第 49 卷 第 10 期
2022 年 10 月

湖南大学学报（自然科学版）
Journal of Hunan University (Natural Sciences)

Vol. 49 No. 10
October 2022

Open Access Article https://doi.org/10.55463/issn.1674-2974.49.10.18

A Non-Invasive Method Applied to Measure Cholesterol and Glucose Levels

Usman Umar*, Syafruddin Syarif, Ingrid Nurtanio, Indrabayu

Electrical Engineering Department, Hasanuddin University, Makassar, Indonesia

Abstract: This research aims to develop an innovative instrument to measure cholesterol and glucose levels non-invasively. The proposed model introduces the idea of measuring cholesterol and glucose levels without a blood sample or physical contact. This is accomplished using a near-infrared (NIR) and a photodiode. To improve accuracy and stability, an optical near-infrared (NIR) wristband sensor was developed to detect electrical pulses in the wrist tissue, which were then converted into values of cholesterol and blood glucose levels. There were 20 participants as clinical referrals in this study to identify invasive cholesterol and glucose levels. To achieve this goal, a mathematical model has been developed to create a non-linear equation between cholesterol and blood glucose levels. The performance of this model was assessed using square error prediction (SEP), the coefficient of determination (R^2) and the Root Mean Square Error (RMSE). To determine the accuracy of this instrument, the ANOVA, T-test, and Clarke EGA analysis of variance were used in this study. The research findings demonstrated that the proposed strategy is practical to apply. Additionally, this instrument was tested on 40 participants with randomized ages between 20 and 60 years.

Keywords: cholesterol, blood, glucose, non-invasive method, sensor.

一种用于测量胆固醇和葡萄糖水平的非侵入性方法

摘要: 本研究旨在开发一种创新仪器，以无创方式测量胆固醇和葡萄糖水平。拟议的模型引入了无需血液样本或身体接触即可测量胆固醇和葡萄糖水平的想法。这是使用近红外(近红外光谱)和光电二极管完成的。为了提高准确性和稳定性，开发了一种光学近红外(近红外光谱)腕带传感器来检测腕部组织中的电脉冲，然后将其转换为胆固醇和血糖水平值。在这项研究中有 20 名参与者作为临床转诊来确定侵入性胆固醇和葡萄糖水平。为实现这一目标，已开发出一种数学模型来创建胆固醇和血糖水平之间的非线性方程。使用平方误差预测(九月)、确定系数(R2)和均方根误差(均方根误差)评估该模型的性能。为了确定该仪器的准确性，本研究使用了方差分析、吨检验和克拉克 EGA 方差分析。研究结果表明，所提出的策略具有实用性。此外，该仪器还对 40 名随机年龄在 20 至 60 岁之间的参与者进行了测试。

关键词：胆固醇，血液，葡萄糖，非侵入性方法，传感器。

1. Introduction

Cholesterol (C27H46O) and blood glucose (C6H12O6) are essential elements in the human body [1]. Cholesterol is a fatty substance that functions as a source of the testosterone hormone in men and the estrogen hormone in women. Cholesterol flows through the blood in body tissues with lipoproteins. Besides, cholesterol can cause clogged arteries by accumulating lipoproteins. Glucose is a carbohydrate element that functions as a source of energy for all body cells, accelerates metabolism by serving as the main fuel for the brain and regulates body temperature [2]. Therefore, cholesterol and glucose are needed to form hormones in human growth.

Generally, cholesterol and glucose levels in the blood have normal limits. According to the NCEP-ATP III, total blood cholesterol and glucose have normal

Received: July 11, 2022 / Revised: August 10, 2022 / Accepted: September 8, 2022 / Published: October 30, 2022

About the authors: Usman Umar, Syafruddin Syarif, Ingrid Nurtanio, Indrabayu, Electrical engineering department, Hasanuddin University, Makassar, Indonesia

Corresponding author Usman Umar, umaru17d@student.unhas.ac.id

standard values < 200 mg/dl and 140-200 mg/dl, respectively. Conversely, excessive cholesterol levels (hypercholesterolemia) will cause cardiovascular disease, namely, the heart, and blood vessel disorders, and cause Diabetes mellitus.

According to [3], cholesterol is essential in the formation of healthy cells. Nevertheless, high cholesterol increases the risk of getting coronary heart disease [4], stroke, peripheral vascular disease, and other cardiovascular diseases [5]. A high cholesterol level has also been tied to diabetes and hypertension [6], and Alzheimer's Disease [7]. Additionally, uncontrolled blood sugar can increase vascular disease [8]. A high glucose level for a long period can cause complications such as diabetes, including nerve damage, vision loss, kidney damage or other problems, and an increased risk of cardiovascular disease. The DM disease currently affecting 1.2 million Australians was investigated in [9]. In 2015, DM was found to be the leading cause of mortality globally and contributed to 5 million deaths around the world [10]. In addition, the global population of individuals with DM will reach 642 million people [9, 10]. According to data from the IDF, in 2017, there were 451 million people with diabetes and this is predicted to increase to 693 million in 2045, causing about five million people to die worldwide each year due to diabetes [11]. As a result, both the cholesterol and glucose levels of patients can affect the disease's progression [12].

