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Electrical Impedance Spectroscopic Analysis on Whole Blood Cells to Correlate Severity Level of Ischemic Stroke Patients

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Abstract: Measuring the impedance value of biological materials in the form of blood samples has been widely used to determine a person's health status. Ischemic stroke patients in terms of impedance values and correlates with morphological tests on changes in red blood cells. The Electrical Impedance Spectroscopy (EIS) method is applied by providing a blood sample which is detected by electrodes and read using a BIA tool set so that the results are obtained on a laptop. The results obtained from the EIS test are in the form of Bode graphs, Bode phase graphs, Nyquist graphs, and impedance values. The EIS method uses a frequency of 100 Hz to 100 kHz by injecting a current of 10 μA. In this study, the impedance value obtained for normal people was 1058 Ω to 709 Ω, while for ischemic stroke patients with various levels of condition, it was from 517 Ω to 761 Ω. When counting the number of morphological cells in the patient's blood, changes were found ranging from the most cell changes to the least, namely with a value of 44% to 19%. The severity level of ischemic stroke patients obtained based on impedance tests and morphological tests includes the order P4, P5, P3, P2, P10, P21, P15, P19, P1, P6, P13, P18, P14, P17, P16, P20, P12, P11, P8, P7, P9.

Keywords: Electrical impedance spectroscopy; Ischemic stroke patients; Severity levels; Whole blood cells

Introduction

Stroke is in third place after coronary heart disease and cancer which has a high mortality rate. Stroke is also the number one cause of disability in the world (Feigin et al., 2021). The World Stroke Organization states that there are 13.7 million new cases of stroke in one year and around 5.5 million people die, the rest suffer mild and severe disabilities. Most stroke sufferers do not know the symptoms of stroke, so when their body condition is serious, they only know that they are experiencing a stroke. This can be caused by the high cost of examinations and fear of the medical equipment used in stroke examinations. The electrical impedance spectroscopy (EIS) method has been widely used in the health sector and to determine a person's health status. The advantages of this method are that it is non-invasive, low cost, portable, gets real-time results and the use process is also easy (Huerta-Nuñez et al., 2019).

Electrical impedance spectroscopy (EIS) is a method used to analyze materials that have electrical properties (Liu et al., 2021). The working principle of the EIS method is to inject an electrical stimulus in the form of potential or electric current into the system and then respond in the form of an output which is measured in the form of a potential signal or current strength (Kong et al., 2020). EIS is used to study cells, especially for live cells and long-term monitoring of living cells. 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. Blood damage can be seen using the morphological method. Morphology can describe blood cells through color, shape, and size which

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can be observed using a microscope (Rahman et al., 2021).

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. 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).

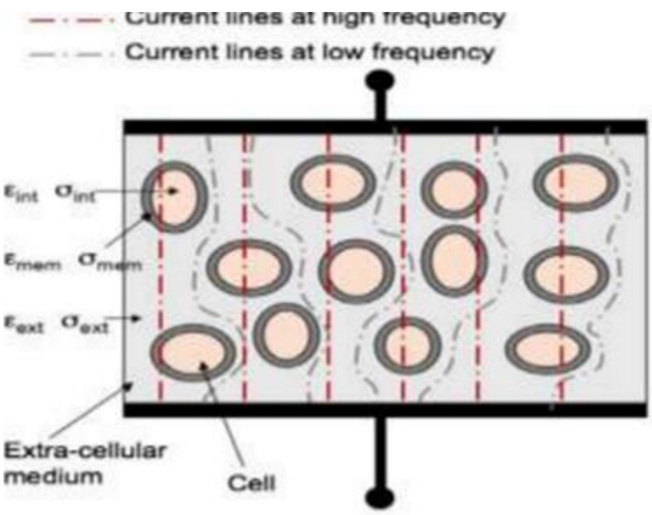


Figure 1. The behavior of electric current when measuring biological tissue

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. At high frequencies, the current penetrates the membrane and provides information about the interior of the cell. There is a frequency dependence of the magnitude of the impedance signal and the phase of the impedance signal of biological tissue (Astashev et al., 2022). Apart from using the EIS method, blood is also tested using the Morphology method to determine the changes that occur. 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 (Mukai & Oka, 2018).

The explanation above made the author interested in researching the severity of ischemic stroke patients which was detected through the medium of blood samples from healthy people and ischemic stroke patients using the electrical impedance spectroscopy method and reviewed with morphological images of peripheral blood smears analyzed using a digital microscope. So, the results are obtained in the form of impedance values and it can be seen the number of erythrocyte cells that experience changes in the blood of ischemic stroke patients.

