Non-invasive blood glucose measurement

Measurement of bioeletrical signal

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Abstract—**Impedance of blood relatively affected by blood-glucose concentration. Blood electrical impedance value is varied with the content of blood glucose in a human body. This characteristic between glucose and electrical impedance has been proven by using four electrode method's measurement. The bioelectrical voltage output shows a difference between fasting and non-fasting blood glucose measured by using designed four tin lead alloy electrode. 10 test subjects ages between 20-25 years old are UniMAP student has been participated in this experiment and measurement of blood glucose using current clinical measurement and designed device is obtained. Preliminary study using the developed device, has shown that glucose value in the range of 4-5mol/Liter having the range of 0.500V to -1.800V during fasting, and 0.100V or less during normal glucose condition, 5 to 11 mol/liter. On the other hand, It also shows that prediction of blood glucose using this design device could achieve relevant for measurement accuracy compared to gold standard measurement, the hand prick invasive measurement. This early result has support that there is an ample scope in blood electrical study for the non-invasive blood glucose measurement.**

Keywords-Blood Impedance, Blood Glucose, Bioelectrical, Four Electrodes Measurement Method

I. INTRODUCTION

A. *Blood Resistivity and Impedance*

Resistivity and impedance value of biological tissue can be measured and has been introduced more than 100 years ago after introduction of techniques to measure resistance and eventually capacitance by alternating currents became available. As discussed earlier in previous papers, blood consists of blood cells, plasma and platet which are these parameters can be modeled by electrical properties by Hober Rudolf as introduce by H.P Schwan in his article [1]. Whenever alternating current or direct current applies to the biological tissue, the voltage measurement can define by its resistance, conductance and the impedance of the tissue. With those values, the biological tissue, itself can be characterized, to some of the application's interest as an example to determine or diagnosis of disease in the human body.

The electrical characteristic of suspensions of blood is model using well known three-element, which has been introduced as electrical equivalent circuit as shown in Figure 1. The resistor R_p stands for the electrical resistance of plasma, while the effect of the cell membrane capacitance of the erythrocytes is modeled by the capacitor C_m. and the resistor R_i, represents the effect of the interior cell resistance of the erythrocytes [2],[3], [4] [5].

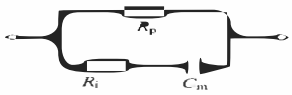

Figure 1- Electrical characteristics of blood [1]

Blood is the medium transportation of glucose and other nutrient to the whole body. Thus, the composition of blood vessels is not only limited to blood but mixing with other components. Basically, blood contains of 55% of plasma and 45% of blood cell, including 99% is red blood cell (erythrocytes) and 1% is a combination of white blood cell (leucocytes) and platelets [6]. The glucose and other nutrient are including in 55% of plasma, which will give influent to the blood resistivity and impedance. In these studies, the electrical properties of erythrocytes only considered because it is the only part of blood constituents who influences the impedance of blood. Leucocytes and the platelets are not importance for the electric properties of blood and can be negligible because they are too small [7]. The higher concentrations of glucose in blood influence the volume of red blood cell in blood capillary. It is shown in this Figure 2.

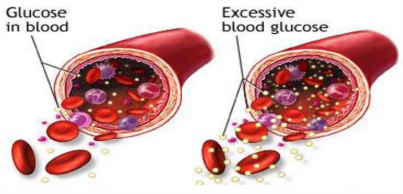

Figure 2: blood with glucose in blood capillary [8]

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B. *Needs of Non-Invasive Technique*

The diabetic patient need to tests blood glucose is less than twice a day with the average of 1.6 times each day [9]. The main issue for the invasive finger pricking for glucose tests are painful. Where requirement need them to prick at least once each time the glucose test is done [10]. Typical invasive glucose measurement device required a small sample blood to do measurement. Contrary, this invasive procedure is not convenient for the long term diabetic patient particularly the type 2 diabetes mellitus as medical recommended self-test is 4 to 7 times per day [11]. This could result in bruising and the high risk of the infection.