The measurement of cholesterol and glucose levels still uses an invasive (auto check) method that uses blood samples for measuring strips. A blood sample is taken by pricking the patient's fingertip, causing pain in the hand. Some of the existing invasive measuring instruments can measure the three components of blood, including glucose, cholesterol and blood uric acid such as Easy Touch GCU, Nesc Multi-check, Autocheck and Accu-Check. Some research has been conducted to minimize the negative impacts of this invasive method. An invasive method was introduced in [13] to continuously monitor glucose in a pain-free way. The proposed concept developed this continuous and pain-free glucose-monitoring model based on a highly porous platinum black. The surface of this platinum black is modified using a Nafion biocompatible ionomer. In the proposed study, SEM and EDX analyses were performed to identify the level of glucose. As a result, this device showed good stability for seven days and lost its functional activity after another seven days. Other research introduces microneedle technology into medical sensing devices. This technology was developed due to its advantages of minimal invasiveness, real-time and convenience. The proposed study was developed based on electrochemical biosensors, CPs, enzymes, nanoparticles and their composites. These results indicate the application of MN that can be used to selectively monitor glucose [14].

However, the impact of an invasive method is to cause pain in the hand. Some patients do not want to be checked for cholesterol and glucose levels continuously. Today, monitoring of total cholesterol and glucose occurs without blood samples. Some researchers introduced a method to measure cholesterol and glucose levels. An amperometry biosensor was applied in [15] to define the cholesterol and glucose levels. Under the optimization conditions illustrated, the proposed sensor has a high sensitivity for detecting the glucose and cholesterol ranges from 0.25 to 6.00 mM and 0.25 to 4.00 mM, respectively. Based on the results, it was found that both sensors displayed good anti-interference ability and clearly exhibited acceptable recoveries for detecting glucose and cholesterol in human serum samples (98.2–104.1%).

The author in [16] applied a visualized sensing method to measure glucose and cholesterol. Under Janus hydrogel microparticles both glucose and cholesterol levels were detected. As a result, the potential of microparticles can be applied to measure the glucose and cholesterol levels. According to [17], a fiber optic bio-sensor can be applied to determine the cholesterol and glucose levels. This sensor can achieve optimal detection with pH 7.0, 40 °C and 10 mg COD (in a 75 mg carrier), and those for glucose were achieved with pH6.5, 35 °C, and 12 mg GOD (in 90 mg carrier). Therefore, the biosensor is effective in conducting repeatability. It is also selective and satisfactorily detects results.

To avoid pain in the patient's hand, most studies examined a non-invasive (sensor) method to measure levels of both cholesterol and glucose, for example: impedance technique [18], eye image analysis [19] and sensor method [20, 21]. A biosensor was developed in [22] using Au nanoparticles to determine the level of cholesterol. In this study, an electrochemical cholesterol biosensor is based on ChOx enzyme immobilized on gold nanoparticles. The Au nanoparticles illustrated a linear response between $2 \times 10{-}3$ to $8 \times 10{-}3$ M in amperometry with sensitivity and detection limit of 10.12 μA mM−1 cm−2 and $0.1 \times 10{-}3$ M, respectively. The author [23] applied AgNPs and GQD nanocomposites as sensor glucose. Moreover, the fabricated sensors exhibited good sensitivity and selectivity with a low detection limit of 162 nM and 30 μM for H2O2 and glucose sensing, respectively.

Additionally, the biosensors have been successfully applied to detect glucose concentrations in human urine. In this research, we developed a disposable electrochemical sensor to detect cholesterol [24]. In this study, this sensor was manufactured by a SPCE, MWCNTs and β-CD. In the proposed technique, it was indicated that the sensor can detect levels of cholesterol ranging from the optimal experimental conditions, however using DPV as the transduction technique, the sensor could detect cholesterol levels ranging from 1

nM to 3 μM, with a detection limit of 0.5 nM.

Other research investigated some methods to detect the levels of glucose. Multi-sensor fusion was applied in [25] to monitor blood glucose. To improve the accuracy in the detection of glucose levels, a K-mean clustering algorithm is used to classify different categories of characteristic parameters of diabetics. As a result, error grids were as follows: 58.33% in Zone A, 39.43% in Zone B and 2.24% in Zone C, with a correlation coefficient of 0.69. This research was conducted at the National Medical Products Administration of China. A non-invasive method was introduced in [26] to detect blood glucose level. The proposed method applied a near infrared optical biosensor. In that study, twelve patients were tested to verify the accuracy of this tool. The results indicated the standard prediction-estimated SPE of 6.16 mg/dl.

