A Low Power Non-Invasive Wrist-Based Approach for Glucose Monitoring

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Abstract. This study presents the development of a prototype non-invasive device for measuring blood glucose levels. It focuses on using photoplethysmography (PPG) and the Beer-Lambert law to measure the absorbance of infrared and red light through the skin of the wrist, offering an alternative to traditional invasive methods, such as commercial glucose meters. This device has the potential to provide a more convenient and less painful approach to continuous glucose monitoring. The study was conducted on a young population in Cartagena, Colombia, where participants used both the prototype device and a commercial glucose meter (Accu-Chek) to compare the results. The data obtained showed a moderate correlation between the two devices (Pearson correlation coefficient of 0.49), with most measurements located in zones A and B of the Parkes error grid, suggesting that the errors are clinically acceptable. However, it is noted that the results should be interpreted with caution in populations with extreme glucose levels. The study concludes that the non-invasive device meets clinical standards for glucose measurement, supporting its future development. It is suggested to move towards a miniaturized wearable device and conduct additional clinical studies to generate more data across a wide range of glucose levels, from hypoglycemia to hyperglycemia.

Keywords: Glucose monitoring · Photoplethysmography (PPG) · Non-invasive Wrist Device · Wrist-based measurement · Parkes error grid.

1 Introduction

In recent years, there has been growing concern in Latin America about the significant impact of chronic diseases such as heart disease, hypertension, respiratory problems, and type 2 diabetes mellitus (T2DM) on the morbidity and mortality of the population [15]. Monitoring these conditions provides crucial information about a person's physiological state, adding healthcare professionals in diagnosing and managing various medical conditions [5,10]. T2DM is the sixth leading cause of death in the region, with a prevalence of 30% to 45% among adults [1]. Constant monitoring of blood glucose levels is essential to prevent severe complications, but traditional invasive methods are costly and uncomfortable, particularly for older patients, children, and people with limited access to healthcare.

Recent technological advancements have led to the development of non-invasive methods for measuring vital signs, reducing the discomfort and risks associated with invasive procedures [9, 10, 13]. Among these, photoplethysmography (PPG) and infrared technology are commonly used for detecting elevated blood glucose levels non-invasively [3, 11, 12]. These approaches offer significant potential for improving disease management by enabling real-time, painless monitoring without the need for frequent blood samples. Our study advances previous research [3, 6] by introducing a prototype designed to measure glucose levels at the wrist, offering a more convenient and user-friendly alternative to traditional fingertip-based methods. The core contribution of this work is the development and validation of a non-invasive wrist-based device that employs photoplethysmography (PPG) and the Beer-Lambert law, utilizing a novel measurement site for glucose monitoring. This innovative approach addresses the discomfort and constraints of traditional invasive methods, making it particularly suitable for continuous monitoring. The results reveal a moderate correlation with a commercial glucose meter, underscoring the device's potential for continuous glucose monitoring, especially in settings with limited resources.

This study was conducted in Cartagena, Colombia, where data were collected from a young population to evaluate the accuracy of the non-invasive device compared to the commercial Accu-Chek glucose meter. The article details both the hardware design and the data collection process, and it presents a comparative analysis aimed at validating the reliability of the prototype for continuous diabetes monitoring. The results obtained have the potential to improve diabetes management in resource-limited settings.

2 Material and Methode

The initial version of the device was introduced in [3]. In this study, we improved both the device hardware and the associated code to improve its performance and functionality.

2.1 Glucose Levels

Glucose levels were categorized as follows: Hypoglycemia is defined as blood glucose levels below 70 mg/dL (3.9 mmol/L) and classified into three levels: mild (54-70 mg/dL, 3.0-3.9 mmol/L), moderate (below 54 mg/dL, 3.0 mmol/L), and severe (requiring external assistance). On the other hand, hyperglycemia is defined as blood glucose levels above 180 mg/dL (10 mmol/L) after meals or above 130 mg/dL (7.2 mmol/L) when fasting. It is classified as mild (180-250 mg/dL, 10-13.9 mmol/L), moderate (250-400 mg/dL, 13.9-22.2 mmol/L), and severe (above 400 mg/dL, 22.2 mmol/L). These thresholds are used to evaluate continuous, non-invasive glucose monitoring [7].

