













ORIGINAL

Non-Invasive Blood Density Measurement using Photoplethysmography Technique

Medición No Invasiva de la Densidad Sanguínea mediante la técnica de fotoplethysmografía

Theo Marcelo Galindo Chicaiza¹  , Luz María Tobar Subía Contenido¹  , Gámez Aparicio Brizeida Nohemí¹  , Marco Antonio Ciaccia Sortino¹  , Cosme Damián Mejía Echeverría¹  , Diego Luis Ortiz Morales¹  

¹Universidad Técnica Del Norte, Facultad de Ingeniería en Ciencias Aplicadas. Ibarra, Ecuador.

Cite as: Galindo Chicaiza TM, Tobar Subía Contenido LM, Gámez Aparicio BN, Ciaccia Sortino MA, Mejía Echeverría CD, Ortiz Morales DL. Non-Invasive Blood Density Measurement using Photoplethysmography Technique. Data and Metadata. 2025; 4:819. <https://doi.org/10.56294/dm2025819>

Submitted: 08-07-2025

Revised: 05-09-2025

Accepted: 03-12-2025

Published: 04-12-2025

Editor: Dr. Adrián Alejandro Vitón Castillo 

Corresponding Author: Luz María Tobar Subía Contenido 

ABSTRACT

Introduction: blood density measurement is a key diagnostic indicator for assessing hematological and cardiovascular conditions. Conventional methods require blood extraction and laboratory equipment. In this context, a non-invasive biomedical device based on photoplethysmography (PPG) and the Beer-Lambert law was developed to estimate blood density through optical parameters.

Method: a prototype was designed using a microcontroller, an optical sensor, and an OLED display. The acquired signals were digitally filtered through FIR and IIR algorithms to separate pulsatile and non-pulsatile components. Twenty-one volunteers were recruited, and sixteen valid recordings remained after artifact removal. Laboratory reference values were compared using linear regression and Bland-Altman analysis to evaluate concordance between clinical and device-derived measurements.

Results: the device achieved an average error of 2,0 % for blood-density estimation, 6,06 % for hematocrit, and 7,01 % for erythrocyte count. The limits of agreement remained within clinically acceptable ranges, with a slight underestimation bias at higher density values. Main limitations were related to the restricted spectral range of the red and infrared LEDs and to physiological variables such as peripheral perfusion and involuntary movements.

Conclusions: the proposed system demonstrated accuracy and stability for non-invasive blood-density estimation, validating PPG as a portable, low-cost diagnostic tool. Future improvements should include a broader calibration dataset and multispectral light sources with higher sensitivity to enhance linearity and dynamic range.

Keywords: Blood Density; Photoplethysmography; Beer-Lambert Law; Non-Invasive Biomedical Device.

RESUMEN

Introducción: la medición de la densidad sanguínea constituye un indicador esencial para evaluar el estado hematológico y cardiovascular. Los métodos convencionales requieren extracción de sangre y equipamiento de laboratorio. En este contexto, se desarrolló un dispositivo biomédico no invasivo basado en fotoplethysmografía (PPG) y la ley de Beer-Lambert, orientado a estimar la densidad sanguínea mediante parámetros ópticos.

Método: se diseñó un prototipo con un microcontrolador, un sensor óptico y una pantalla OLED. Las señales captadas fueron filtradas digitalmente mediante algoritmos FIR e IIR para separar componentes pulsátiles y no pulsátiles. Se reclutaron 21 voluntarios (16 registros válidos). Los valores obtenidos se compararon con datos de laboratorio, empleando regresión lineal y análisis estadístico de Bland-Altman para validar la concordancia.

Resultados: el dispositivo presentó un error promedio de 2,0 % en densidad sanguínea, 6,06 % en hematocrito y 7,01 % en conteo eritrocitario. Los límites de concordancia se mantuvieron dentro de rangos clínicamente aceptables, evidenciando una tendencia leve a la subestimación en valores altos. Las principales limitaciones se relacionaron con el rango espectral restringido de los diodos emisores y la influencia de la perfusión periférica.

Conclusiones: el sistema propuesto demostró precisión y estabilidad para la estimación no invasiva de la densidad sanguínea, validando el uso de la PPG como herramienta diagnóstica portátil y de bajo costo. Se recomienda ampliar la muestra de calibración e incorporar fuentes ópticas multiespectrales para mejorar la linealidad y el rango dinámico del dispositivo.

Palabras clave: Densidad Sanguínea; Fotoplethismografía; Ley de Beer-Lambert; Dispositivo Biomédico no Invasivo.

INTRODUCTION

Measuring blood density is a fundamental diagnostic tool for assessing a person's health, as it reflects the concentration of red blood cells and other blood components. This parameter acts as a key indicator of blood viscosity and overall functionality, as abnormal levels may be associated with various clinical conditions. For example, a high blood density may suggest dehydration or circulatory disorders, while a low density is often associated with anemia or significant blood loss.

Over time, measurement techniques have evolved from traditional methods, such as the hematocrit procedure—which estimates red blood cell volume by centrifugation—to more advanced technologies such as automated hematology analyzers and portable densitometers. These modern tools enable faster, more accurate quantitative assessments, which are especially valuable in emergencies and remote healthcare settings.⁽¹⁾ Variations in normal blood density levels can aid in diagnosing various diseases. In healthy adults, this value typically ranges from 1,050 to 1,065 g/mL, although it can be influenced by factors such as age, sex, hydration status, and overall health.⁽²⁾ Blood density directly influences the interpretation of hematocrit levels, which is why its measurement is indispensable in clinical diagnosis. A low hematocrit indicates fewer circulating red blood cells, which could be due to overhydration or reduced oxygen-carrying capacity.⁽³⁾ This phenomenon may point to conditions such as anemia, characterized by a significant decrease in the total number of erythrocytes.⁽⁴⁾

On the other hand, abnormally high hematocrit levels—called polycythemia—have been linked to high blood pressure and other cardiovascular risk factors.⁽⁵⁾ Likewise, the relationship between hematocrit and vascular health is particularly relevant, as both low and high levels have been associated with vascular smooth muscle dysfunction. This link underscores the importance of considering both blood density and hematocrit to assess the patient's cardiovascular status comprehensively. Even conditions such as acute blood loss can alter density, affecting the clinical interpretation of hematological values.