Non-invasive blood glucose was investigated in [27] monitoring laser light, according to transmittance and refraction. In this research, red laser light with a wavelength of 650 nm is selected, as this device is simple, cheaper and compact. The results indicated that it has high accuracy in measuring blood glucose. According to [28], an optical sensor can be applied to monitor blood cholesterol. This study focused on the use of an infrared lighting emitting diode with a wavelength of 940 nm. The result illustrated that the variance analysis by comparing both invasive and non-invasive methods can be accepted, such as p-value is less than 0.05. Bioimpedance was applied and neural network methods to measure the cholesterol levels in blood [29]. This paper demonstrated that of 260 participants, 190 subject data were applied to the artificial neural network method and the remaining 70 subjects' data were applied to the testing model. As a result, such a model showed high prediction accuracy, sensitivity and specificity.

However, as mentioned above, none of these studies can monitor both cholesterol and glucose at the same time. This study aims to design a device to detect cholesterol and glucose simultaneously by increasing the accuracy and stability of the sensor by using a wristband as a holder for the NIR sensor that is attached to the wrist. In this study, the sensor uses a 940 nm IR LED and a photodiode that is generally used to detect glucose levels and is also applied to detect cholesterol and glucose levels directly with the same sensor. In addition, the proposed method allows patients to measure cholesterol and glucose with high accuracy and independently at a lower cost.

This paper is structured into four sections: section 2 presents methodology; section 3 discusses results and discussion and section 4 presents the conclusions.

2. Research Method

2.1. Sensor Design

Figure 1 shows the structural layout of the sensor system for measuring cholesterol and blood glucose levels. A reflecting optical sensor uses an infrared LED with a wavelength of 940 nm as a transmitter, receiving light, and a photodiode as a detector. The sensor is fastened to a wrist strap, and the infrared LED's light is reflected and captured by the photodiode after being absorbed by the tissue in the wrist. The light that the photodiode receives is transformed into light at the attenuation value and into an electric current. A load resistor is then coupled to the anode to convert the electric current into a voltage. The voltage amount depends on the amount of light received by the photodiode. The voltage value on the photodiode is still too low so the difference in voltage values is less visible. A voltage amplifier must increase the low voltage value by inserting an IC LM358N amplifier circuit that can amplify the voltage from the sensor. The voltage value of the amplifier circuit is sent to Pin A0 of the ADC microcontroller to be converted into a digital voltage value. The voltage value is entered into a mathematical equation in the program's algorithm to classify the total cholesterol and blood glucose values displayed on the monitor.

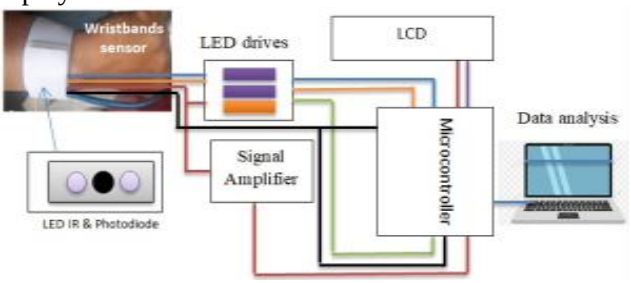

Fig. 1 Architecturally designed instrument for monitoring blood glucose and cholesterol levels

In designing this device, three steps were conducted, as illustrated in the following statement, namely:

2.1.1. Instrument Design

A schematic diagram of the sensor LED is shown in Fig. 2. The patient's output voltage is measured using a photodiode and an IR LED 940 nm. The output voltage of this sensor must be increased and converted into readings of cholesterol and glucose using an IC LM358N amplifier circuit. To alter the voltage value, an algorithm software is employed. This mathematical model uses polynomial regression to estimate the levels of glucose and cholesterol in each patient. Cholesterol and glucose can therefore be identified.

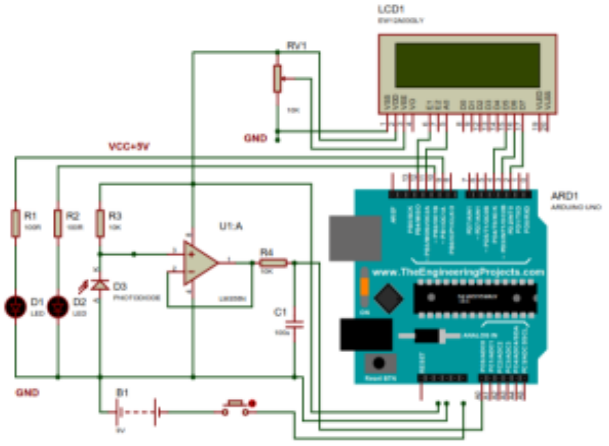

Fig. 2 Schematic diagram of the IR LED sensor

2.1.2. Processing

Twenty patients were taken as clinical references in determining cholesterol and glucose levels. The age limit for each patient was between 20 and 60 years old. The output voltage of each patient was measured using the auto check tools. To ensure accuracy, the sampling was carried out five times for each patient. The resulting output voltage will be correlated with cholesterol and glucose levels to obtain mathematical equations in the form of polynomial equations. The resulting mathematical equation will be used as the basis to identify the values of cholesterol and glucose in the patient's blood.