Method

The material used was blood samples with a total of 21 samples consisting of 5 blood samples from healthy people as a control group and 21 blood samples from ischemic stroke patients with various levels of condition severity. The blood sample will be tested using electrical impedance spectroscopy with a BIA tool set, laptop, and electrodes, and a peripheral blood smear will be made and the morphological image of the blood cells will be tested using a digital microscopic tool labeled Pico Scope.

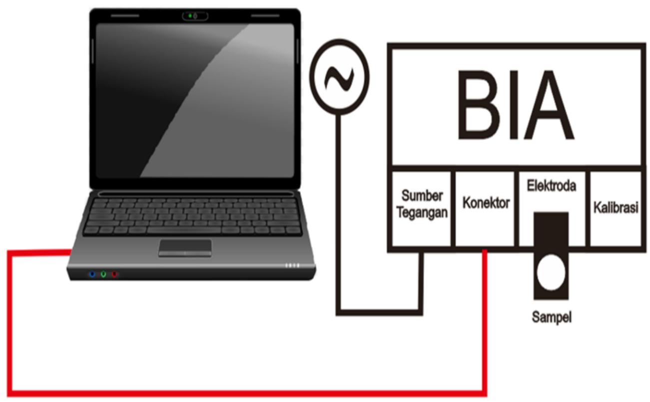
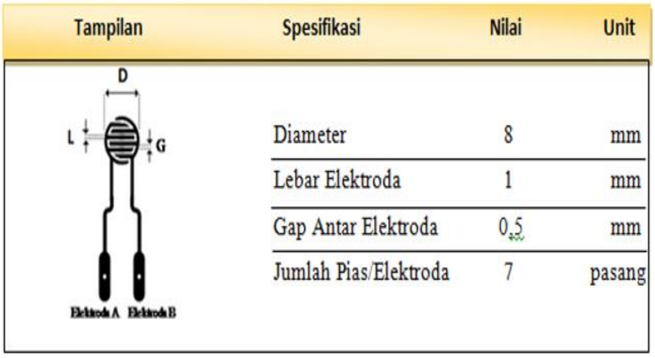


Figure 2. Series of electrical impedance spectroscopy test equipment with blood sample medium

Set of BIA (Bioimpedance Analyzer) tools connected to a current of 10 μA and a laptop to produce results. Blood samples are read using electrodes connected to a BIA device. IDE (interdigitated electrode) has a working principle that is very similar to the more conventional parallel plate capacitor. A voltage is applied to the electrode, and the impedance across the electrode is measured. One side of the electrode is connected to an AC voltage source and the other side is connected to ground. This property can be used to measure the impedance value of a material. In interdigitated electrodes, the measured impedance value depends on the properties of the material.

The electrodes are then placed in a container that has a block shape and is made of acrylic material with a volume of 0.2 mm^3. This container functions as a control for the blood volume used in each measurement and as a place to isolate samples from the open environment. The design of the container can be seen in Figure 4.



Tampilan	Spesifikasi	Nilai	Unit
	Diameter	8	mm
	Lebar Elektroda	1	mm
	Gap Antar Elektroda	0,5	mm
	Jumlah Pias/Elektroda	7	pasang

Figure 3. Electrode design and specifications

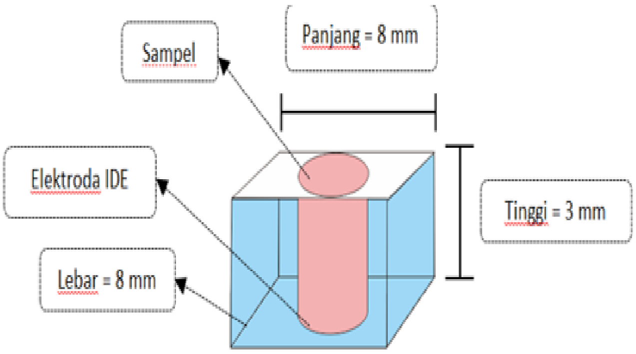


Figure 4. Container design

Impedance measurements were carried out using blood samples from 26 samples, namely 5 blood samples from healthy people which will be given codes K1 to K5, and 21 blood samples from stroke patients with various levels of severity of the patient's condition which will be given codes P1 to P21. Blood samples were obtained from a hospital in the city of Mojokerto. The impedance measurement process is carried out at room temperature with the blood condition also following room temperature (Liao et al., 2022). The blood obtained was divided into two tubes, namely one tube for the electrical impedance spectroscopy test and one tube for making peripheral blood smears (Kim et al., 2022). Meanwhile, a set of BIA tools that have been connected to a laptop to see the results of the readings and connected to an electric current are equipped with electrodes to read blood samples. The circuit design of the impedance test can be seen in Figure 2. The results read by the laptop are in the form of graphs and impedance values from the blood sample. The result graphs are Bode graphs, Bode phase graphs, and Nyquist graphs. The results can be seen in Figure 5.

