International Journal of Biological, Physical and Chemical Studies
ISSN: 2709-1554
DOI: 10.32996/ijbpcs
Journal Homepage: www.al-kindipublisher.com/index.php/ijbpcs

IJBPCS
AL-KINDI CENTER FOR RESEARCH AND DEVELOPMENT

| **RESEARCH ARTICLE**

Correlation of Whole Blood Cell Morphology on Electrical Impedance Spectroscopic Characteristics on the Severity Level of Ischemic Stroke Patients

Ferhiyan Nabila[1] ✉ Chomsin Sulistya Widodo[2] and Didik Rahadi Santoso[3]
[123]Department of Physics, Faculty of Mathematics and Natural Sciences, Brawijaya University
Corresponding Author: Ferhiyan Nabila, **E-mail**: profesormuda876@ub.ac.id

| ABSTRACT
This paper discusses the influence of peripheral blood smear morphology methods on the electrical impedance spectroscopic characteristics of blood samples from ischemic stroke patients. In this study, there were 26 blood samples, consisting of a control group with 5 blood samples and a group of ischemic stroke patients with 21 samples with varying degrees of severity. The methods used are electrical impedance spectroscopy (EIS) and whole blood cell morphology methods. The EIS method was carried out using the BISDAQ tool and application, and results were obtained in the form of Bode Plot, Bode Phase Plot, Nyquist Plot, and measurement data values in the form of Ms. Excel. Meanwhile, the Morphological method is carried out by making a peripheral blood smear, then viewing and obtaining an image using a digital microscope, and then counting the number of cells using the Image Raster application. Based on the results of the method carried out, the correlation can be seen to conclude that whole blood cell morphology greatly influences the characteristics of EIS and determines the severity of ischemic stroke patients.

| KEYWORDS

Electrical Impedance Spectroscopy, Whole Blood Cell Morphology, Severity Levels in Ischemic Stroke Patients

| ARTICLE INFORMATION

ACCEPTED: 02 November 2023 **PUBLISHED:** 30 November 2023 **DOI:** 10.32996/ijbpcs.2023.5.2.5

1. Introduction
Stroke is a disease that has the third highest death rate after coronary heart disease and cancer. Stroke is the biggest contributor to disability in the world, so stroke is still one of the main problems in the world health sector (Mutiarasari et al., 2019). According to World Stroke Organization data, every year, there are 13.7 million new cases of stroke in the world, and around 5.5 million people die. The rest suffer mild or severe disabilities. Every year, cases of stroke sufferers always increase (Bilqis, 2022).

Stroke is a condition when the blood vessels in the brain become blocked and rupture so that blood circulation to the brain will be disrupted due to reduced brain function and can even stop the supply of oxygen and nutrients from being distributed to the brain bnormalities in the blood lipid profile cause stroke, the main ones being an increase in total cholesterol, triglycerides, and LDL (Low Density Lipoprotein) levels as well as a decrease in HDL (High Density Lipoprotein) cholesterol levels. These deposits are fat that lines the walls of blood vessels, and it is called atherosclerosis. Atherosclerosis is the main cause of ischemic stroke (Mandala, 2015) .

The death of stroke sufferers occurs due to several causes, one of which is the fear of being examined at the hospital, either because they are afraid of the examination methods provided, equipment that is considered scary because of the effects of radiation, or expensive costs. However, now many new methods have been used with the advantages of being non-invasive, low cost, portability, getting real time results, and the use process is also easy. This method is called Electrical Impedance Spectroscopy (EIS), which is a method of measuring the electrical properties of an object through surface measurements. This method shows

Copyright: © 2023 the Author(s). This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC-BY) 4.0 license (https://creativecommons.org/licenses/by/4.0/). Published by Al-Kindi Centre for Research and Development, London, United Kingdom.

promise for detecting diseases that may have previously gone undetected. This is based on measurements of normal and abnormal electrical impedance (Braun et al., 2017).
Electrical impedance measurement technology in detecting disease has become a topic of great interest to scientists. Because tissue consists of cells and an extracellular medium, their electrical properties will determine the properties of the tissue. The extracellular medium consists mainly of ionic solutions. Cells consist of a cell membrane and an intracellular medium. The cell membrane consists of a lipid and protein bilayer. Due to this structure, cell membranes are primarily capacitive, with the exception of selective permeability (the ability of a substance/membrane to pass a certain number of particles that penetrate or pass through it), which defines membrane conductivity. Selective permeability is a function of the physiological processes of living cells. This can be illustrated in Figure 1, which shows that the circuit is equivalent in cells and has different conductance and dielectric properties. The cell membrane has properties like a capacitor; if in an electrical circuit, it can be analogous to the components R and C. Cm is the capacitance of the double layer membrane, Ri is the resistance inside the cell, Re is the resistance outside the cell, and Rm is the membrane resistance.