2.1.3. Validating

For the justification, 40 patients were tested at random ages between 20 and 60 years. In this research, the ANOVA and T-test were applied to determine the error value of each test carried out. Additionally, the Clarke EGA was used to analyze the accuracy of the measurement results of this tool compared with the test results using the auto check method as a clinical reference.

2.2. Statistical Analysis

In this research, non-linear regression has been applied to determine the correlation between the sensor output and auto check result from both cholesterol and glucose levels, as illustrated in the equation (1).

$$Y_{C/G} = \beta_0 + \beta_1 X + \beta_2 X^2 + \varepsilon \quad (1)$$

In equation 1, Y is the estimated value of cholesterol or blood glucose, X is the sensor output voltage value, and β_O, β_1, β_2 are the parameter vector constants determined from the sum square error derivative of the existing X and Y values, with ε is the residual value.

The square error prediction (SEP) can be calculated based on equation (2):

$$\mathrm{SEP}_{C/G} = \sqrt{\frac{\sum_{i=1}^{n}\{(Y_p - \bar{Y}_p) - (Y_{ref} - \bar{Y}_{ref})\}^2}{n}} \quad (2)$$

In addition, the performance of this model was evaluated using the coefficient of determination (R^2) and Root Mean Square Error (RMSE). The R^2 factor determines how well the dataset matches the model. R^2 is measured between 0 and 1. When R2 equals one, it indicates that the input variables can explain all variations in the dependent variables. Whereas R2 equals 0 indicates that none of the variability in the dependent variables can be accounted for by the input variables. The RMSE assists in determining the amount to which the data are concentrated around the line of best fit. The R2 and RMSE were demonstrated in equations (3) and (4) [30]:

$$R^2 = \left[\frac{n.\sum xy - \sum x.\sum y}{\sqrt{n.\sum x^2 - (\sum x)^2 . n.\sum y^2 - (\sum y)^2}}\right]^2 \quad (3)$$

$$RMSE = \sqrt{\frac{\sum_{y=1}^{n}(y - y_p)^2}{n}} \quad (4)$$

To define the error value of each test, variant analysis ANOVA and T-test were applied to analyze the average differences in significant data in the performance of the tests conducted [27]. According to [28, 31], ANOVA is used to analyze the differences among the group means and their associated procedures (such as "variation" among and between groups). In its simplest form, ANOVA provides a statistical test of whether or not the means of several groups are equal. The ANOVA test illustrates the variables by mean squaring and estimates the experimental errors at specific levels [29]. ANOVA is a method that can be used to compare the means of two or more samples using the F distribution. This method can be used only for numerical response data. In this research, data measurement of invasive and non-invasive methods for cholesterol (C) and glucose (G) act as a variable for input data.

To define summation, total Cholesterol or glucose (SST_{CG}) can be identified by equation (5):

$$SST_{C/G} = \sum(Y_{tCG})^2 - \frac{(\sum Y_{tCG})^2}{N_{tCG}} \quad (5)$$

The Summation square between the groups ($SSB_{C/G}$) can be calculated according to equation (6):

$$SSB_{C/G} = \left\{\sum_{i=1}^{a}\frac{(Y_{tCG})^2}{N_{tCG}}\right\} - \frac{(\sum Y_{tCG})^2}{N_{tCG}} \quad (6)$$

The Summation square within the group (SSW_{CG}) can be computed according to equation (7):

$$SSW_{C/G} = \sum_{i=1}^{a}(\sum Yt_{CG}^2) - \frac{(\sum Y_{tCG})^2}{N_{tCG}} \quad (7)$$

The degree of freedom (*df*) is used to compare the observed and expected data based on equations (8), (9) and (10) below:

$$df(T)_{C/G} = N_{tCG} - 1 \quad (8)$$

$$df(B)_{C/G} = N_{aCG} - 1 \quad (9)$$

$$df(W)_{C/G} = N_{tCG} - N_{aCG} \quad (10)$$

The MS deviation is calculated to measure the average square difference between the estimated and the actual value of cholesterol and glucose, as illustrated in equations (11) to (12) below:

$$MSB_{C/G} = \frac{SSB_{C/G}}{df(B)_{C/G}} \quad (11)$$

$$MSW_{C/G} = \frac{SSW_{C/G}}{df(W)_{C/G}} \quad (12)$$

Finally, to analyze whether the hypothesis is

accepted or rejected then the value of *F*-count is compared to the value of *F*-distribution (*F-critic*). Equation (13) illustrates the formula of value *F*-count for cholesterol *(Fc)* and glucose (F_G):