Morphological testing is carried out by making preparations or peripheral blood smears from each blood sample. After that, observations and images were taken using a digital microscope so that researchers could determine the shape, color, and changes in the blood cells. Then the number of cells was calculated using the Image Raster application.

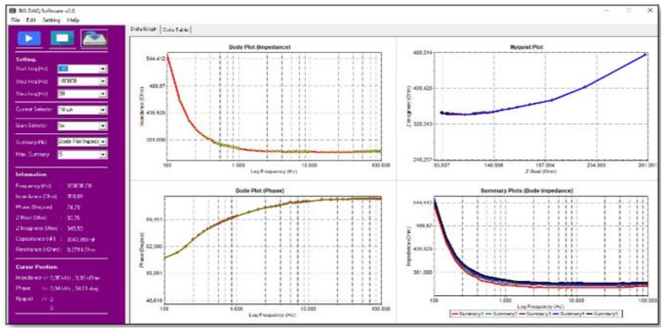


Figure 5. BIA tool measurement results

Result and Discussion

Measurements using the electrical impedance spectroscopy method are currently widely used. Because this method is a simple, inexpensive, non-invasive method, portability and results are obtained directly (Serrano-Finetti et al., 2023). One of the biological media used by the electrical impedance spectroscopy method is blood (B. Pedro et al., 2020). Impedance is measured with a frequency value range of 100 Hz to 100 kHz by providing a current injection of 10 µA and in an alternating current (AC) circuit (Pîslaru-Dănescu et al., 2022). In this study, measurements were carried out using the electrical impedance spectroscopy (EIS) method on blood samples which were divided into two groups, namely the control group (healthy people) and the ischemic stroke patient group (ischemic stroke patients with various levels of severity). The BIS tool is used for sample measurements and the BISDAQ application is an application that provides results from blood sample measurements. The measurement results that will be obtained are in the form of bode graphs, nyiquist graphs and values in Excel software (Santoso et al., 2020). Bode impedance graph provides a display of the relationship between frequency and impedance with a predetermined frequency range.

Bode impedance graph provides a display of the relationship between frequency and impedance with a predetermined frequency range. The impedance spectra produced from 26 different blood samples, namely 5 blood samples from healthy people and 21 blood samples from ischemic stroke patients with various levels of condition severity, can be seen in Figure 3.

Based on impedance measurements in the control group and ischemic stroke patient group with a given frequency range of 100 Hz to 100 kHz, differences can be seen based on variations in the quantity of red blood cells (erythrocytes) in individuals (Urbanowicz et al., 2023). In Figure 6 it can be seen that healthy people have the highest impedance value of 1058 Ω at low frequencies and decreases logarithmically to 309 Ω at the highest frequencies. The control group in the study had an electrical impedance value of 1058 Ω to 709 Ω at the lowest frequency. Low frequency values mean that the electric current is unable to penetrate the cell and only passes through the electrolyte solution on the cell surface (Meddings et al., 2020). This can provide information about the physiology and characteristics of the cell. Figure 6 shows that the bottom graph line is P4 (Patient 4) which has the lowest electrical impedance value compared to the other samples. The electrical impedance value of ischemic stroke patients at a frequency of 100 Hz is 517 Ω and at the highest frequency, namely 100 kHz, is 348 Ω (Yang et al., 2017).

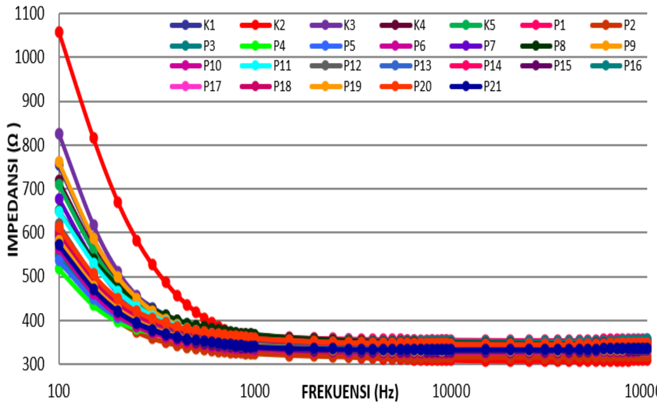


Figure 6. Bode plot impedance of blood samples of healthy people and ischemic stroke patients

Based on Figure 6 which consists of 26 blood samples, it can be seen that the impedance value tends to be relatively stable at values of more than 5 kHz. In the frequency range of 100 Hz - 5 kHz, it can be seen that the impedance value has decreased, this indicates the capacitive nature of the system behavior (phenomena in materials that are given an electric current) which is measurable (Cabrera-Peña et al., 2023). Electrical impedance measurements that have been carried out on ischemic stroke patients with varying levels of severity from the Sakinah Islamic Hospital (Patil et al., 2022), Mojokerto, can provide results from the highest to the lowest, namely P4, P5, P3, P2, P10, P21, P15, P19, P1, P6, P13, P18, P14, P17, P16, P20, P12, P11, P8, P7, P9. The phase change values from blood samples from healthy people and ischemic stroke patients can be seen more clearly in Figure 7 and Figure 8.