2.2 Photoplethysmography (PPG)

We analyzed the optical properties of glucose, as its concentration in blood affects the refractive index and absorption properties, altering the amount of light absorbed at specific wavelengths. The methodology is based on photometry and light absorbance. Photoplethysmography (PPG) measures changes in blood flow through direct sensing, while the Beer-Lambert Law calculates the absorbance of infrared and red light as a function of glucose concentration. Glucose levels are then estimated using a linear regression model that correlates absorbance values with blood glucose concentrations, leveraging glucose's effects on light absorption and scattering.

To minimize noise, the following techniques were applied: 1. Averaging: The sensor averages eight samples in its buffer, reducing high-frequency noise. 2. Signal Validation: Low "red reading" values (< 1000) trigger a wait state, avoiding processing erroneous data. 3. Sampling Rate Adjustment: A sample rate of 400 Hz balances resolution and noise suppression by oversampling.

2.3 Hardware Design

We use a wearable device designed for wrist-based measurements, potentially for medical monitoring purposes. The components are organized to ensure functionality, comfort, and reliable data collection, with a focus on proper sensor placement and data display, see Fig. 1.

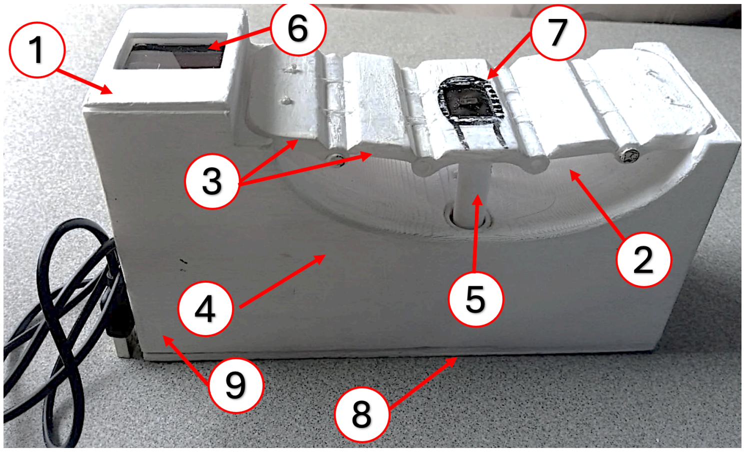

Fig. 1: Prototype developed to measure glucose at the wrist.

The device features an arch-shaped design that wraps around the wrist, with links Fig. 1 number 3) functioning as bracelet segments to allow flexibility and adjustable fitting, similar to a watch strap. The main body (see Fig. 1 number

4) holds the components, providing structural integrity to the system. We use a pulse oximeter biosensor (Fig. 1 number 7) to collect the patient's data samples. Pressure mechanism (Fig. 1 number 5) ensures proper contact between the sensor and the wrist, which is crucial for accurate measurements by maintaining optimal sensor positioning. A small OLED display (Fig. 1 number 6) shows readings or device status information. The sensor, positioned in close contact with the skin, is responsible for detecting glucose levels. The bottom cover houses additional components, protecting the microcontroller and power system (see Fig. 1 number 8). The microcontroller (Fig. 1 number 9) processes the data collected by the sensor and controls the overall functionality of the device. A power cable is used to charge the device, enabling the system to function.