$$F_{C/G} = \frac{MSB_{C/G}}{MSW_{C/G}} \quad (13)$$

To identify the error value of this instrument, ANOVA analysis was performed to determine the result of analysis. ANOVA test results obtained P-value and *F*-count *(F)*, which can be used to determine whether the data is very statistically significant and whether the data is very discriminatory. The hypothesis is accepted if the *P*-value is greater than the specified level of significance (α = 5%) and the hypothesis is rejected if the *P*-value is smaller than the significant level. If the *F*-count value is smaller than *F*-critical or *F*-table, there is no significant difference between the measurement values of invasive and non-invasive techniques. Alternatively, if the *F*-count is greater than the F-table (*F*-critical) there is a significant difference between the two measurement techniques.

According to [32], the t-test is a statistical hypothesis test that determines whether there is a significant difference between two groups' averages. In this case: invasive and non-invasive data. The T-test statistic (T) is illustrated in the following equation (14):

$$T = \frac{\sum d_Y}{\sqrt{\frac{n\left(\sum d_{Y2}\right)-\left(\sum d_Y{}^2\right)}{n-1}}} \quad (14)$$

To justify the clinical accuracy of glucose, some researchers have applied the Clarke EGA as an essential tool to monitor levels of blood glucose [33, 34]. In this research, EGA is used to analyze the accuracy of the results of measuring cholesterol and glucose levels by comparing measurement instruments with sensors and reference values. The Clarke EGA was developed as one of the main standards in determining the accuracy of blood glucose measurements. Clarke EGA is divided into five zones A, B, C, D, and E by using Beckman Analysis, where Zones A and B are accurate glucose values that are acceptable, Zone C glucose values need correction so as not to be a poor result, Zone D the detected value is deviant and can be corrected, and, finally, Zone E is the wrong value of glucose level. The Clarke EGA was developed to analyze the accuracy of the results of measuring cholesterol levels using sensors by comparing reference values.

3. Results and Discussion

3.1. Clinical Reference Data

Figure 3 depicts the data collection process for measuring cholesterol and glucose using a non-invasive approach. To ensure accuracy, data collection was repeated five times for each sample.

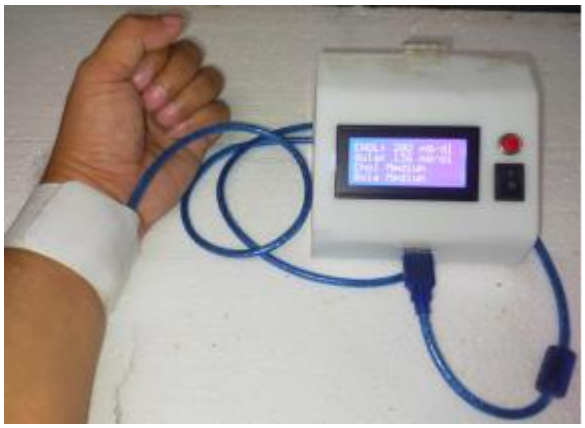

Fig. 3 Data collection process

Table 1 illustrates the result of measurements for 20 participants as a clinical reference for cholesterol and glucose, respectively.

Table 1 Clinical references of cholesterol and glucose

No.	Output Sensor for Cholesterol (Volt)	Cholesterol Invasive (mg/dl)	Output Sensor for Glucose (Volt)	Glucose Invasive (mg/dl)
1	0.59	145	0.77	335
2	0.6	150	0.62	92
3	0.61	173	0.61	89
4	0.66	226	0.61	86
5	0.63	192	0.65	107
6	0.68	256	0.65	116
7	0.58	140	0.8	390
8	0.71	275	0.65	104
9	0.73	280	0.67	126
10	0.74	293	0.76	292
11	0.70	256	0.71	190
12	0.69	240	0.73	230
13	0.56	125	0.6	76
14	0.55	129	0.6	72
15	0.62	200	0.74	260
16	0.63	210	0.68	163
17	0.62	188	0.73	215
18	0.68	236	0.69	180
19	0.63	216	0.67	150
20	0.60	153	0.66	120

Table 1 illustrates the results of measuring the voltage values for cholesterol and glucose in each participant. All data were obtained simultaneously using the auto-check invasive method. Due to the differences in the absorption of light into body tissues and the reflection of light, the value of the output, voltage is different for each participant. Therefore, the values of total cholesterol and blood glucose in each participant were also different.

3.2. Mathematical Prediction Model

The relationship between sensor output value and cholesterol and glucose levels can be characterized using statistical analysis results and mathematical equations, as shown in Figures 4, 5, and equations (15) and (16).

