The authors have no conflicts of interest to declare.

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## Author Contributions

N.H.G.-P. enrolled patients and performed the mDLS measurements, conducted data analyses, and had the lead in manuscript writing. T.E. supported patient enrolment and participated in data analyses. T.G.G. contributed to technical documentation and the study setup. R.C.J.J. participated in the study setup. I.K.M.R. initiated the study and provided clinical input throughout the study. W.W. performed the study and analyses design, ethics board submission, technical documentation, and manuscript writing.

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