3 Methodology

The data collection protocol for all study participants was conducted as follows:

3.1 Non-Invasive Device

The procedure for Non-Invasive Blood Glucose Measurement is as follows:

Clean the wrist with alcohol, as this surface will be used for the sample collection. The user places their wrist over the sensor and presses down. The person conducting the test should turn on the device once the user has positioned their wrist as indicated. At the start of the test, the user should gently press the bracelet and maintain the position for one minute to obtain an accurate measurement. Once the result is displayed on the screen, the user can remove their wrist from the device.

This procedure was performed three times with each user to eliminate any potential measurement errors.

3.2 Commercial Device - Invasive Method

The comparative analysis was conducted using the Accu-Chek Instant device (Accu-Chek; Roche, Basel, Switzerland) [8], following the operating principles detailed in [14], along with Accu-Chek Instant test strips [2]. The procedure was as follows:

Clean the sample area, usually the side of a finger, with alcohol. Use a lancet, a small needle in a lancing device, to obtain a drop of blood, with a new lancet used for each user. Place the drop of blood on a test strip, which is then inserted into the glucose meter. An enzyme on the strip reacts with the glucose, generating an electrical current measured by the device, which then displays the glucose level in milligrams per deciliter (mg/dL) or millimoles per liter (mmol/L).

3.3 Study Population

The study involved a young population, comprising 60% women and 40% men. All participants were between 18 and 40 years of age, and the study took place at sea level. Participants were fasting at the time of data collection. The individuals involved were students from the Universidad Tecnológica de Bolívar - Cartagena-Colombia. This City is known for its diverse racial and ethnic composition, the result of centuries of interaction between various groups. Generally, the population has a mix of Afro-descendant, Indigenous, and European (Spanish) heritage. This unique blend of ethnic backgrounds provides a rich cultural context for the study, as the participants reflect the diversity inherent in the local population.

BMI values range from 18.61 to 39.84, with a mean of 24.03, indicating a sample that includes individuals from normal weight to those with obesity.

3.4 Linear regression model

The linear regression model proposed in this study establishes a direct relationship between absorbance (A), calculated using the Beer-Lambert law, and glucose concentration (G), expressed as:

$$G = A \cdot m + b, \tag{1}$$

where the slope ($m =$): represents the rate of change in glucose concentration for each unit increase in absorbance. The intercept (b): represents the baseline glucose level when absorbance approaches zero. The absorbance (A) is calculated using the following equation:

$$A = \log_{10}\left(\frac{peakvoltage}{valleyvoltage}\right). \tag{2}$$

The peak and valley voltages are derived from PPG signal readings at infrared and red wavelengths, representing the light absorbed by the blood. This absorbance value is assumed to correlate directly with glucose concentration based on its optical properties. The model presumes a linear relationship between A (absorbance) and G (glucose concentration), where higher absorbance values indicate greater glucose levels. Calibration data, obtained in preliminary studies [3, 6], is used to determine the parameters m and b, fitting a straight line to known glucose levels and their corresponding absorbance values. For a measured A, the glucose level (G) is predicted using the equation 1, providing a real-time blood glucose estimation.

4 Results

This section presents the preliminary results of tests conducted on 25 participants. However, the results from two individuals were excluded as their values fell outside the limits of the mathematical model used to estimate blood sugar levels.

All participants provided informed consent, confirming their understanding and voluntary acceptance of the procedures. The study was also approved by the ethics committee of Universidad Tecnológica de Bolívar, ensuring compliance with ethical principles and regulations to protect participants' rights and well-being.

One factor influencing the sensor's accuracy is its dependence on proper placement. Correct positioning ensures effective light penetration into the skin and minimizes light scattering. Misalignment or insufficient contact reduces the signal-to-noise ratio (SNR), resulting in unreliable absorbance values (A), which directly impact glucose estimation using the linear regression model. Improper placement can lead to significant underestimation or overestimation of glucose levels. Another challenge identified is that darker skin tones, which have higher melanin concentrations, absorb more light, reducing the amount of light detected by the photoplethysmography (PPG) sensor. This can decrease signal intensity and compromise accuracy [4].