Figures 4 and 5 depict the statistical analysis of the output sensor (voltage) and both cholesterol and glucose levels. It is possible to monitor variations in the levels of cholesterol and glucose by 20 individuals ranging in age from 20 to 60 years old. Voltage and mg/dl are the units of measurement. Overall, the cholesterol and glucose levels increased as a result of the voltage applied.

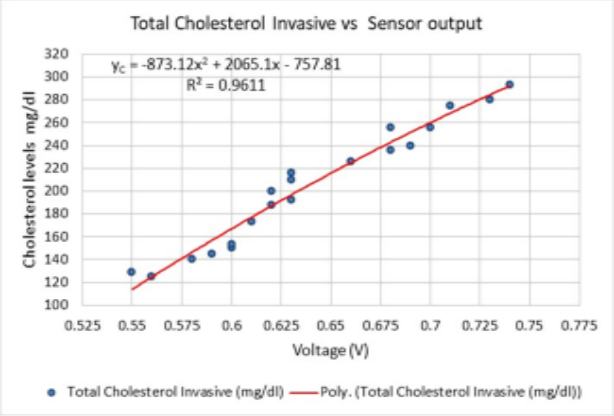

Fig. 4 Statistical analysis result of regression non-linear voltage output of sensor with blood cholesterol

The relationship between the sensor output and each participant's blood cholesterol level is shown in Figure 4. The output sensor of the individuals had a baseline of 0.55 Volt and a maximum of 0.74 Volt, which corresponded to cholesterol levels of 129 mg/dl and 293 mg/dl, respectively. According to Figure 4, non-linear regression depicts the relationship between them. For example: when the sensor output of 0.55 Volt resulted in a cholesterol level of 129 mg/dl. In contrast, when the sensor output was 0.56 Volt, the cholesterol level measured 125 mg/dl. This type of characteristic continued until the maximum value of sensor output was achieved. Therefore, the polynomial quadratic regression creates a mathematical model as illustrated in the following equation:

$$Y_C = -873.12x^2 + 2065.1x - 755.81 \quad (15)$$

This model explained approximately (R-squared) of the variability (R^2= 0.96). This indicated that blood cholesterol for every participant is based on the sensor output. Therefore, the null hypothesis is rejected and the alternative hypothesis is retained.

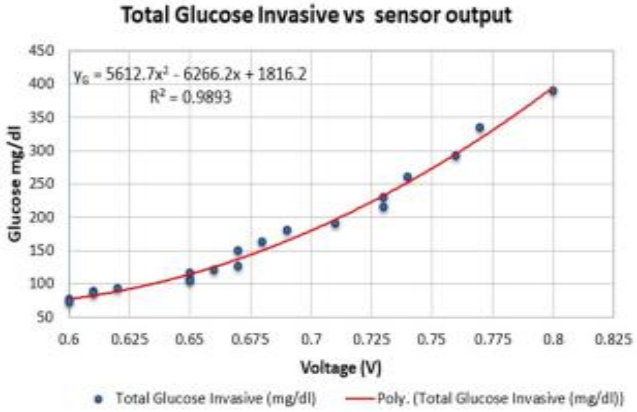

Fig. 5 Statistical analysis result of regression non-linear voltage output of sensor with blood glucose

Figure 5 demonstrates the relationship between the blood glucose level and the sensor output. The participant's output sensor began at 0.6 Volt and peaked at 0.8 Volt with glucose levels of 72 mg/dl and 390 mg/dl. As shown in Figure 5, non-linear regression is used to demonstrate the relationship between both of them. For example, 0.6 Volt of sensor output resulted in cholesterol readings of 72 mg/dl and 76 mg/dl. This pattern of behavior continued until the sensor output reached its maximum value. As a result, the polynomial quadratic regression generates a mathematical model, as seen in the equation below:

$$Y_G = 5612.7x^2 - 6266x + 1816.2 \quad (16)$$

This model clarified approximately (R-squared) of the variability (R^2 = 0.94). This model illustrates that sensor output and blood glucose levels for each participant indicate a strong relationship between the two variables. Consequently, the null hypothesis is therefore rejected and the alternative hypothesis is accepted.

3.3. Tool Testing

To justify the result of tool testing, 40 participants were chosen to compare the results of measurement of total cholesterol and glucose under the auto check (invasive) and sensor (non-invasive) methods, as illustrated in Table 2.