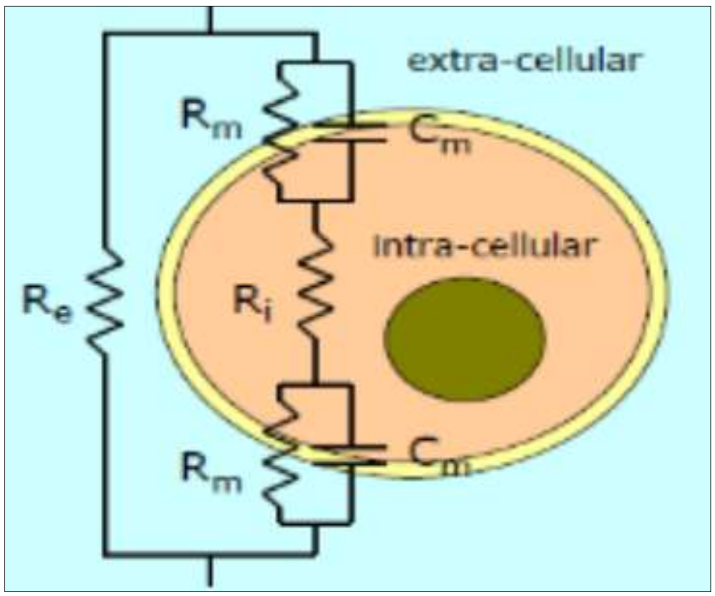

Figure 1. Equivalent Circuits in Cells

The values of Cm, Ri, Re, and Rm are characteristics of a tissue which are related to the nature of the cell membrane and the number of ions contained in the tissue. Based on these indicators, it can be the cause of differences in normal and abnormal/damaged tissue impedance values (Salamena et al., 2017). The biological material that will be used as a medium for measuring the impedance value of ischemic stroke sufferers is blood. Blood has a very important role in circulating oxygen, nutrients and functional components throughout the body. Blood is composed of red blood cells (Erythrocytes), white blood cells (Leukocytes), blood platelets (Platelets) and blood plasma. Blood components will be damaged when someone suffers from a stroke (Roubinian et al., 2019).

When erythrocytes pass through the narrow surface of a capillary, they need to change shape to allow passage. Thus, in microcirculation, resistance flow is mainly influenced by the ability of individual cells to change shape, or what is called cellular rheology. This is a way for cells to adapt so they can pass through narrow surfaces and a way for cells not to die easily.

Damage to blood cells can be seen using morphological methods. Peripheral Blood Morphology or Blood Smear is used to determine and evaluate red blood cells, white blood cells and platelets. The number of blood cells and their shape can be seen using the morphological method, which is commonly used to help diagnose and monitor various disease deficiencies and disorders that involve the production, function and lifespan of blood cells. Morphology can describe blood cells through color, shape and size, which can be observed using a microscope (Bunga et al., 2019).

There are several types of damage that occur to red blood cells (erythrocytes), namely damage based on color, size and shape. In damage based on color, there are 4 types of erythrocyte color variation conditions, namely Normochromia, Hypochromia, Hyperchromia, and Polychromasia. Normochromia is a condition of erythrocytes with normal hemoglobin concentration, where the color is red, with the central area (central pallor) being paler. The red color of erythrocytes is a reflection of the presence of hemoglobin in the cells. Meanwhile, the pale color is a thin part of the cell, with a diameter not exceeding one third of the cell. Hypochromia is a condition where erythrocytes have a hemoglobin concentration that is less than normal. Hypochromia has a central pallor measuring more than one third of the cell diameter. Hyperchromia is a condition of erythrocytes with a hemoglobin concentration that is more than normal. Polychromasia is a condition where erythrocytes are larger and bluer in color than normal erythrocytes.

Based on the size of erythrocytes, there are 4 types of size, namely normative, macrocytosis, microcytosis and anisocytosis. Normocytic has a normal size of 6.8 – 7.5 µm. Macrocytosis is a condition where erythrocytes have a diameter of more than 8.2 µm, while microcytosis is a condition where the average diameter is less than 6.2 µm. Anisocytosis is a variation in the size of erythrocytes or erythrocyte volume on peripheral blood smears (HDT), which is usually found in patients with chronic anemia in the severe category. Apart from changes in color and size, there are changes in shape in erythrocytes; these changes include blister cells, acanthocytes, spherocytes, target cells, stomatocytes, burr cells, sickle cells, leptocytes, helmet cells, schistocytes, teardrop cells, oval macrocytes, elliptocytes, crenation cells, poikilocytosis. Changes in shape in erythrocytes can be seen in Figure 2 as follows (Magne et al., 2015).

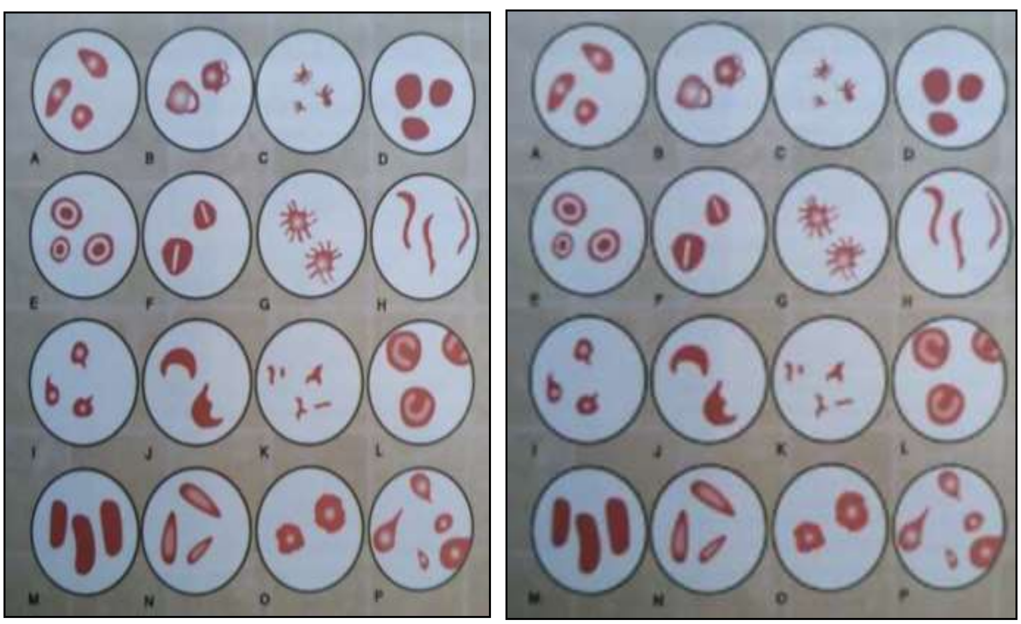

Figure 2. Several shape changes in erythrocyte cells, (a) Normal erythrocyte E cells, (b) Blister cells, (c) Acanthocyte cells, (d) Spherocyte cells, (e) Target cells, (f) Stomatocyte cells, (g) Burr Cells, (h) Sickle Cells, (i) Leptocyte Cells, (j) Helmet Cells, (k) Schistocyte Cells, (l) Tear Drop Cells, (m) Oval Macrocyte Cells, (n) Elliptocyte Cells, (o) Crenation cells, (p) Poikilocytosis cells