The Pearson correlation coefficient for the device is 0.49, indicating a moderate positive correlation. This suggests that, while there is some relationship between the device's measurements and those of the reference method, the relationship is not very strong, pointing to additional factors influencing the non-invasive device's measurements. Fig. 2 shows the diversity of the participants in terms of skin tone. Three sample tests are presented, conducted on the wrists of different young individuals, each with a distinct skin tone: a) darker skin tone, b) intermediate skin tone, and c) lighter skin tone. In each case, the non-invasive device is placed around the wrist. The image illustrates how the device adjusts and functions on different skin types.

We present the results of comparative analysis bewteen both devices (see Fig. 3). The blue lines represent glucose levels measured by a commercial Accu-Chek device, while the red lines represent levels measured by a non-invasive wrist device. Both lines show fluctuations in glucose levels among the participants, with some notable peaks and valleys. In general, the two devices seem to follow a similar trend, although there are minimal differences at several points. Until participant 5, the measurements from the commercial device tend to be slightly higher than those from the non-invasive device. Between participants 6 and 10, the measurements from the non-invasive device are very close to or coincide with those from the commercial device. From participant 15 onwards, the measurements again show variations, with some points where the non-invasive device shows higher levels and others where it shows lower levels compared to the commercial device. The commercial device (blue line) shows glucose levels ranging approximately between 85 and 100 mg/dL, while the non-invasive device (red line) shows glucose levels that also vary within a similar range, albeit with some occasional differences.

We present the results of comparative analysis of gender with the both devices. Fig 4 shows a comparison of glucose levels measured by a commercial Accu-

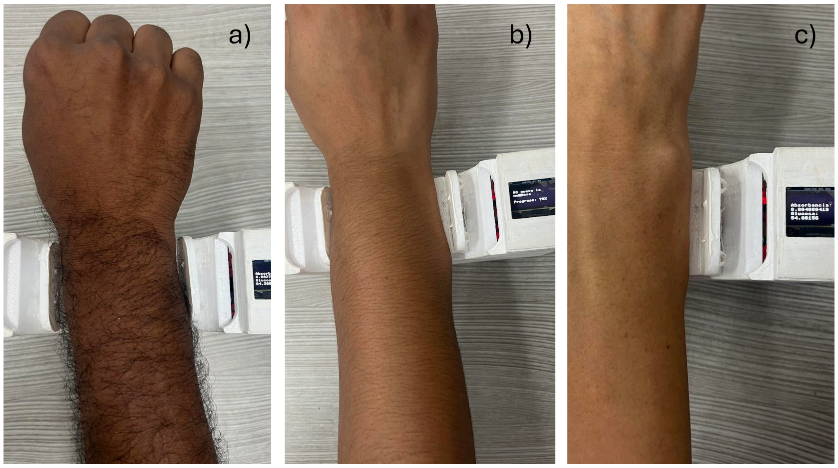

Fig. 2: Testing examples of the participants, a) darker skin tone, b) intermediate skin tone, and c) lighter skin tone