Non-invasive measurement device do not need of drawing a blood sample from biological body. This technique is applied to overcome the pain, scare procedure, infections and also to avoid damage of nerve endings because of blood draw frequently [12]. In electrical impedance measurement, it is importance that current source supply must be regulated to avoid the tissues or cells damage. Webster purposed to use a current greater than 1 mA to 10mA at low frequencies. Mohamed et al shows frequencies above 20 kHz are used to avoid perception of the current as the previous researchers they used 2 mA current supplies with 50 kHz .

Many researcher groups, prove that some factors that influence the value of blood impedance such as the orientation and shape of erythrocytes [13,[14]. Moreover, the temperature of blood and amount of erythrocytes also will affect the impedance of blood [15]. Impedance of the blood is also different during systolic and diastolic cardio cycle and during flowing and resting blood [16]. These factors should be considered when to develop a device to diagnose the abnormalities such as of blood flow, to measured aggregation of erythrocytes, to measure changes in tissue volume, to detect venous thrombosis and to monitor infant apnea by using blood impedance concept [17],[18].

II. METHODOLOGY

A. *Hardware*

In measuring the blood electrical impedance, the electrode was made with using four tin-lead solder electrode. Tin-lead solders is choose only for the electrical connection and ease of electrode design. Alloy's material commonly used in the electrical solder to improve connection and having a lower impedance value to reduce error in measurement. Four rows of electrodes with length 10 mm and width of 2 mm is applied. The distance between the two inner electrodes is 3mm, while the distance between the two outer electrodes is 13mm. The finger area placed on the electrode must be constant to ensure correct voltage reading. Hence, subject finger should touch all 4 electrodes on the correct length and width. Figure 3 shows the design of the electrode.

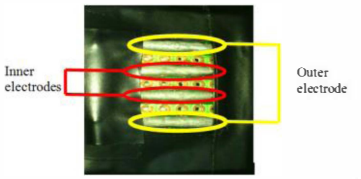

Figure 3: Finger electrode

Figure 4 shows the measurement setup. It consists of three parts, constant current source, finger electrode placement and differential voltage circuit. The current source is applied to the outer electrode with label as 1 and 4. The other electrode which is electrode 2 and 3 is a differential voltage electrode which measures the voltage drop by finger.

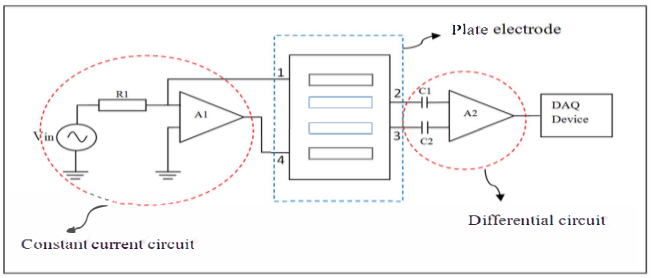

Figure 4: Hardware Circuit

In a current source circuit, the current output from this circuit is 1.14mA constant. As presented earlier, the suitable range of current flow to the human body electrical measurement is about 1mA to 10mA with frequency set to be 55KHz. Output voltage will be connected to the data-acquisition device for output sampling, reading, and writing to a file.

B. *Software*

Output from the circuit will be feed to LabVIEW for sampling, filtering and writing data. Using data acquisition from National Instrument, It will be a sample the analog data or voltage to the digital data with 100 samples at 100 Hz and will stop the sampling at 200th seconds. The filtering type is using Butterworth high pass with cutoff frequency of 50 KHz. This is because, this project hardware used the 50 KHz supply to run the circuit. The filter will remove the entire signal below 50 KHz, including power line noise at 50 Hz.