In recent years, photoplethysmography (PPG) has evolved from basic clinical applications to advanced physiological monitoring tools, thanks to the integration of optical models and machine learning algorithms that improve the accuracy of hemodynamic parameter estimation.⁽⁶⁾ These innovations have expanded their use in real-time blood density and flow monitoring, both in hospital settings and in portable telemedicine systems.

In this context, recent technological advances have driven the development of portable densitometers, which are emerging as a viable solution for remote healthcare settings. These devices allow rapid testing at the patient's bedside, thereby improving medical care in underserved populations.⁽¹⁾

Non-invasive methods for measuring blood density and hematocrit have gained relevance for their ability to provide accurate readings without blood extraction. According to the patent⁽⁷⁾ a non-invasive technique is described that uses principles such as fluid pressure and volume to assess density. This innovation highlights the potential of blood as a diagnostic fluid and promotes the development of less invasive methods with lower risks and greater patient comfort.

Among these technologies, photoplethysmography (PPG) stands out as an optical technique that measures volumetric variations in blood in tissues, facilitating real-time monitoring of parameters related to blood density. The development of this technique dates back to 1936, when Alrick B. Hertzman first documented a photoplethysmogram using a light source and a photodiode to detect light interactions with tissues.⁽⁸⁾ Since then, its evolution has allowed for greater precision in hemodynamic assessment without the need for invasive techniques.

The integration of these technologies represents a notable advance in non-invasive measurement methods, offering healthcare professionals tools with high diagnostic efficiency and lower clinical risk. In addition, these systems enable large volumes of data to be analyzed to identify predictive patterns, thereby improving the accuracy of assessments and promoting more equitable and accessible medical care globally.

In this context, the present study aims to design and validate a non-invasive device for estimating blood density using optical principles and photoplethysmography (PPG) techniques. To achieve this goal, a measurement system based on Beer-Lambert's law was implemented, which allows light absorption to be related to the optical properties of biological tissue. Subsequently, the device was calibrated using laboratory experimental data to establish reliable quantitative relationships between the recorded optical signals and the actual blood density. Finally, the system was validated through comparative statistical analyses to evaluate the accuracy and consistency of the proposed method relative to reference measurements.

The expected results of this research aim to contribute to the development of safer, more accessible biomedical tools, to consolidate the use of non-invasive optical technologies in clinical monitoring, and to improve the quality of medical care.

METHOD

System design

The device's structure was designed according to technical criteria derived from literature reviews of non-invasive biomedical optical systems,^(9,10) with an emphasis on those based on the principles of photoplethysmography (PPG) and Beer-Lambert's law.

A multi-criteria weighting matrix was applied to select the components, which allowed the optimal configurations to be identified considering variables such as: 1) spectral range of the optical sensor at wavelengths of 660 nm and 880 nm, 2) electrical and digital compatibility with low-power microcontrollers, and 3) compact size of the elements for integration into an ergonomic and portable housing.

This design methodology ensured that the system could capture photometric signals with high fidelity, minimizing optical and electronic noise, and allowing real-time processing of the acquired data.

Implementation

The device was printed in PLA, a polymer designed to reduce optical interference. The system consists of a dual-wavelength optical sensor (660 nm and 880 nm), a microcontroller for signal acquisition, filtering, and digital processing, and an OLED display for viewing results. The algorithm was programmed in C++ and configured for periodic reading and storage of both pulsatile and non-pulsatile signals.

Data acquisition

The device developed was evaluated in twenty-one (21) participants, from whom sixteen (16) valid records were obtained after eliminating artifacts caused by movement or optical interference. During each experimental session, the device signals and the laboratory data for complete blood count were collected simultaneously to enable a direct comparison between the two measurement methods.

The sample was selected using non-probability convenience sampling, considering the availability of volunteers and the controlled experimental conditions. Exclusion criteria were established to ensure the validity and reliability of the measurements: 1) The test subject must not have nail polish on their nails or apply cosmetic products that could interfere with the measurement. 2) The subject must remain at rest with minimal body movement during sampling. 3) The subject must be fasting at the time of measurement to avoid variations in physiological parameters. 4) Subjects with Parkinson's disease were excluded due to the presence of high-frequency involuntary tremors that generate artifacts in the PPG signal. 5) Subjects with low blood pressure or bradycardia were excluded, as these factors may compromise the reliability of the data obtained.

During data acquisition, the test subject remained at rest for at least 5 minutes before the measurement. The contact area was disinfected with isopropyl alcohol to avoid contamination of the sensor and ensure accurate readings. The device was connected to the computer via a serial communication link, and the user placed their finger on the sensor for at least 30 seconds, ensuring that the screen recorded and updated the data at each cardiac cycle. After the set time elapsed, the signals were automatically stored in digital format (.txt and .csv) and encoded with the date and volunteer number for later analysis.

Conventional filters were used to reduce noise during signal processing. However, recent studies have shown that combining FIR and IIR filters with adaptive algorithms or convolutional neural network models can significantly reduce the impact of noise and motion artifacts on PPG signals.⁽⁸⁾ Therefore, future versions of the device could incorporate intelligent processing strategies to improve the signal-to-noise ratio in real clinical conditions.

Statistical analysis

The Bland-Altman method and box plots were used to validate the device's estimated values against clinical values, using key metrics such as upper and lower limits, bias, median, and average.

DEVELOPMENT

To assess whether erythrocyte number responds to optical stimuli, a photoplethysmography (PPG) technique

is used.⁽¹¹⁾ This technique allows the analysis of changes in light absorption through tissues associated with the pulsatile activity of the cardiovascular system.

$$A = -\ln\left(\frac{I_o}{I_a}\right) \quad (1)$$

To improve signal quality and extract relevant information from the PPG signal (figure 1), FIR (Finite Impulse Response) and IIR (Infinite Impulse Response) digital filters are applied. This allows the pulsatile component, which corresponds to arterial blood flow, to be separated from the non-pulsatile component, which contains information on static tissue, ambient light, and motion artifacts. For FIR low-pass filters (order 100, $f_c = 0,5$ Hz) for IDC, and an IIR Butterworth band-pass filter (order 5, 0,4-5 Hz) for IAC.