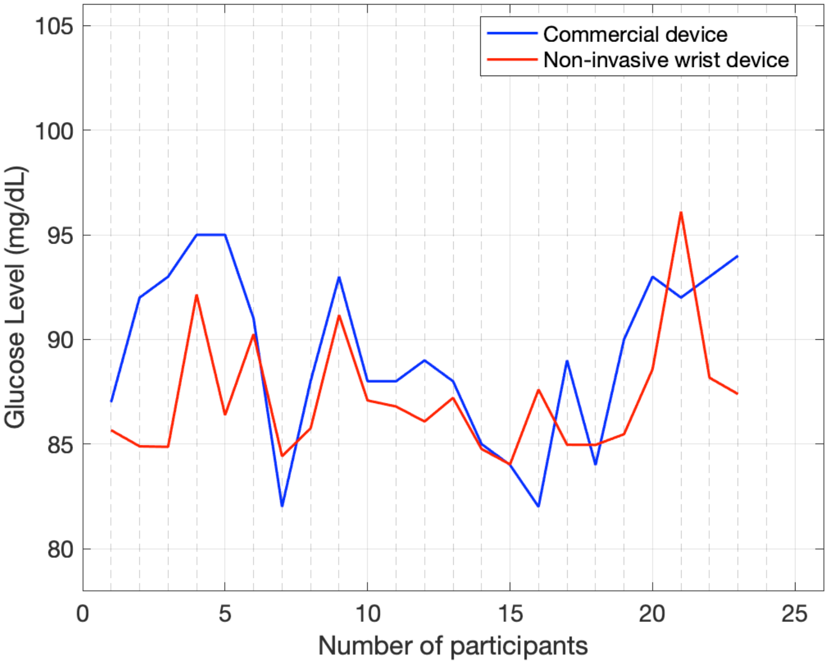

Fig. 3: General results

Chek device (blue bars) and a non-invasive wrist device (red bars) in a group of 15 female participants. The results indicate that, in general, both devices present a similar trend in glucose measurements, although there are minimal differences at certain points. Up to participant 6, the measurements from the commercial device tend to be slightly higher than those from the non-invasive device. Between participants 7 and 9, the measurements from the non-invasive device are very close to or coincide with those from the commercial device. From participant 10 onwards, the measurements show variations again, with some points where the non-invasive device shows higher levels and others where it shows lower levels compared to the commercial device. The glucose levels measured by both devices vary approximately between 80 mg/dL and 100 mg/dL, although with some specific differences.

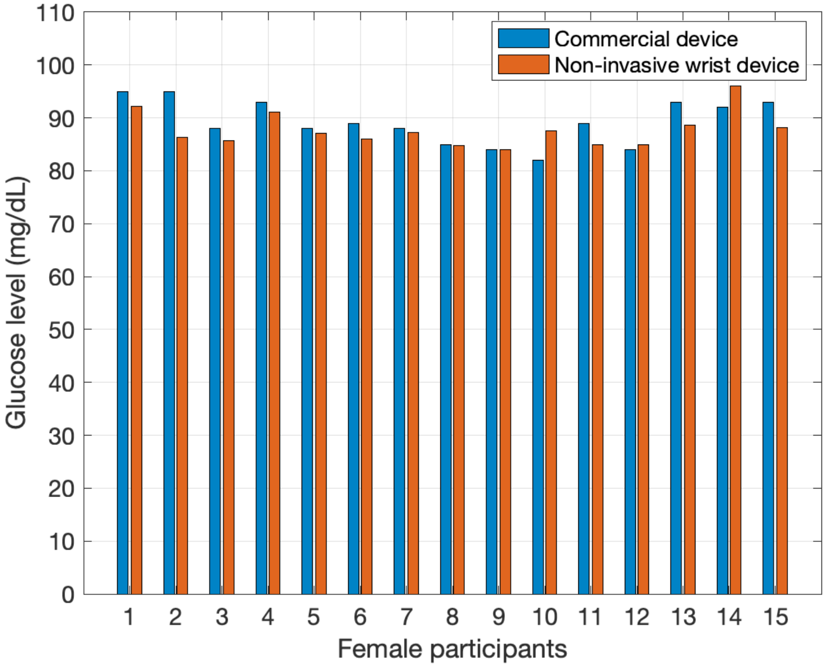

Fig. 4: Representation of female participants

Fig. 5 presents glucose levels (mg/dL) for a group of male participants, comparing the measurements obtained with a commercial device (in blue) and a non-invasive wrist device (in red). Glucose levels remain within a narrow range (approximately 80-100 mg/dL) for all participants, and there is a general trend in which the commercial device measures slightly higher glucose levels compared to the non-invasive wrist device.