Impedance measurements on cells are carried out using small AC signals in the frequency range of 100 Hz to 100 kHz; this is done so as not to damage or affect the cells. The small signal does not damage or affect the cell and limits the measurement to the pseudo-linear region. In this method, the input voltage $V(f)$ is applied through an electrode that is in direct contact with the material. Electrical impedance (f) is measured as a function of frequency and can be represented by $(f) = V(f)/I(f)$, where $I(f)$ is the electric current injected by the electrode. Such measurements provide a safe, non-invasive, and relatively inexpensive method for measuring tissue properties. Then, the value of the resulting current or voltage will be measured. When the cells stick and spread on the electrode, the impedance value increases. This is because the cell membrane is an insulator that blocks current. (Wegener et al., 2000).

Based on the explanation above, there are many stroke sufferers around us. Apart from that, stroke is a dangerous disease because it has the third highest death rate in the world and is the largest contributor to disability. So, the author wants to research the influence of whole blood cell morphology on electrical impedance spectroscopic characteristics on the severity of ischemic stroke patients. This research aims to provide information about the severity of ischemic stroke suffered by stroke patients so that they can prevent it from progressing to the next stage of severity.

2. Research Methods

This research was conducted at the Faculty of Mathematics and Natural Sciences, Brawijaya University, Malang, and samples were taken at Sakinah Islamic Hospital, Mojokerto. The tools and materials needed include a thermometer, vacuum tube, humidity meter, shrynge, alcohol and cool box. The tools used for microscopic testing of blood cells are a computer microscope, spreader and glass slide/preparation. The tools used for spectroscopic measurements of electrical impedance are a series of BISDAQ test equipment, the BISDAQ application on a laptop, and IDE electrodes. The materials used for this research were blood samples or Whole Blood Cells from ischemic stroke patients and healthy people.

In this study, the samples used were blood samples from ischemic stroke patients with various levels of conditions, namely from mild levels in the form of stroke symptoms, moderate levels in the form of ischemic stroke with various conditions, and severe levels in the form of paralysis. Two methods are used in this research, namely the EIS test method and the morphology test method.

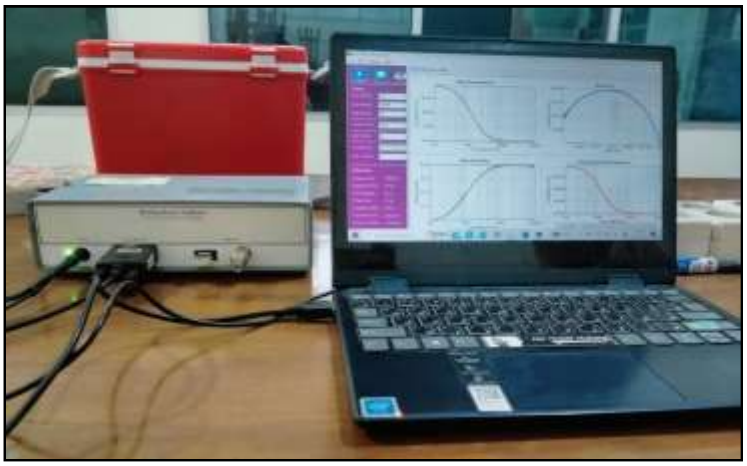

Figure 3. EIS (Electrical Impedance Spectroscopy) Test with Samples of Ischemic Stroke Patients and Healthy People

The EIS test is used to measure the impedance value of a biological material; in this study, the biological material is blood. The set of tools BIS used to measure impedance values has a system that includes a set of BIS tool sources, AC current by injecting 10 μA current, IDE electrodes and a display of results from the BISDAQ application on a laptop. The system will be integrated into an impedance measurement system based on the Bioelectrical Impedance Spectrometer, which can measure biological materials with IDE-based electrodes. Data from the measurements will be displayed via the BISDAQ application on the laptop. The data display will be plotted in the form of Bode and Nyquist graphs. The Bode Plot is a graphic plot that shows the relationship between the electrical impedance value of the sample and the frequency given to the sample. Bode Plot is used to graph phase differences, which have a relationship between the frequency given to the sample and the phase difference obtained. Nyquist Plot is a graph that connects Zreal and Zimaginer values. The EIS test can be used to detect a person's disease status and its severity.

Figure 4. Morphology Test Using a Digital Microscope of Blood Samples from Ischemic Stroke Patients and Healthy People

The Morphological Test can be used to find a lot of information from the results displayed in terms of changes in shape, color, and number of blood cells. The morphological tests used are blood samples that are formed into peripheral blood smears (ADT), digital microscopes, and image raster applications on laptops. ADT placed on a Digital Microscope can be viewed using 10x magnification to obtain morphological images of whole blood cells. Then, an application in the form of an Image Raster is used to calculate the number of each desired cell so that the results obtained are the number of erythrocyte cells (normal and abnormal), leukocyte cells and platelet cells.

3. Results and Discussion

Measurements using the EIS method are currently widely used because this method is simple, non-invasive, and portable; results are obtained immediately and are not expensive. The EIS method uses a medium in the form of biological material, which in this study were blood samples from ischemic stroke patients with a total of 21 samples and blood samples from healthy people with a total of 5 samples. The sample of ischemic stroke patients will be given codes P1 to P21, while 5 healthy people will be given codes K1 to K5 as the control group. Electrical impedance measurements were carried out in the frequency range of 100 Hz to 100 kHz by injecting an AC current of 10 µA. Low frequencies can be used to determine the characterization of biological cells regarding cell morphology, adhesion and movement information. This happens because low to medium frequencies mostly flow current around the dielectric cell membrane. Frequency dependence of impedance signal magnitude and impedance signal phase of biological tissue. The plot of impedance dependence on frequency shows three regions, namely alpha (α), beta (β) and gamma (γ) dispersion, respectively, at low, medium and high frequencies (Y. Xu et al., 2016). When the measurement frequency increases, the phase of the impedance signal will increase, and the magnitude of the impedance signal will decrease.