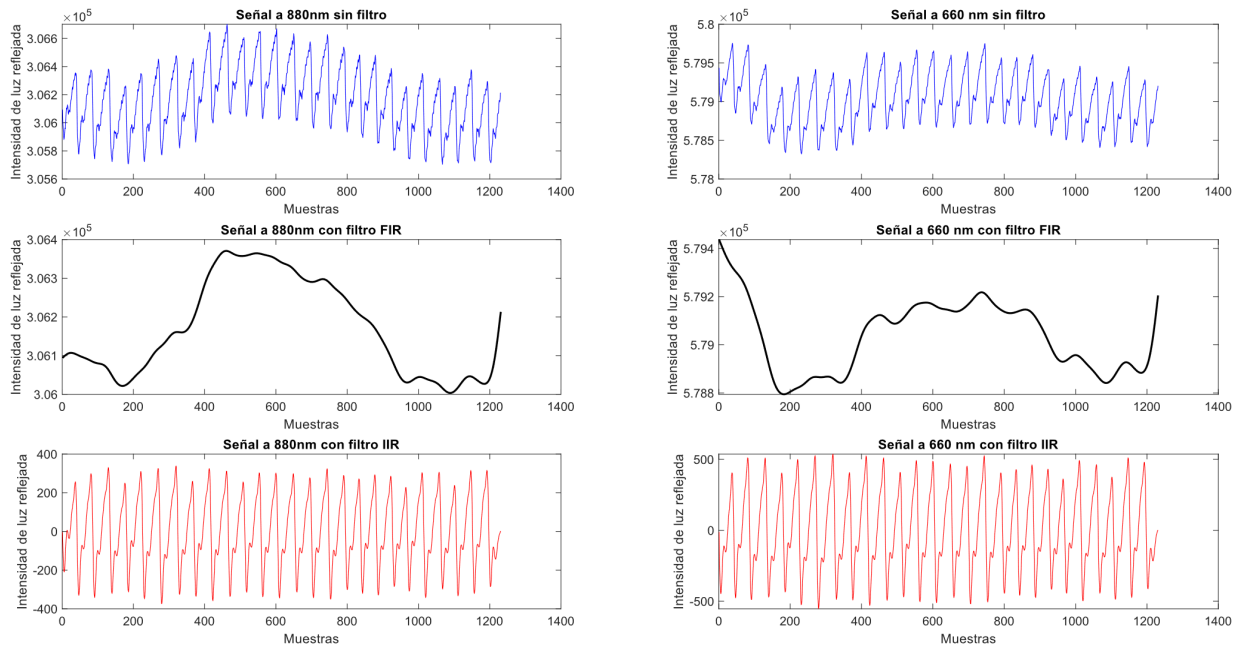


Figure 1. Filtering of red and infrared signals in pulsatile and non-pulsatile

Understanding that the useful signal is the sum of the pulsatile and non-pulsatile signals.

$$S_{TIR} = Sp_{IR} + Snp_{IR} \quad (2)$$

$$S_{TRED} = Sp_{RED} + Snp_{RED} \quad (3)$$

Where: Sp_{IR} is the total signal from the infrared sensor, Sp_{IR} is the total signal from the red sensor, Sp_{IR} is the pulsatile signal from the infrared sensor, Snp_{IR} is the non-pulsatile signal from the infrared sensor, Sp_{RED} is the pulsatile signal from the red sensor, Snp_{RED} is the non-pulsatile signal from the red sensor.

The relative intensity value is needed, not an absolute value, so the incident light intensity value is assumed to be one relative unit, and the transmitted light signal is equivalent to the ratio of pulsed and non-pulsed signals combined.

$$A_{TIR} = -\ln\left(\frac{1}{S_{TIR}}\right) \quad (4)$$

$$A_{TRED} = -\ln\left(\frac{1}{S_{TRED}}\right) \quad (5)$$

Where: A_{TRED} is equivalent to the absorptivity in the 660 nm sensor, and A_{TIR} is equivalent to the absorptivity in the 880 nm sensor. In this study, the Beer-Lambert law model is used, which establishes that light absorption is exponentially related to the concentration of an absorbent and the length of the optical path. Since the specific absorptivity of erythrocytes (molar extinction coefficient) is not accurately tabulated for this type of optical configuration, an empirical calibration is performed, correlating optical intensity measurements with clinical laboratory values, mainly hematocrit and red blood cell count.

$$R_p = \frac{A_{TIR}}{A_{TRED}} \quad (6)$$

Where: R_p equals the ratio of red and infrared signals.

Although the pulsatile signal contains most of the dynamic information related to the heartbeat, the non-pulsatile signal is also included, as it serves as a reference value or baseline absorption level for relative calculations. The pulsatile signal tends to oscillate around zero after centering and normalization, so the sum of the two signals provides a more robust representation of the absorbed optical intensity.

Finally, the intensity ratio between the two spectral channels (red and infrared) is calculated, yielding a relative absorbance value. This relative absorbance correlates with hematological parameters such as erythrocyte count and hematocrit, allowing blood density to be estimated using calibrated models.

$$\text{hematocritos} = a1 \times R + b1 \quad (7)$$

$$\text{hematíes} = a2 \times R + b2 \quad (8)$$

Where: $a1$ is the dependent coefficient of linear regression and is equal to 56,38, $b1$ is the independent coefficient of linear regression and is equal to -60,28, $a2$ is the dependent coefficient of linear regression and is equal to 62,02, $b2$ is the independent coefficient of linear regression and is equal to -66,30. These calibration coefficients were determined by linear regression of the normal hematocrit and red blood cell values corresponding to the red-to-infrared signal ratio.

Calibration with laboratory parameters (hematocrit and erythrocyte count) was used as a reference to obtain the regression coefficients ($a1$, $b1$).

Typical values for plasma and cell densities are used to estimate blood density,⁽¹²⁾ since only information on red blood cells is available, not on white blood cells or platelets.

$$DS = \frac{Hcto \times DC}{100} + \frac{(100 - Hcto) \times DP}{100} \quad (9)$$

Where: SD equals blood density (kg/m³), CD equals cell density (kg/m³), PD equals plasma density (kg/m³), Hct equals hematocrit (%).