C. *Electrical equivalent circuit*

In order to get correct measurement practice, electrical equivalent circuit must be understand clearly to improve error in measurement. Figure 5 shows that due to electrode circuit and effects of skin impedance in measuring the level of glucose in the blood, mathematically it can be calculated as,

$$Zs = Zt // Zab // Zib \quad (1)$$

$$Zd = Zt // Zab \quad (2)$$

Where Zt is the tissue's impedance, Zab is the artery blood impedance, and Zib is incremental blood in artery, and Zd is the total summation of impedance [19], which is more than a total of impedance during blood incremental, Zs. Based on this equations, it is show that changing of blood volume will also be changing the impedance value based on this equation.

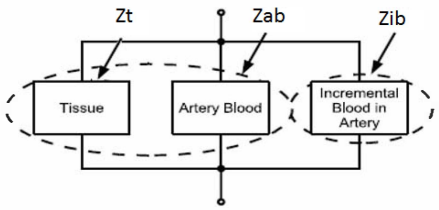

Figure 5: Electrical components in finger during measurement [17]

The electrode use on this measurement also contribute another impedance which normally has been identify and known as electrode electrolyte interactions [20]. As example shows in figure 6, model of electrode equivalent circuit.

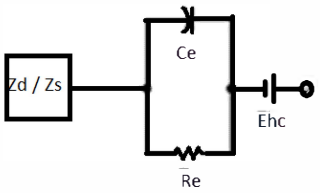

Figure 6: Equivalent circuit of the biopotential electrodes

Ehc is the half-cell potential, Re and Ce impedance components associated with the electrode-electrolyte interface and polarization effects, and connected in series; Zd / Zs is an electrical equivalent model for human finger as shows in Figure 5. However, in this study, assumption has been made such as by applying frequencies more than 20Khz. The impedance of skin (epidermis,dermis) could be neglected and constant resistance-impedance of the finger electrodes. The blood pulse from equation (1) and equation (2) also neglected and an average of reading within 3 minutes during impedance measurement is applied.

D. Protocol and Data Collection

The subjects experimented is considered are fit and free from any disease. 10 healthy female volunteers in the range of age from 20 to be 25 years old for the experiment. The subject weight and height are in range 50 to 70 kg and 150 to 170 cm is recorded. During the experiment, temperature measured on subjects is 36.8 to 36.9 Celsius.

Before the experiment begins, the subjects have been briefing with the procedure of the experiment, where this experiment need performs two conditions, fasting and non-fasting. Firstly, subject need to fasting for eight hours before the experiment start. In this condition, the normal of glucose level in blood can be measured [21]. This experiment started with the measured the glucose level during fasting at the end of the eight hours' time, using the glucometer. Then, subject need to place a fingertip on top of the electrodes. Data (voltage) will be collected in 3 minutes using the design device. Then, subject need to drink or break their fasting with juice drink with the estimation of 30 grams of glucose per serving. After 40 minutes of drinking, glucose level needs to measure again using the glucometer and using designed device for 3 minutes. Figure 7 shows the experiment flow.

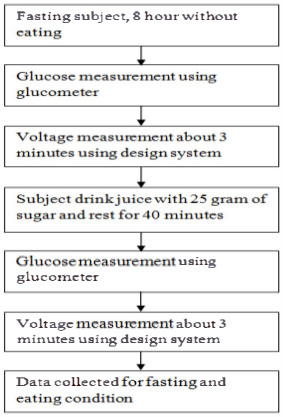

Figure 7: block diagram of the procedure

E. Data Analysis

Regression analysis is a technique for modeling and analyzing several variables, when the focus is on the relationship between a dependent variable and independent variables as an example in this project voltage as independent and mol/liter of glucose as a dependent variable. In the other word, regression analysis helps value of the dependent variable's changes when the independent variable is varied [22]. Usually, regression analysis estimates the conditional expectation of the dependent variable given the independent variables. Regression analysis is widely used for prediction glucose prediction by many research groups, in this studies the prediction of blood glucose in mol/liter is based on the value of output voltage from the design device.