Impedance measurements using the Electrical Impedance Spectroscopy (EIS) method produce results in the form of Bode plots, Nyquist plots and data tables on Mc. Excel, which can be seen in Figure 5.

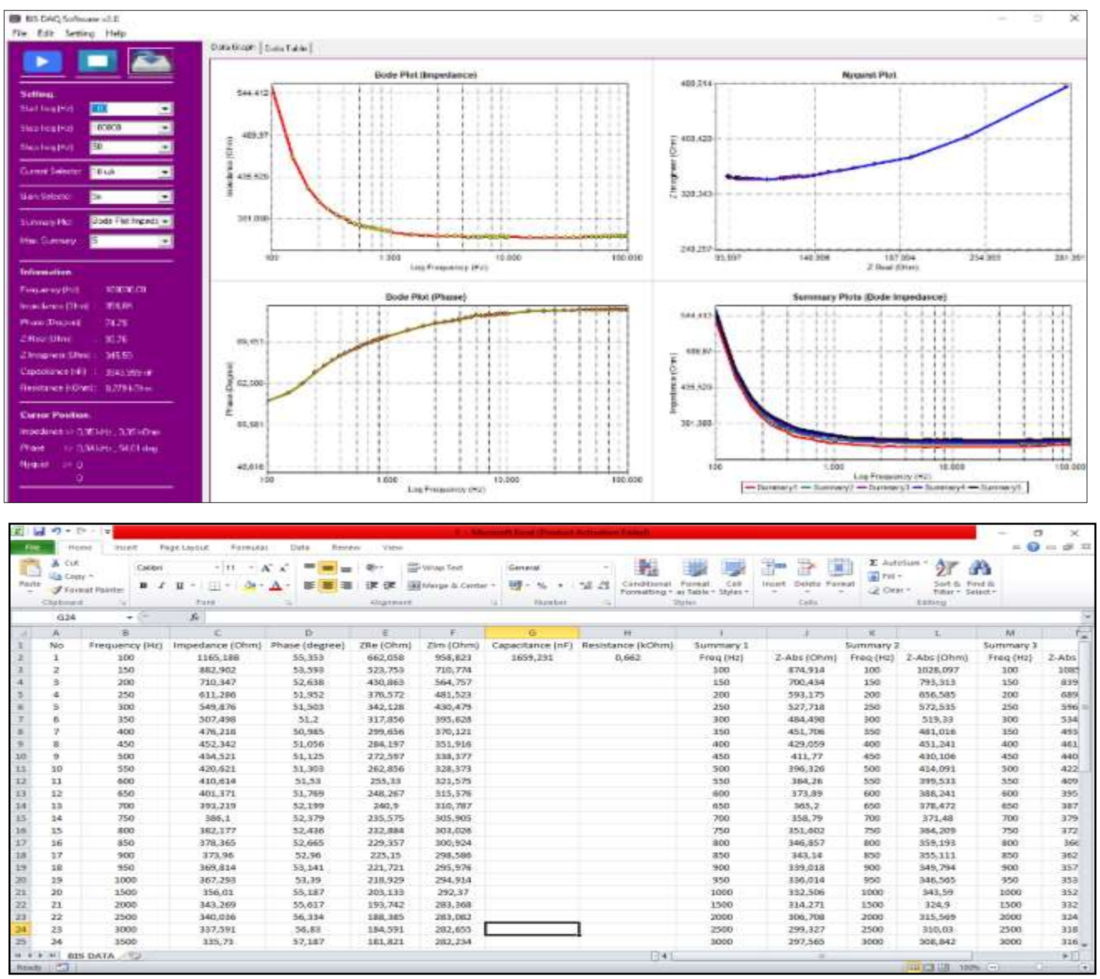

Figure 5. a) Display results in the BISDAQ application, b) Data table of BIS tool measurement results

The bode plot consists of two graphs, namely, a graph of the relationship between frequency and impedance and frequency and phase difference. The information displayed is in the form of impedance values (total, real and imaginary impedance), phase difference values, and component values (resistance and capacitance). Based on the research obtained, the results of the bode plot are shown in Figures 6 and 7. Figure 6 will provide information about the bode plot of the relationship between frequency and electrical impedance. Figure 7 provides information about the measured phase differences. Figure 7 a shows the plot of the control group, and Figure 7 b shows the plot of ischemic stroke patients with various levels of severity.