RESULTS

Table 1. Laboratory results for red blood cell and hematocrit blood counts, and mathematical estimation of blood density

No.	Red blood cells (millions/mm ³)	Hematocrit (%)	Blood density (kg/m ³)
1	5,05	0,44	1054,5
2	6,22	0,50	1047,8
3	6,11	0,50	1064,7
4	5,89	0,51	1065,9
5	5,79	0,52	1046,1
6	5,81	0,52	1048,0
7	5,62	0,50	1050,3
8	5,28	0,47	1048,5
9	5,48	0,46	1064,4
10	5,61	0,48	1046,5
11	4,87	0,37	1064,6
12	5,62	0,50	1050,3
13	6,40	0,52	1068,5
14	5,93	0,52	1059,5
15	4,98	0,40	1046,6
16	4,74	0,42	1048,1
Average	5,59	0,48	1054,65

The laboratory values for red blood cells, hematocrit, and estimated blood density using the Philips-Van Slyke ratio are presented in table 1.

The values recorded by the device include average measurements in the infrared (IR) and red (RED) channels, the optical absorption ratio, and parameters derived from red blood cells, hematocrit, and blood density. Table 2 shows the results obtained and their overall averages.

Table 2. Laboratory results for red blood cell and hematocrit blood biometrics, mathematical estimation of blood density

No.	IR value	RED value	Ratio parameter	Red blood cells (Millions/mm ³)	Hematocrit (%)	Blood density (kg/m ³)
1	301 890	582 420	1,93	536 454	0,49	1063,8
2	303 820	580 620	1,86	4 888 430	0,44	1052,1
3	304 390	582 330	1,86	4 931 490	0,45	1052,9
4	307 920	587 730	1,93	5 364 880	0,49	1060,2
5	309 180	586 760	2,00	5 777 000	0,53	1069,2
6	301 610	579 750	1,86	5 925 400	0,55	1053,2
7	310 810	589 860	1,88	5 350 450	0,46	1058,5
8	305 780	580 670	1,81	5 612 480	0,51	1048,0
9	307 960	587 450	1,90	5 142 470	0,47	1056,3
10	303 180	582 840	1,90	5 145 730	0,47	1056,2
11	316 170	589 840	1,87	4 963 760	0,40	1053,2
12	308 420	598 060	1,90	5 123 170	0,47	1056,3
13	308 090	583 750	1,90	5 876 550	0,47	1057,7
14	306 740	585 100	1,82	5 682 220	0,51	1050,0
15	308 280	585 260	1,81	4 822 610	0,42	1048,7
16	302 220	589 640	1,82	4 630 440	0,42	1049,6
Average	306 654	549 449	1,88	5 287 601	0,47	1055,4

Table 3. Average errors between device values and clinical laboratory values in blood biometry

No	Average error between red blood cells from the device and red blood cells from the laboratory	Average error between device red hematocrit and laboratory hematocrit	Average error between blood density estimates
1	6,23	10,81	1,42
2	21,41	11,41	3,05
3	19,29	10,36	3,38
4	8,92	4,39	0,15
5	0,22	0,98	2,92
6	1,99	5,31	1,19
7	4,80	8,20	1,50
8	6,30	8,51	0,71
9	6,16	1,61	1,27
10	8,28	2,57	0,55
11	1,93	8,42	2,79
12	8,84	6,87	1,29
13	8,18	9,52	3,61
14	4,18	2,79	0,22
15	3,16	5,03	3,13
16	2,31	0,20	0,98
Average	7,01	6,06	1,76

Table 3 summarizes the average errors between the values obtained by the device and those obtained in the laboratory. The average errors were 7,01 % for red blood cells, 6,06 % for hematocrit, and 1,76 % for blood density.

The Bland-Altman analysis for hematocrit (figure 2) shows that the laboratory tests exhibit greater dispersion than the device measurements, suggesting less variability in electronic measurements. This stability is attributed to the linear regression adjustment used in calibration, which generates more consistent results within typical ranges.

The median of the laboratory data is slightly higher than that of the device, indicating an underestimation bias. To correct this, it is recommended to recalibrate the device by expanding the data range and adjusting the linear regression coefficients.⁽¹³⁾