III. RESULTS

The experiment for measure voltage of blood glucose during fasting was done to the 10 fasting for eight-hour subjects while for non-fasting, ready after 40 minutes the

subject drink juice with an estimate 50 grams of glucose. Figure 8 shows the voltage measured for fasting and non-fasting condition of each subject. As plotted on graph, voltage measured during both conditions exposed the difference between them. Voltage during fasting represented by blue line mostly indicates higher than the non-fasting voltage represent by red line. The voltage for fasting condition obtained by 8 from 10 subjects is higher than reading voltage for non-fasting condition, while for other 2 subjects, it vice versa. This can be simply concluded that the voltage is higher to lower glucose level. This graph has shown proved that voltage measurements during fasting and non-fasting. It can be concluded, there has a different voltage with the glucose level varied.

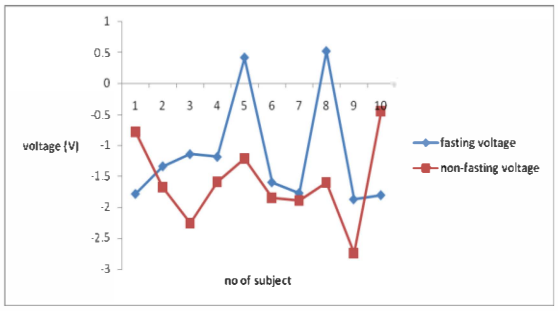

Figure 8: Voltage measured from a design device.

Early prediction of blood glucose is made by using regression analysis. 20 data have been using for this analysis and plotted by a scatter graph to expose the relation between voltage and glucose level as shown in Figure 9. To obtain accurate relationship between two variables, the polynomial trend line created to form an equation. The table of prediction able to form based on the equation from the polynomial trend line.

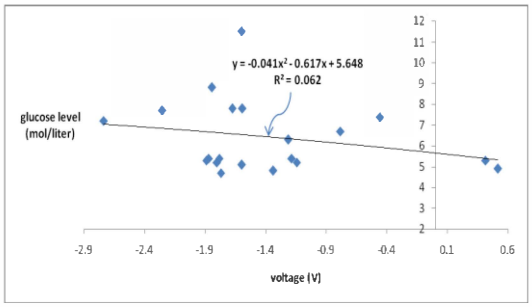

Figure 9: Scatter graph for both conditions

Unknown y from equation (3) is representing mol/liter of glucose and x is representing a voltage. The value of y can be able to determine at the present of value x.

$$y = -0.041x^2 - 0.617x + 5.648 \quad (3)$$

TABLE I BLOOD GLUCOSE PREDICTION USING DESIGN DEVICE

Voltage	Prediction mol/liter
1.6251	4.5
0.2198	5.5
-1.6549	6.5
-4.1985	7.5

Table 1 had presented the sample of prediction using (3). The predictions of mol/liter from value of voltage have been done with the acceptable measurement accuracy. The value of accuracy will based on the value of Standard Error of Prediction. Samples of prediction were the value of voltage selected to predict the output of mol/liter. The voltage around 1.6251V to -4.1985V had predicted the value of glucose around 4.5 to 7.5 mol/liter of glucose. The negative voltage shown that measurement from inner electrode is dominant by negative current. It also shows that, measurements is influenced by the individual biological differences.

TABLE II: BLOOD GLUCOSE MEASUREMENT USING DESIGN DEVICE AND COMPARISON WITH CURRENT STANDARD

Voltage (V)	Prediction (mol/liter)	Current standard (mol/Liter)
-1.071	5.7	5.4
0.212	5.3	5.2
-3.017	6.8	7.2

Table 2 shows some result of measurement between design device with conventional current method. From the experiment using the design device, the output voltage is not much stable during first and second reading within 1 minutes average value and compared to the hand-prick method which provide more precise reading. Comparison one to one device still having a large differences of blood glucose reading.

IV. DISCUSSIONS

The electrical signal measure from biological body having a potential to be used for determination of blood glucose non-invasively. In this studies, early result shows that design device and the blood glucose prediction can be achieved the objective to overcome the finger-prick blood glucose measurement.

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