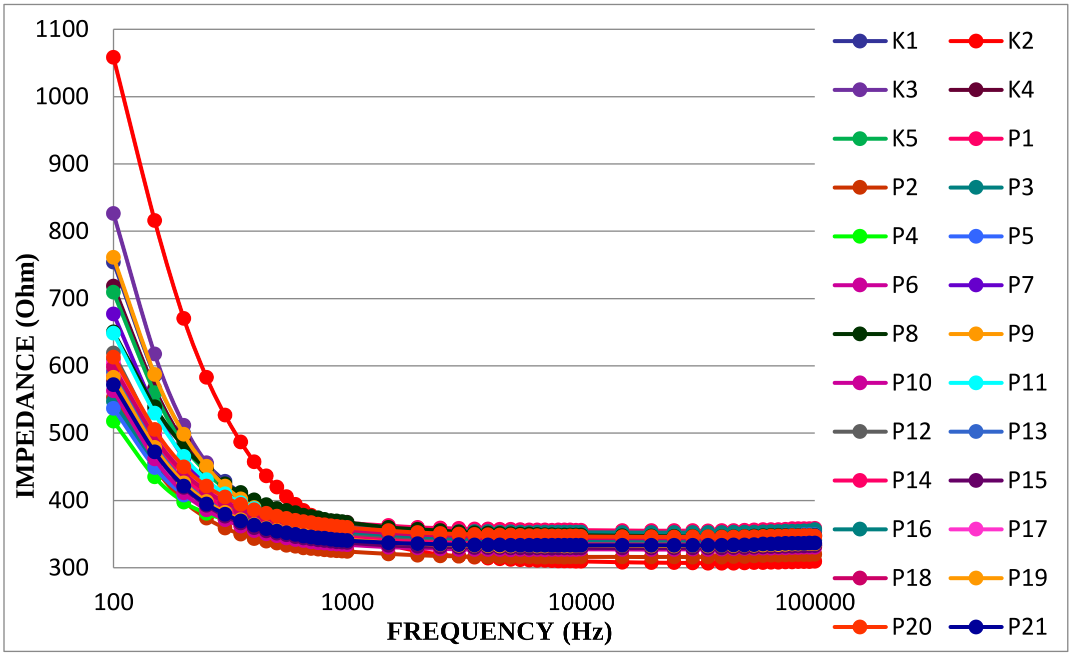

Figure 6. Bode Plot of Ischemic Stroke Patients and Control Group

Figure 6, which is a bode plot of impedance from the measurement results, shows that there are differences in the characteristic impedance values of various variations in the number of red blood cells with a frequency range of 100 Hz to 100 kHz. At frequencies between 100 Hz to 1 kHz, there is a decrease in impedance values; this occurs due to the capacitive nature of the measured system behavior or phenomena that occur in materials when an external current is applied. When the frequency is 1 kHz to 100 kHz, a relatively stable impedance value is obtained. In this measurement, it can be ascertained that the impedance value of a biological material will be inversely proportional to the given frequency value because the smaller the given frequency, the greater the measured impedance value.

The results shown by the impedance bode plot show that the higher the graph line shown in Figure 6, the higher the electrical impedance value obtained in blood cells. The top graph line is the control group, which was measured on healthy people with the impedance value obtained being 1058 Ohms at the lowest frequency, namely 100 Hz. Meanwhile, the lowest graph line is in patient 4, who is suffering from an ischemic stroke and is in the acute category of severity, namely having an impedance value of 517 Ohm at a frequency of 100 Hz. According to the results obtained in the control group, the impedance value produced at the lowest frequency was 1058 Ohm to 709 Ohm, while for the group of ischemic stroke patients, it was between 761 and 517 Ohm.

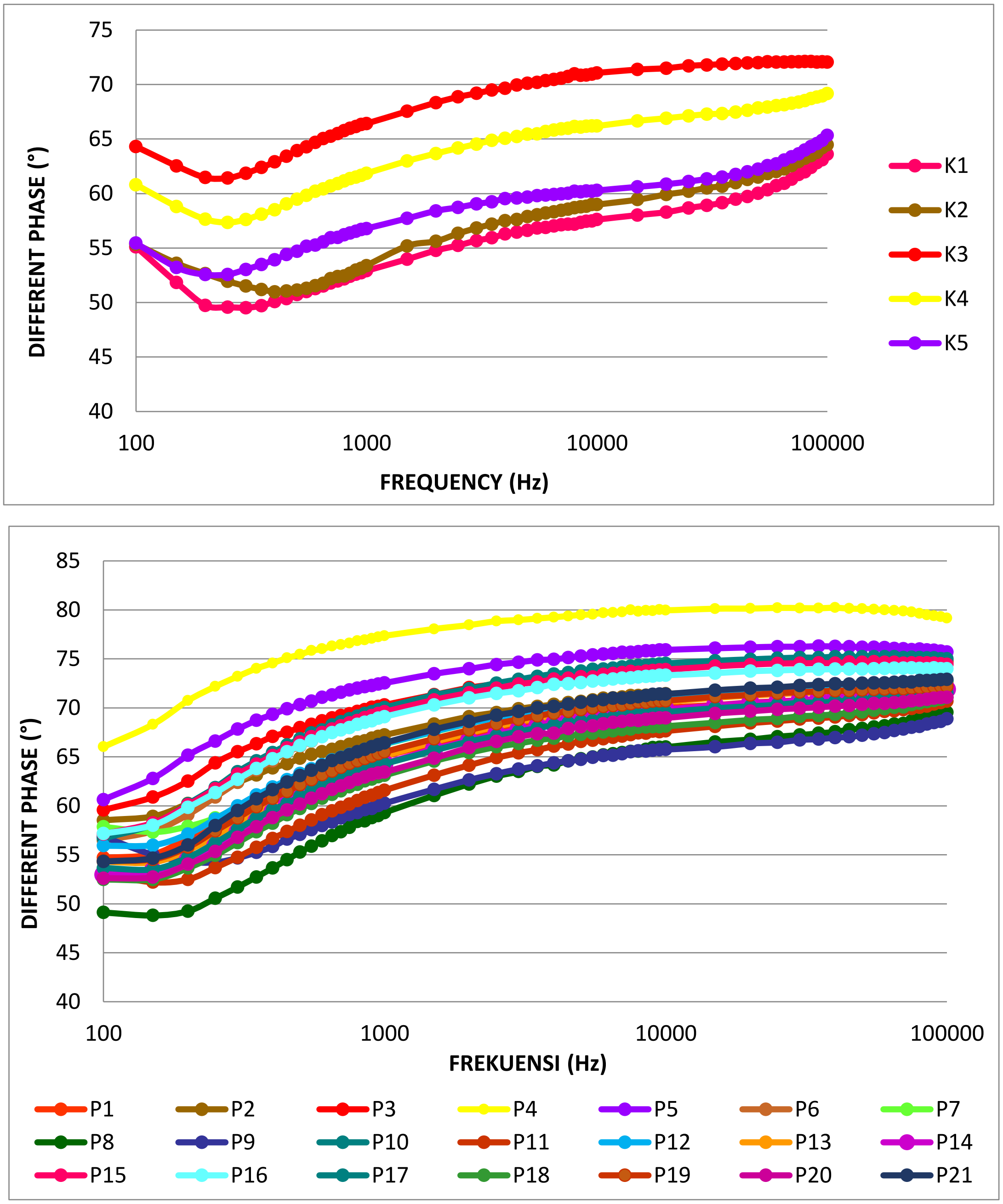

Figure 7. a) Phase Difference Plot in the Control Group; b) Phase Difference Plot in Ischemic Stroke Patients.