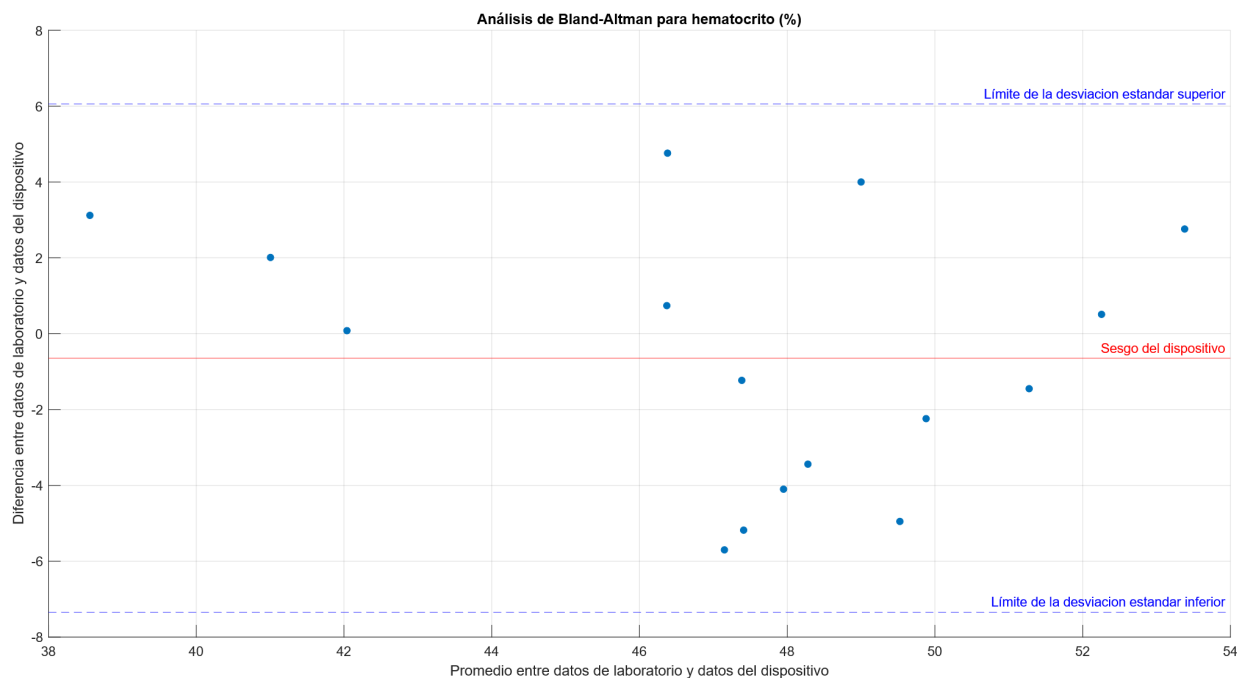


Figure 2. Bland-Altman analysis for hematocrit

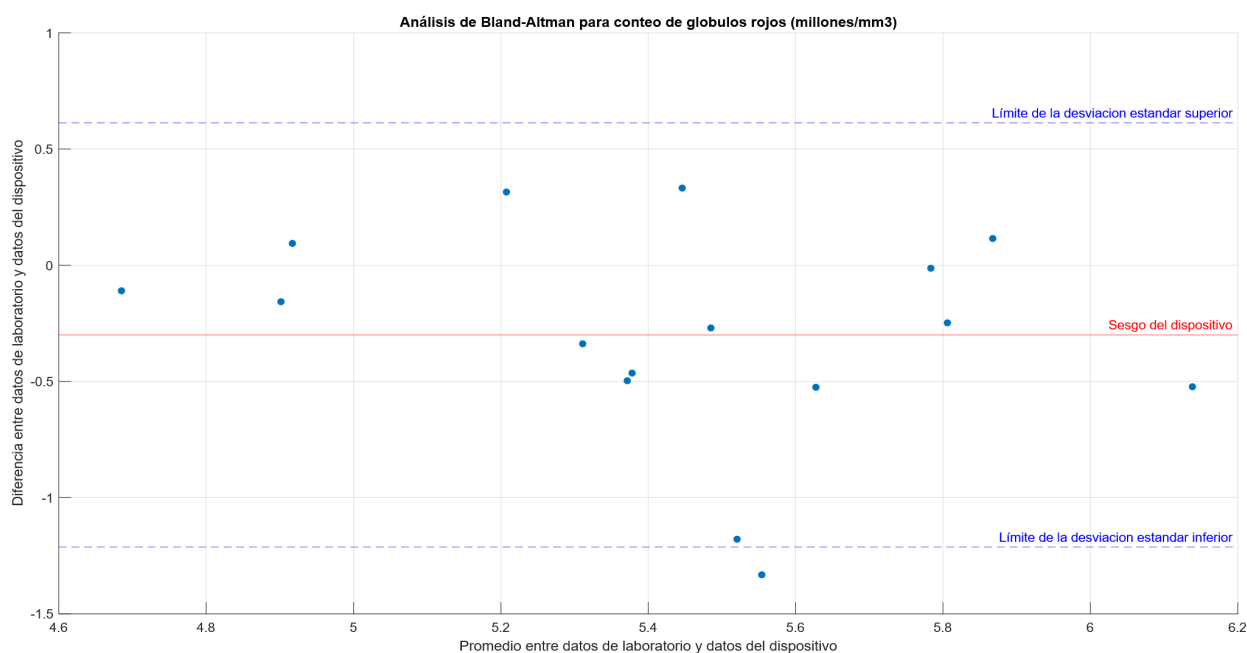


Figure 3. Bland-Altman analysis for red blood cells

In the red blood cell analysis (figure 3), the range of variation of the device is slightly greater than that of the laboratory, indicating greater dispersion in the electronic measurements. This suggests that the device

requires calibration adjustments, although not necessarily an increase in the sample range.

The median of the laboratory data is below that obtained with the device (figure 4), confirming an overestimation bias in the measurement of blood density.

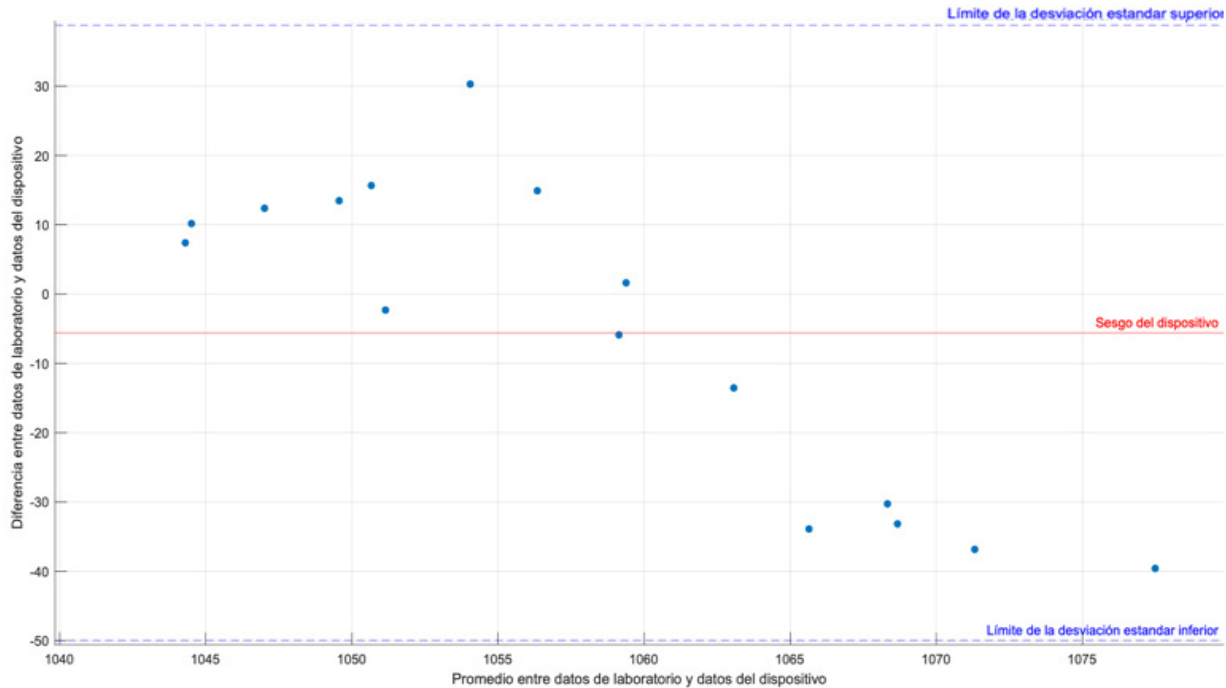


Figure 4. Bland-Altman analysis for blood density

Figure 5 shows that the laboratory data present greater dispersion, evidencing higher variability between experimental values.