For most participants, the measurements taken with the commercial device (blue bar) are consistently higher than those from the wrist device (red bar), although the differences are minimal. The recorded glucose levels are within a healthy range (below 110 mg/dL) in both cases.

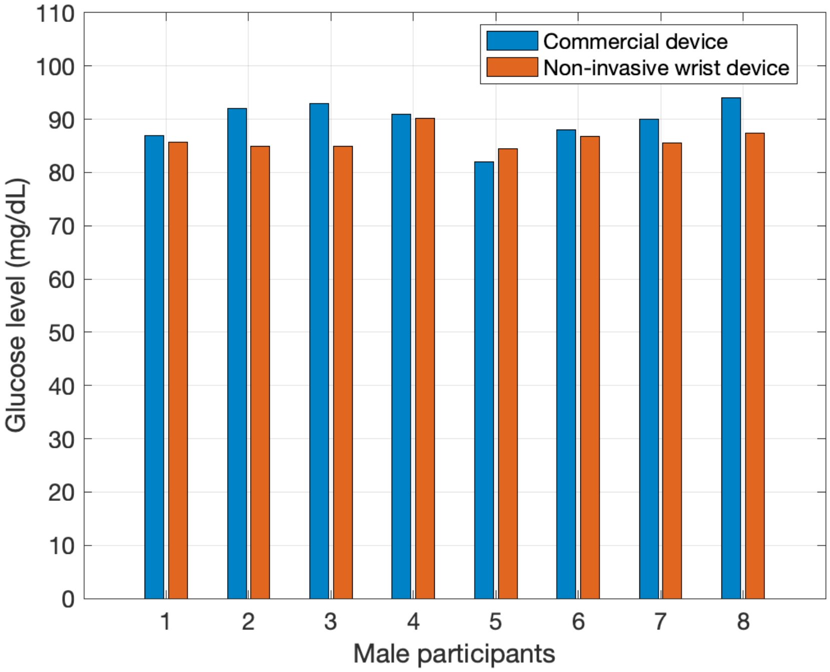

Fig. 5: Representation of male participants

4.1 Parkes error analysis

Figure 6 shows the Parkes error grid plots for both the Commercial Device and the Non-invasive Wrist Device which is used to evaluate the accuracy of glucose measurement. In this graph, the X-axis presents the glucose values from the commercial device, while the Y-axis shows the values from the non-invasive wrist device. The solid diagonal line indicates perfect equivalence between the two devices, while the dashed lines represent different zones of clinical error. The red dots, representing the measurements, are mostly grouped near the equivalence line, suggesting that the non-invasive device has reasonable accuracy. Most of the points fall within zones A or B of the grid, indicating that the errors are clinically acceptable and would not negatively impact decision-making. Therefore, the non-invasive device demonstrates performance comparable to the commercial device within clinically safe margins.