Figure 7 shows the different phases obtained in the control group and in ischemic stroke patients. There is a slight difference in the image; this is influenced by the capacitance and reactance values obtained on blood samples with a frequency of 100 Hz to 100 kHz. The capacitance value in the control group obtained the highest value of 2656 nF, with the resistance value obtained being 0.412 kOhm, while the lowest capacitance value in the control group was 1659 nF, and the resistance obtained was 0.662 kOhm. Meanwhile, in the ischemic stroke patient group, the highest capacitance value was 3368 nF with a resistance value of 0.266 kOhm, while the lowest capacitance value was 2478 nF, and the resistance obtained was 0.419 kOhm. From the presentation of these results, it can be seen that the lower the capacitance value obtained, the more the resistance value will increase, so it can be said that the capacitance value and resistance value are inversely proportional. So, the total impedance value will be influenced by the resistance value; at lower frequency values, the influence of the resistance value will begin to appear (Ryan et al., 2013).

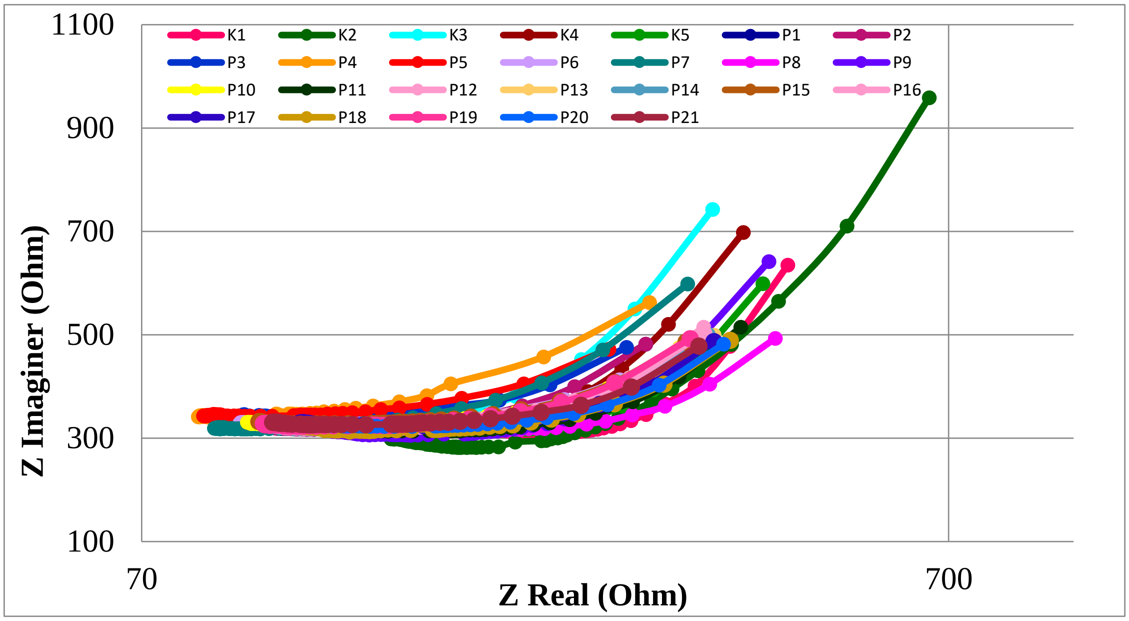

Figure 8. Nyquist Plot in the Control Group and Ischemic Stroke Patients.

After obtaining the phase difference, as in Figure 7, the Nyquist plot can be obtained. Figure 8, which is a Nyquist plot, will provide information about real Z, which represents the resistance value and imaginary Z, which represents the reactance value. The resulting Nyquist plot consists of a semicircular line shape at high frequencies and will be nonvertical at medium frequencies in accordance with the Randles circuit model. The semi-circular line at high frequencies can be seen in the real Z value with a value of 90 Ohm to 300 Ohm, which can be interpreted as internal resistance, which is the sum of the resistance of the bulk electrolyte and the charge which can be called transfer resistance. On non-vertical lines that occur at medium frequencies, such as Z real with a value of 300 Ohm to 662 Ohm, this can be interpreted as a limit on ion transport in the bulk electrolyte or referred to as equivalent distribution resistance. Transfer resistance can also be called bulk electrolyte resistance (R ∞), while equivalent distribution resistance can be called diffusion layer resistance (R D) (Sugianto, 2019).

In Figure 8, it can be seen that the lowest line is green, which is the control group with the highest electrical impedance value, while the highest line is the orange line with the electrical impedance value obtained previously, which is the lowest value. The imaginary z in Figure 8 shows that in the control group, it can be seen that the resulting value is above 598 Ohm, while in the picture, there are 7 lines that have a value above 598 Ohm, where 2 of them were patient 7 (P7) and patient 9 (P9). P7 and P9 were the two patients who had the best electrical impedance values compared to the other 19 patients and were patients with symptoms of ischemic stroke, so their severity was included in the mild category, with the first and second ratings being the lightest of the 21 ischemic stroke patients. The reactance obtained at the end point has a constant tendency at a value of 300 Ohm to 350 Ohm; this shows that the measured electrode interface has the same characteristics.