In contrast, the device demonstrates greater stability, although lower sensitivity at the extremes of the range—values above 1065 kg/m³ and below 1045 kg/m³—where its accuracy decreases.

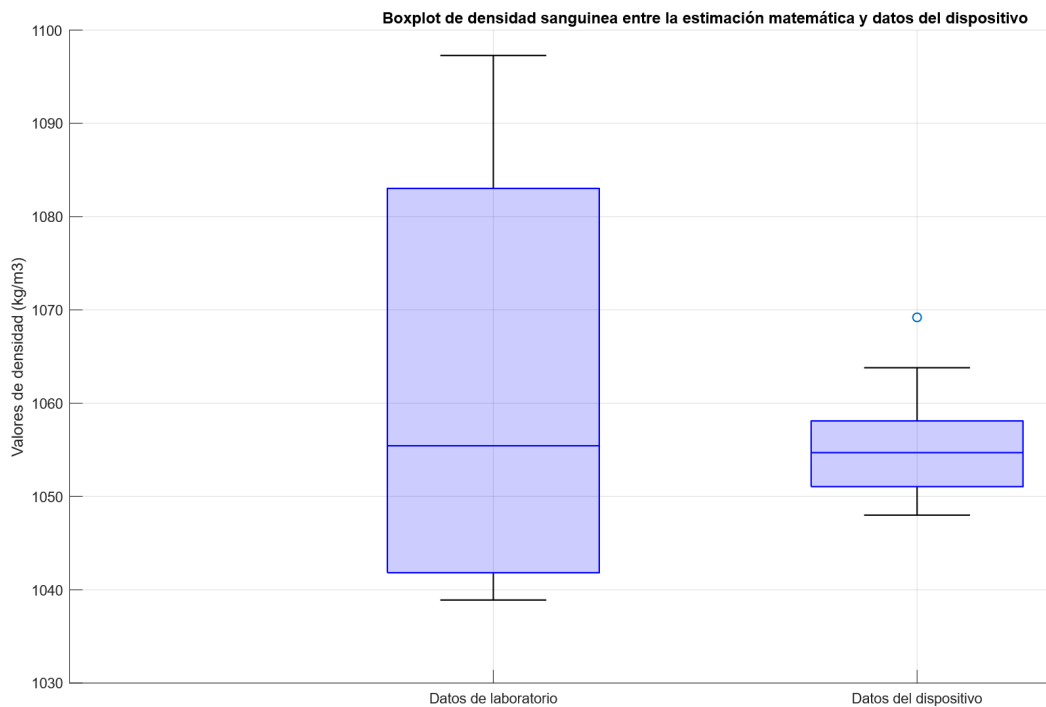


Figure 5. Box plot for blood density

The comparative analysis presented in figures 6 and 7 confirms the patterns identified in the previous measurements. In the case of hematocrit, the device slightly underestimates the values obtained in the

laboratory.

In contrast, for red blood cells and blood density, there is a tendency to overestimate, which is more pronounced for values above the average. These differences are due to limitations of the linear regression model used; it is recommended to recalibrate the system by expanding the training set and optimizing the sensor’s optical coefficients.