Table 2 Measurement results of cholesterol and glucose under invasive and non-invasive (sensor) methods

No.	Cholesterol invasive (mg/dl)	Cholesterol non-invasive (mg/dl)	Glucose invasive (mg/dl)	Glucose non-invasive (mg/dl)
1	145	157	335	320
2	150	167	92	90
3	173	177	89	83
4	226	225	86	83
5	192	197	107	116
6	256	243	116	116
7	140	146	390	397
8	275	268	104	116
9	280	284	126	138
10	293	292	292	297
11	256	260	190	198
12	240	251	230	234
13	125	125	76	78
14	129	114	72	78
15	200	187	260	254
16	210	197	163	152
17	188	187	215	234
18	236	243	180	166
19	216	197	150	138
20	153	167	120	126
21	189	186	108	107
22	253	248	99	96
23	217	231	94	92
24	206	221	127	127
25	191	206	139	131
26	306	324	109	120
27	231	246	124	130
29	285	267	152	149

Continuation of Table 2

30	214	216	125	126
31	191	201	119	127
32	225	232	104	110
33	244	227	114	114
34	169	169	95	101
35	288	292	108	111
36	209	198	100	102
37	183	182	123	114
38	174	178	153	157
39	168	180	95	105
40	177	193	114	110

Table 2 illustrates the measurement results of cholesterol and glucose under invasive and non-invasive methods for 40 participants. The measurement results show that there are differences in measurement results between invasive and non-invasive methods. The results are stable, but there are still differences in the results of the two measurement techniques.

3.4. Statistical Analysis Result

Equations (2), (3) and (4) are applied to define the statistical error analysis presented using the SEP, R2 and RMSE approaches. The research results specified that the values of SEP are 10,202 mg/dl and 9,236 mg/dl for blood cholesterol and glucose levels, respectively. The R2 of cholesterol and glucose were 0.94 and 0.95, respectively. This shows that the regression analysis implies that more than 94% and 95% of the data set can explain the variation in the predicted final cholesterol and glucose level. Similarly, the results of RMSE for cholesterol and glucose levels were 13.262 mg/dl and 7.45 mg/dl levels, respectively. This indicates that the value of error standard prediction under the SEP and RMSE methods is lower than the reference value. According to [35], the reference values for cholesterol and glucose are 30 mg/dl and 14.94 mg/dl based on the national cholesterol education program and the national committee for clinical laboratory standard, respectively. As a result, the measurement results for both cholesterol and glucose are within the acceptable range.

To define the accuracy of measuring results of both the invasive and sensor method show that the concept of ANNOVA and T-test comes into play in this research. ANOVA was used to analyze the results of measuring blood glucose and cholesterol components with invasive and sensor techniques. Equations (4) to (12) are applied to define the analysis variant of ANOVA, as illustrated in Tables 3 and 4.

Table 3 ANOVA analysis variant for cholesterol

Group	SS	df	MS	F-Count	T-Table (α = 0.05)
BG	87.94504	1	87.94		
WG	171149.1	78	2194.2	0.04008	3.96
Total	171237.1	79			

Table 4 ANOVA analysis variant for glucose

Group	SS	df	MS	F-Count	T-Table (α = 0.05)
BG	27.73955	1	27.7395		
WG	386401.8	78	4953.89	0.006	3.96
Total	386429.5	79			

Tables 3 and 4 above illustrate that the results of the F-count are 0.04008 for cholesterol levels and 0.006 for glucose levels. The value of F-table is 3.963 for cholesterol and glucose levels. This means that the F-count is lower than the F-table. From these results, it can be interpreted that the hypothesis is accepted, with the measurement results showing that there is no significant difference between invasive and non-invasive methods. Consequently, the NIR wristband sensor has good stability and accuracy.

For additional testing, T-test is applied to determine whether there is a significance difference between measurement results of invasive and non-invasive methods for cholesterol and glucose. Equation (13) is applied to calculate T-test analysis, as illustrated in Tables 5 and 6.

Table 5 T-test analysis variant for cholesterol

Group	Invasive	Non-invasive
Mean	210.05	212.1469626
Variance	2222.35641	2166.082771
Observations	40	40
Pearson Correlation	0.973774739	
Hypothesized Mean Differences	0	
Df	39	
t-value	-1.234365574	
P(T<=t) one-tail	0.112226479	
t Critical one-tail	1.684875122	
P(T<=t) two-tail	0.224452959	
t Critical two-tail	2.02269092	

Table 6 T-test analysis variant for glucose

Group	Invasive	Non-invasive
Mean	142.475	143.6527
Variance	4985.383974	4922.353965
Observations	40	40
Pearson Correlation	0.994149284	
Hypothesized Mean Differences	0	
Df	39	
t-value	-0.976624286	
P(T<=t) one-tail	0.167387254	
t Critical one-tail	1.684875122	
P(T<=t) two-tail	0.334774508	
t Critical two-tail	2.02269092	

Table 5 illustrates that t-value (-1.234) is less than t-table (1.684). This indicates that the difference in blood cholesterol levels from the results of invasive and non-invasive measurements is not significant. Similar to glucose analysis, Table 6 presents the t-value (-0.976) is less than t-table (1.684). This illustrates that there is no substantial difference in blood glucose levels

between invasive and non-invasive tests. Consequently, this sensor is stable and accurate for measuring both cholesterol and glucose levels.