Apart from using the EIS method, this research also used the Morphology method and counting the number of blood cells. Morphology in Peripheral Blood Smear is a method used to determine and evaluate red blood cells, white blood cells and platelets. The morphological method describes blood cells through color, shape and size, which can be observed using a microscope (Bunga et al., 2019). The research showed that there were 14 damages that occurred in the blood samples of ischemic stroke patients. This damage includes the form of Blister Cells, Spherocyte Cells, Target Cells, Stomatocyte Cells, Burr Cells, Sickle Cells, Leptocyte Cells, Helmet Cells. Schistocyte Cells, Tear Drop Cells, Oval Macrocyte Cells, Elliptocyte Cells, Crenation Cells and Poikilocytosis Cells.

Changes that occur in erythrocytes have a correlation with the Nyquist graph where Z real informs about resistance, and Zimaginary informs about reactance. Resistance is the resistance provided by a resistor, while reactance is resistance that reacts to changes in voltage or changes in electric current. What is described in this research is that when an electric current of a certain frequency goes to the blood cells, it creates resistance, and if, after passing the edge surface, the electric current is transmitted or reflected according to the condition of the blood cells' shape, this can be said to be reactance.

The changes that occur in erythrocytes will be described by the percentage value of blood cells in the peripheral blood smear, both from the control group and ischemic stroke patients, so that the diagram in Figure 9 is obtained.

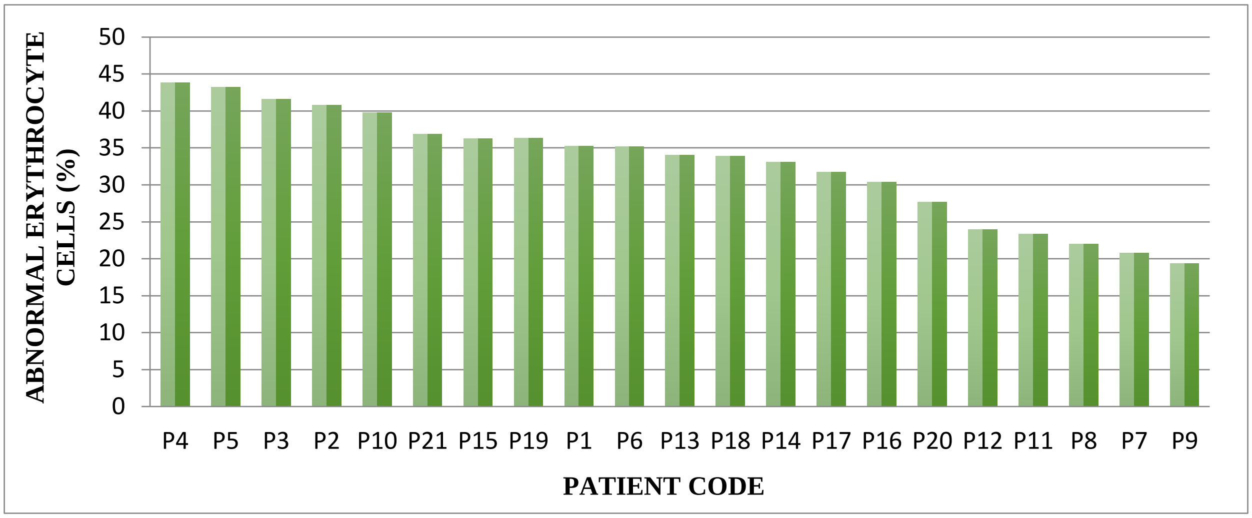

Figure 9. Diagram of the Percentage of Erythrocytes Experiencing Changes.

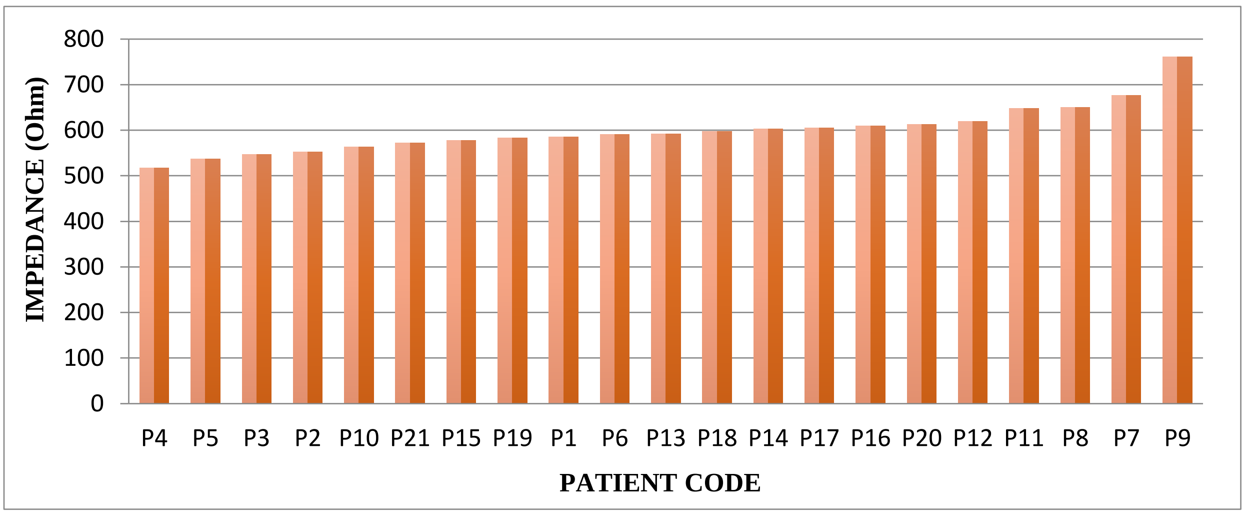

Figure 10. Impedance Diagram Based on the Severity Level of Ischemic Stroke Patients