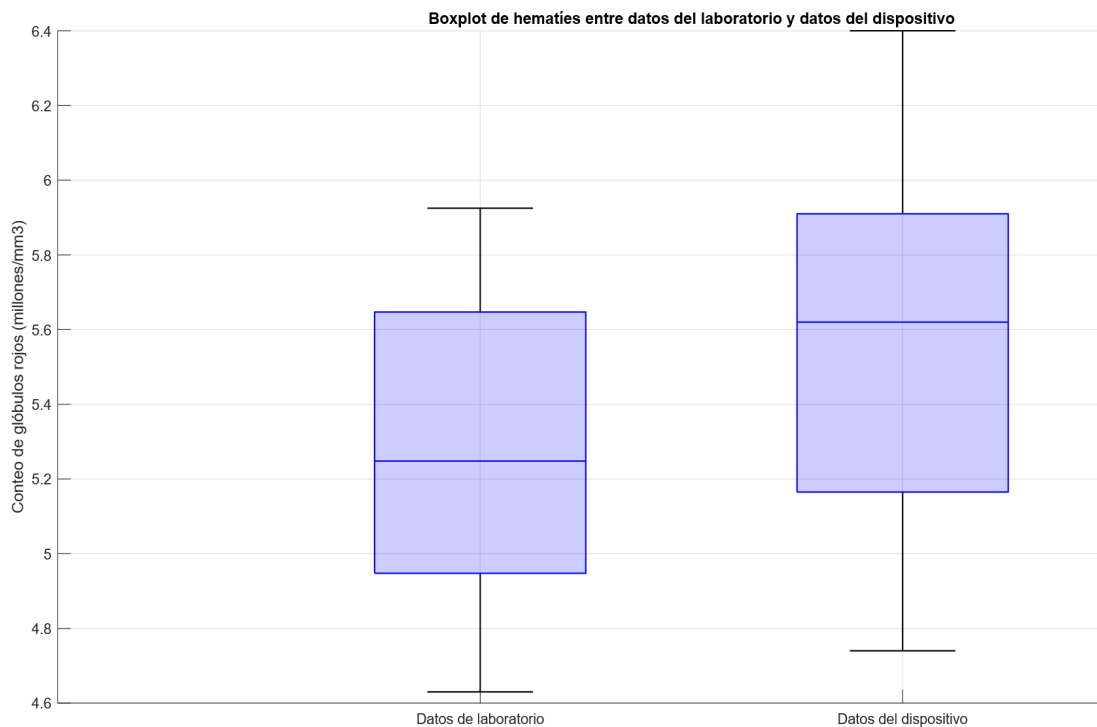


Figure 6. Comparative box plot for red blood cells

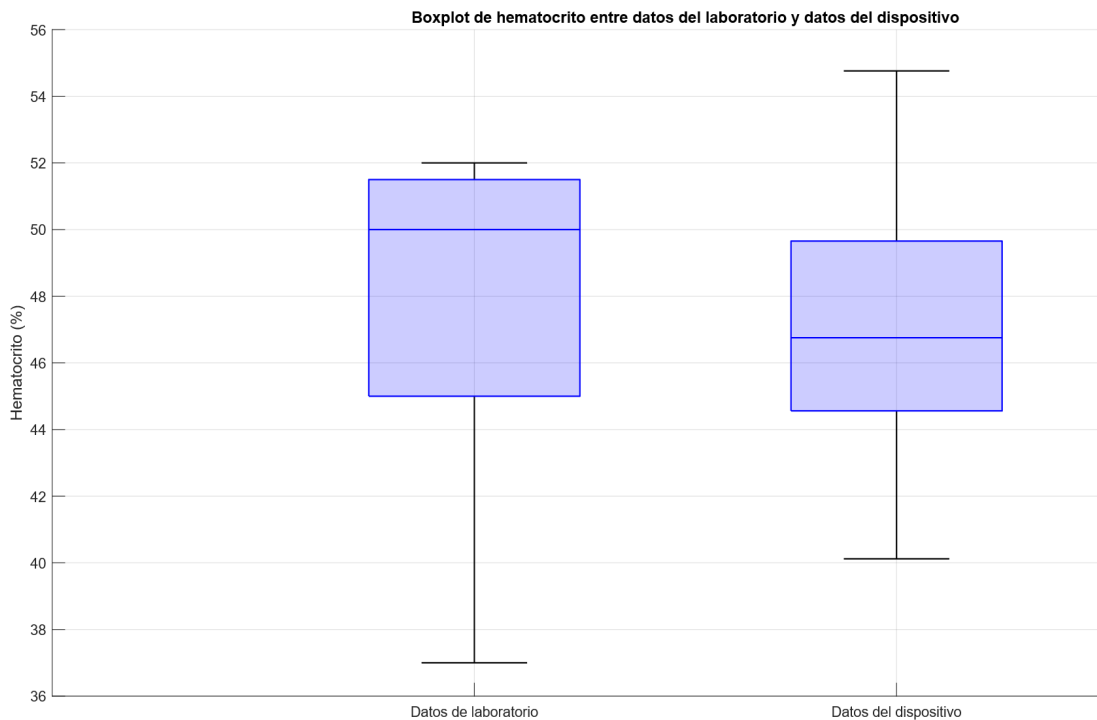


Figure 7. Comparative box plot for hematocrit

DISCUSSION

The results show a strong correlation between the proposed optical device and clinical blood density values, with low, clinically acceptable bias according to the Bland-Altman analysis. This behavior supports the validity

of the method as a non-invasive alternative for real-time estimation of hematological parameters. However, slight discrepancies were observed in participants with extreme hematocrit values, possibly associated with individual variations in optical absorption and light scattering in biological tissues, a phenomenon widely described in studies on (PPG).^(6,11)

The average 2 % error in blood density estimation is attributed to the use of standard reference values for plasma and cell density, which reflect normal physiological ranges. Since the study was conducted in subjects without significant hematological abnormalities, these calibration parameters yielded reliable, clinically consistent results. Consequently, the combination of hematocrit and erythrocyte count proves to be sufficient for an approximation of blood density, provided that cell and plasma density values remain within stable biological ranges.

From an instrumental point of view, the system implemented with a microcontroller, an optical sensor, and an OLED display demonstrated stable performance in the acquisition and processing of PPG signals. The system architecture enabled the acquisition of pulsatile signals with adequate temporal resolution and an acceptable signal-to-noise ratio, confirming its effectiveness for real-time optical measurements. These results are consistent with recent research on PPG-based portable biomedical devices, which highlights their potential for telemedicine and remote monitoring applications.⁽⁸⁾

The spectral behavior observed in the experiments confirms that hemoglobin is the primary chromophore responsible for optical absorption and dispersion at wavelengths of 660 nm (red) and 880 nm (infrared). This characteristic explains the device's sensitivity to variations in erythrocyte concentration, whereas other blood components, such as leukocytes and platelets, exhibit minimal optical responses. This finding reinforces the relevance of photoplethysmography as a selective technique for the non-invasive analysis of parameters related to the cellular fraction of blood.

Comparatively, the results obtained are consistent with those reported by other authors,^(11,13) who demonstrated that PPG, combined with optical models based on Beer-Lambert's law, allows for reliable estimates of tissue and hematological properties. In addition, recent studies in bioengineering and telemedicine have highlighted the importance of PPG as a complementary diagnostic tool in resource-limited clinical settings, owing to its low cost, portability, and continuous monitoring capabilities.⁽¹⁴⁾

Despite the positive results, limitations have been identified that need to be addressed in future research. First, the underestimation bias observed in high blood density values suggests the need to recalibrate the regression coefficients using a larger and more heterogeneous sample. Second, variations in skin tone, peripheral temperature, and involuntary movements can affect measurement accuracy, as noted in recent studies on motion artifacts in PPG.⁽¹⁵⁾ Finally, it is recommended to incorporate multispectral optical sources and more sensitive sensors to improve the system's linearity and dynamic range.

In addition, advances in remote photoplethysmography (rPPG) using RGB cameras have demonstrated the feasibility of estimating hemodynamic parameters without physical contact, offering an opportunity to extend this technology to integrated telemonitoring platforms. The incorporation of these technologies would expand the device's scope, especially in primary care settings or areas with limited resources.

Overall, the results confirm the viability of the developed device as a non-invasive tool for estimating blood density and validate the application of photoplethysmography as a robust method for real-time physiological monitoring. Its potential integration into portable systems and telemedicine platforms opens new opportunities for early detection of hematological disorders, continuous assessment of hemodynamic status, and the implementation of patient-centered digital health strategies.