In addition, the Clarke EGA is applied to quantify the clinical accuracy of both patients' cholesterol and glucose compared to reference values. Figures 6 and 7 (below) illustrate the Clarke EGA analysis for both cholesterol and glucose.

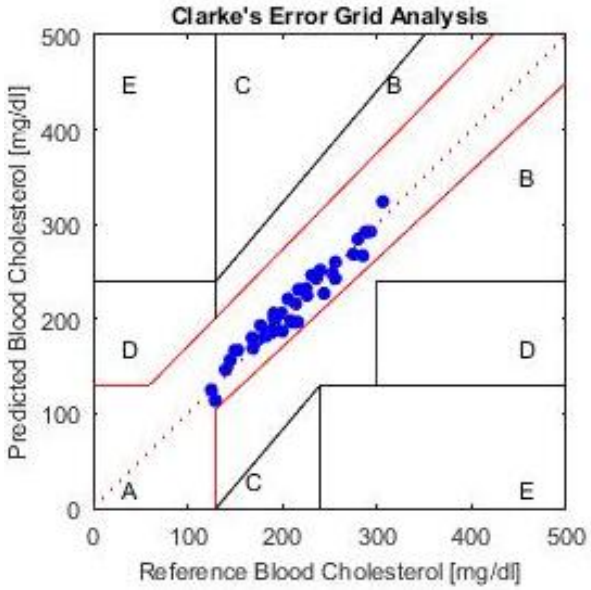

Fig. 6 Clarke error grid analysis for cholesterol

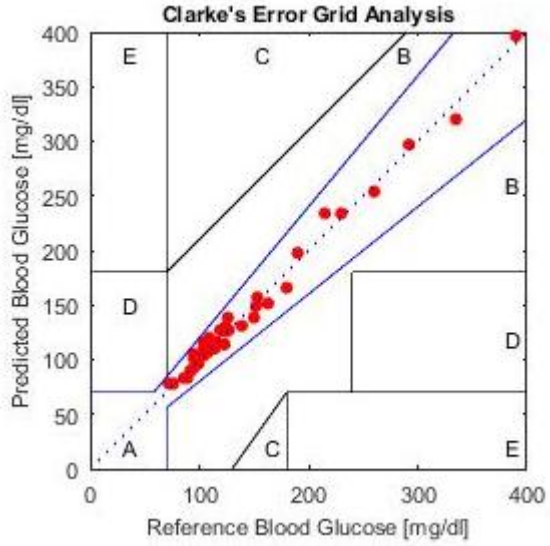

Fig. 7 Clarke error grid analysis for glucose

Figure 6 depicts the Clarke EGA based on graphical plotting of the invasive (reference) and non-invasive (predicted) cholesterol values of the volunteer participants obtained during the experimental pilot study. The Clarke EGA-based respective cholesterol determining accuracy-dependent percentage values from Figure 6 above are categorized as follows: A zone=100%, B zone=00.00%, C zone=00.00%, D zone=00.00% and E zone=00.00% respectively. The analysis's findings show that the predicted values of blood cholesterol concentration obtained using the invasive models are more concentrated in region A. This indicates that the proposed model is clinically acceptable.

Figure 7 illustrates the Clarke EGA based on the glucose determination accuracy. Based on this, Figure 7 indicated that the predicted value of glucose for every zone can be classified as follows as: A zone equals 100%, B zone equals 0%, C zone equals 0%, D zone equals 0%, and E zone equals 0%. Therefore, the predicted value of glucose was evenly distributed across region A. This suggests that the prediction accuracy of the non-invasive model is clinically acceptable.

The combination of infrared light and a photodiode adds a new dimension to non-invasive blood cholesterol and glucose levels measurement. However, a few undesirable erroneous signals were acquired as a result of numerous factors such as skin tissue pigmentation, background light intensity, pulsatile blood flow, machine-associated drifts, time dependent drifts, motion related artifacts, other physiological or pathological causes, etc. All of these conflicting factors alter the blood tissue complex-induced bio-signals and have an incorrect impact on blood cholesterol and glucose levels readings.

4. Conclusion

The proposed research developed an innovative method that allows patients to measure cholesterol and glucose with high accuracy and independently at a lower cost. The result of the statistical analysis indicated that both cholesterol and glucose levels were measured in accordance with the standard. Blood cholesterol and glucose levels do not differ significantly between invasive and non-invasive examinations. Consequently, the proposed method can be applied to detect cholesterol and glucose simultaneously. Additionally, the analysis using the Clarke EGA method, shows that the level of data accuracy for non-invasive cholesterol and glucose compared with invasive measurements, predicts 100% of patients in the zone A category, but not in zones B to E. Therefore, the NIR bracelet sensor is feasible to implement. The proposed method is only appropriate for 20-60-year-old patients.

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