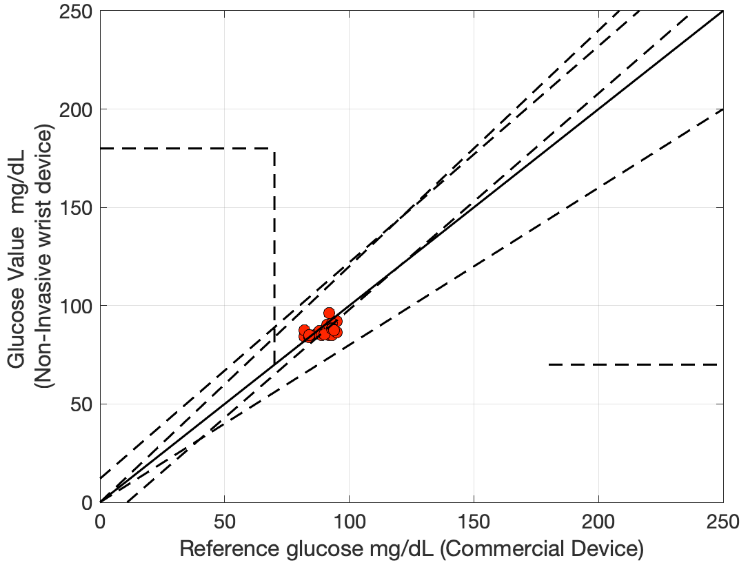

Fig. 6: Parkes error grid

4.2 Bland-Altman analysis

The Bland-Altman analysis (see Fig 7) revealed a mean difference (bias) of −2.19 mg/dL between the wrist-based device and the Accucheck reference, indicating a slight systematic underestimation by the wrist-based device. The calculated limits of agreement (LoA) range from −9.15 mg/dL to 4.77 mg/dL, encompassing 95% of the differences. Most data points fall within these limits, demonstrating reasonable agreement between the two methods. However, the presence of some outliers suggests areas for improvement, such as refining the device's algorithm and addressing variability caused by factors like skin tone, or wrist pressure.

5 Conclusions

In conclusion, the device meets the measurement standards for reading glucose levels non-invasively at the wrist. In this study, a prototype non-invasive wrist device was used to collect absorbance data and successfully estimate blood glucose levels (BGL). This result shows that it is feasible to continue developing the prototype, moving towards a miniaturized wearable device and conducting additional clinical studies to generate large volumes of accurate BGL data, covering a broad range from hypoglycemia to hyperglycemia.

Although most measurements fall within zones A and B of the Parkes grid, the results suggest that further refinements are needed. It is important to note that while zones A and B represent clinically acceptable margins, they do not guarantee absolute equivalence in the measurements.

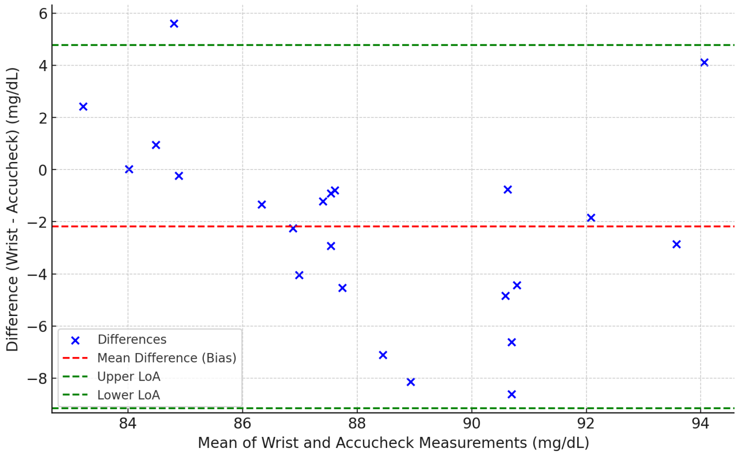

Fig. 7: Bland - Altman analysis results

Since the results are within clinically safe margins, some users might confuse the applicability of the non-invasive device in different medical contexts or for different types of patients. However, it is crucial to consider that the results obtained in this study may not apply uniformly to populations with more extreme glucose conditions (severe hypoglycemia or hyperglycemia), as most of the measurements analyzed seem to fall within a moderately healthy range.

As future work, additional tests of the non-invasive device are planned in populations with extreme glucose conditions, such as individuals with hyperglycemia and hypoglycemia. These tests are crucial to validate the device's accuracy across a wide range of glucose levels, ensuring its applicability in more complex clinical scenarios. Furthermore, the miniaturization process of the device will be prioritized to make it a portable and convenient tool for continuous use in patients' daily lives. Finally, the device's performance will be evaluated in environments with lower blood oxygenation, such as high altitudes, to assess its ability to accurately measure glucose under adverse physiological conditions.

Furthermore, future research will incorporate feedback mechanisms to alert users when placement is suboptimal, such as real-time visual or haptic feedback to ensure proper positioning and improve data reliability.

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