CONCLUSIONS

This study enabled the development and validation of a non-invasive device for estimating blood density, obtaining an average error of 1,76 % in density measurement, 6,06 % in hematocrit estimation, and 7,01 % in red blood cell count. These results demonstrate that photoplethysmography, in combination with Beer-Lambert's Law, is a viable alternative for measuring hematological parameters without blood sampling.

The device developed, based on red and infrared light, allowed the characterization of blood components with acceptable accuracy. However, it was found that specific parameters, such as plasma density, do not respond directly to these wavelengths, suggesting the need for complementary techniques to improve analysis accuracy. Nevertheless, data analysis revealed a bias in the device's measurements, indicating the need for recalibration to improve concordance with reference methods. In particular, it is recommended that the calibration database be expanded to include subjects with greater variability in blood density to optimize the adjustment coefficients of the estimation model.

In conclusion, the developed prototype represents an advance in the research of non-invasive biomedical devices, with the potential to contribute to the early detection of hematological disorders and facilitate access to frequent measurements in populations with limited access to conventional laboratory tests. However, future research should focus on optimizing signal processing and integrating more robust models to improve accuracy.

and reduce the system's margin of error.

The device tends to underestimate blood density, resulting in a bias of 2 points (kg/m^3) below actual laboratory values. However, no blood density data falls outside the lower (-25 kg/m^3) or upper ($+30 \text{ kg/m}^3$) limits, suggesting similarity in the data.

In addition, the device is accurate when measuring density values between 1048 kg/m^3 and 1065 kg/m^3 , but for values between 1065 kg/m^3 and 1080 kg/m^3 , it is less accurate, and dispersion increases. This phenomenon occurs because people with normal blood density values were used to calibrate and normalize blood parameters in the Philips Van-Slike mathematical model.

Blood density has not been a field of study as extensive as other medical parameters. Although low and high blood density directly influence health, some parameters are easy to diagnose and simple to measure. However, pathologies such as dehydration and cardiovascular problems, such as high blood pressure and aneurysms, could be effectively diagnosed with this methodology.

In the future, integrating the device with artificial intelligence and machine learning platforms would allow for real-time calibration optimization and personalized blood density estimation based on the patient's physiological characteristics. These improvements aim to consolidate its application in continuous monitoring and preventive medicine, strengthening the paradigm of digital health and remote medical care.

BIBLIOGRAPHIC REFERENCES

1. Gamas L, Lee JS. Density indicator method to measure pulmonary blood flows. *J Appl Physiol*. 1986;60(1):327-34. <https://journals.physiology.org/doi/epdf/10.1152/jappl.1986.60.1.327>
2. Yilmaz F, Gundogdu MY. A critical review on blood flow in large arteries: relevance to blood rheology, viscosity and elasticity. *J Med Sci*. 2008;10-15.
3. Wennecke G. Hematocrit - a review of different analytical methods. *Acute Care Testing*. 2004 Sep;1-9. <https://acutecaretesting.org/en/articles/hematocrit--a-review-of-different-analytical-methods>
4. Brodkey FD. Hematocrit. *MedlinePlus*. 2024 Nov. <https://medlineplus.gov/ency/article/003646.htm>
5. Kishimoto S, Maruhashi T. Hematocrit, hemoglobin and red blood cells are associated with vascular function and vascular structure in men. *Sci Rep*. 2020 Jul;10:68319. <https://www.nature.com/articles/s41598-020-68319-1>
6. Park J, Seok HS, Kim SS, Shin H. Photoplethysmogram analysis and applications: an integrative review. *Front Physiol*. 2021; 12:808451. <https://www.frontiersin.org/articles/10.3389/fphys.2021.808451/full>
7. Davis CL, Harrison PD, Bronson JE. Noninvasive method of measuring blood density and hematocrit. US Patent US7011631B2. 2004. <https://patents.google.com/patent/US7011631B2/es>
8. Chen W, Yi Z, Lim LJR, Lim RQR, Zhang A, Qian Z, et al. Deep learning and remote photoplethysmography powered advancements in contactless physiological measurement. *Front Bioeng Biotechnol*. 2024;12:1420100. doi:10.3389/fbioe.2024.1420100
9. Miele Freire MS. Dispositivo para medir la cantidad de hemoglobina en la sangre. Ibarra (Ecuador): Universidad Técnica del Norte; 2023. p. 88-90.
10. Celleri S. Sistema no invasivo de medición de azúcar en la sangre utilizando diferentes longitudes de onda infrarroja. Ibarra (Ecuador): Universidad Técnica del Norte; 2023. p. 80-100.
11. Allen J. Photoplethysmography and its application in clinical physiological measurement. *Physiol Meas*. 2007;28(3):R1-10.
12. Kenner T. The measurement of blood density and its meaning. *Basic Res Cardiol*. 1989;84(2):111-24.
13. Elson DS, et al. Quantitative optical spectroscopy for tissue diagnosis and monitoring. *J Biomed Opt*. 2009;14(6):064015. doi:10.1117/1.3259370
14. Sridhar AR, Cheung JW, Lampert R, Silva JNA, Gopinathannair R, Sotomonte JC, et al. State of the art of mobile health technologies use in clinical arrhythmia care. *Commun Med*. 2024;4:218.

15. Penmetcha V, Rambabu L, Smith BG, Mantle O, Edmiston T, Hobbs L, et al. Evaluating diversity in open photoplethysmography datasets: protocol for a systematic review. JMIR Res Protoc. 2025;34:e73040.

FINANCING

The authors did not receive funding for the development of this research.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

AUTHORSHIP CONTRIBUTION

Conceptualization: Theo Galindo.

Data curation: Theo Galindo.

Formal analysis: Theo Galindo.

Research: Theo Galindo.

Methodology: Theo Galindo, Luz María Tobar, Briseida Gámez.

Project management: Luz María Tobar, Cosme Mejía, Marco Ciaccia.

Resources: Theo Galindo, Diego Ortíz.

Software: Theo Galindo.

Supervision: Luz María Tobar.

Validation: Theo Galindo, Luz María Tobar.

Visualization: Theo Galindo.

Writing - original draft: Theo Galindo.

Writing - review and editing: Marco Ciaccia.