Figures 9 and 10 show that the electrical impedance value and the percentage change value of erythrocyte cells are inversely proportional because the higher the impedance value obtained, the healthier they are, while the higher the percentage change in erythrocyte blood cells in a person, the worse their body condition is. In Figures 9 and 10, we get the order based on the level of severity in the patient, starting from the lightest level of severity P9, P7, P8, P11, P12, P20, P16, P17, P14, P18, P13, P6, P1, P19, P15, P21, P10, P2, P3, P5, P4. In the normal group, electrical impedance values were obtained ranging from 709 Ohm to 1058 Ohm, and the percentage change in erythrocytes was 2% to 5%. The electrical impedance value in ischemic stroke patients is 517 Ohm in P4 patients with acute ischemic stroke category and 761 Ohm in ischemic stroke patients with symptoms, namely P9. Meanwhile, changes in erythrocyte cells in acute ischemic stroke patients were 44%. So, it can be inferred that the severity level is most acute at P4 and lightest at P9.

4. Conclusion

The blood morphology of ischemic stroke patients has a correlation with the electrical impedance spectroscopic characteristics of blood samples from the control group and the group of ischemic stroke patients. The electrical impedance of a blood sample can be measured correctly using this method because it provides a well-measured impedance value that changes significantly. This method has also been proven to be able to measure resistance and reactance values as well as phase differences using the BIS tool and the BISDAQ application. Apart from the EIS method, the morphology method also has results that match the results of the EIS method data so that these two methods can correlate with each other to determine the severity of ischemic stroke patients. Apart from ischemic stroke patients, this method can also be used to detect patients with other medical diseases.

Funding: This research received no external funding.
Conflicts of Interest: The authors declare no conflict of interest.
Publisher's Note: All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers.

References

[1] Bilgis, B., Sumardiyono, S., & Handayani, S. (2022). The Relationship Between Hypertension Prevalence, DM Prevalence and Stroke Prevalence in Indonesia (Analysis of Riskesdas Data and Health Profile 2018). *Journal of Public Health (Undip), 10* (3), 379–384. https://doi.org/10.14710/jkm.v10i3.33243

[2] Braun, R.P. et al. (2017) Electrical Impedance Spectroscopy in Skin Cancer Diagnosis, Dermatologic Clinics. Elsevier Inc, 35(4), pp. 489–493. doi: 10.1016/j.det.2017.06.009.

[3] Bunga, M., Widi, A., & Pandarangga, P. (2019). Hematological Profile and Blood Morphology Images of Bali Cattle (Bos Sundaicus) Kept at the Alak Final Disposal Site in Kupung City. Veterinary Archipelago, 2 (2), 72–84.

[4] Huerta-Nuñez, L.F.E., Gutierrez-Iglesias, G., Martinez-Cuazitl, A., Mata-Miranda, M.M., Alvarez-Jiménez, V.D., Sánchez-Monroy, V., Golberg, A., & González-Díaz, C.A. (2019). A biosensor capable of identifying low quantities of breast cancer cells by electrical impedance spectroscopy. Scientific Reports, 9 (1), 1–12. https://doi.org/10.1038/s41598-019-42776-9

[5] Nadhira, P, PN (2020). The Relationship Between Hypertension and Stroke Association Between Hypertension and Stroke Article info Article history. https://doi.org/10.35816/jiskh.v10i2.435

[6] Magne, J., Guy, J., & Maynadié, M. (2015). Hematology. In Revue Francophone des Laboratoires (Vol. 2015, No. 471). https://doi.org/10.1016/S1773-035X(15)30080-0

[7] Mandala, Z. (2015). Comparison of Blood Lipid Profile Levels in Ischemic Stroke and Hemorrhagic Stroke at RSUD Dr. H. Abdoel Moeloek Bandar Lampung 2014. In Journal of Medika Malahayati (Vol. 2, Number 2).

[8] Mutiarasari, D., Health, BI, Community, M.-K., & Medicine, F. (2019). Ischemic Stroke: Symptoms, Risk Factors, And Prevention. In Medical Scientific Journal (Vol. 6, Number 1).

[9] Pretini, V., Koenen, M.H., Kaestner, L., Fens, M.H.A.M., Schiffelers, R.M., Bartels, M., & Van Wijk, R. (2019). Red blood cells: Chasing interactions. Frontiers in Physiology, 10 (JUL), 1–17. https://doi.org/10.3389/fphys.2019.00945

[10] Roubinian, NH, Plimier, C., Woo, JP, Lee, C., Bruhn, R., Liu, VX, Escobar, GJ, Kleinman, SH, Triulzi, DJ, Murphy, EL, & Busch, MP (2019). Effect of donor, component, and recipient characteristics on hemoglobin increments following red blood cell transfusion. Blood, 134 (13), 1003–1013. https://doi.org/10.1182/blood.2019000773

[11] Ryan, Cooper, & Tauer. (2013). Development of a Bioelectrical Impedance Spectrometer (Bis) that works quickly with Bode and Nyquist Plot facilities. Paper Knowledge. Toward a Media History of Documents, 12–26.

[12] Salamena, GA, Abdurrouf, A., & Santoso, DR (2017). Analysis of Experimental Results Measurement of Electric Impedance Value on Liquid with Injection Flow on Parallel Plate. Natural-B, 4 (1), 31–36. https://doi.org/10.21776/ub.natural-b.2017.004.01.4

[13] Sugianto, W. (2019). Detection of Red Blood Cell Quantity Using the Electrochemical Impedance Spectroscopy Method. Trends In Science, 8 (5), 55.

[14] Wegener, J., Keese, C.R., & Giaever, I. (2000). Electric cell-substrate impedance sensing (ECIS) as a noninvasive means to monitor the kinetics of cell spreading to artificial surfaces. Experimental Cell Research, 259 (1), 158–166. https://doi.org/10.1006/excr.2000.4919