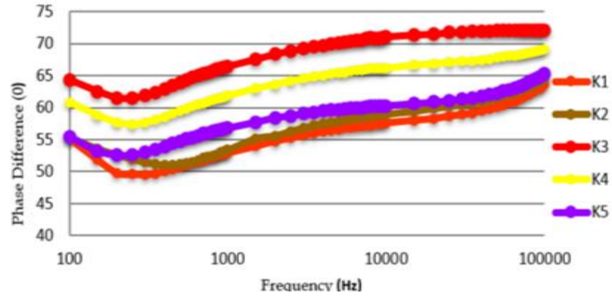


Figure 7. Bode data phase healthy people/control group

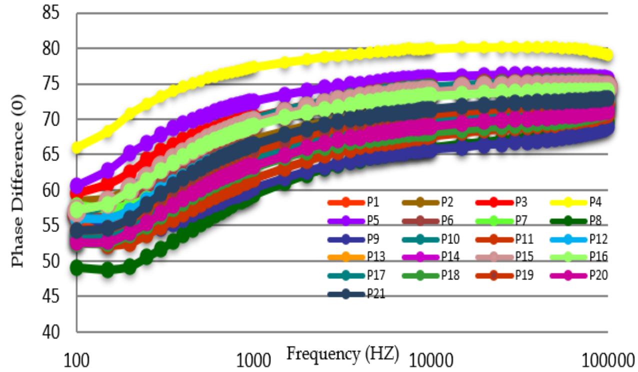


Figure 8. Bode phase data for ischemic stroke patients

In the bode phase, different results were obtained from the control group and in ischemic stroke patients which are presented in Figure 7 and Figure 8. Electrical impedance spectroscopy is used to characterize biological materials in certain frequency ranges. Impedance has a dependence on frequency to obtain specific information from the biological medium, it is called dispersion. In this study, the results showed that alpha dispersion occurred at low frequencies, thereby obtaining information about cell morphology, adhesion and cell movement because the frequency used was less than 10 kHz (Kwon et al., 2020). This occurs because most of the current flows around the blood cell membrane. In Figure 7 and Figure 8 we can see the phase differences because the morphology of blood cells in healthy people and ischemic stroke patients has very significant differences

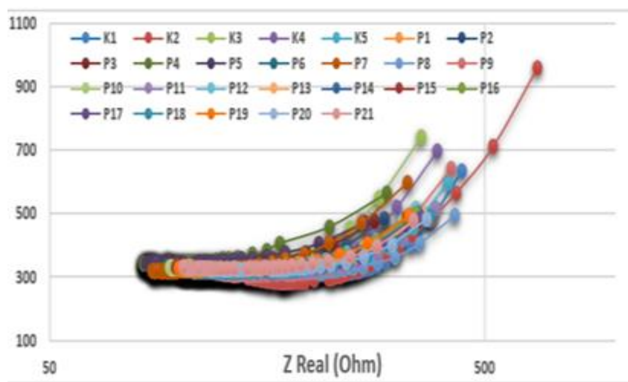


Figure 9. Nyquist graphs on various blood samples

The Nyquist graph is a graph that shows the relationship between real impedance and imaginary impedance values. Nyquist graphs are also called cole-cole graphs. Nyquist charts show the measurement process clearly based on the patterns produced on the graph. An example is the semicircle (arc) pattern on the Nyquist graph showing that the time constant (τ) in the measurement system (Chowdhury et al., 2015).

Whole blood is composed of 55% liquid components (plasma) and 45% solid components (erythrocytes, leukocytes and platelets). Erythrocytes can make up 95-98% of the solid components of blood, while the rest is the buffy coat (thrombocytes and leukocytes). Blood is considered a suspension of particles (erythrocytes or red blood cells) with high resistivity in a conducting fluid (plasma) (Yokoyama et al., 2022). Other cells and platelets are considered to play an unimportant role in the electrical properties of blood because they are too small in size and number (Seyoum et al., 2018).

The resistivity of a particle suspension can be related to the resistivity of the suspended medium and the suspended particles. Most mammals, including humans, have lower plasma resistivity compared to erythrocyte resistivity (B. G. Pedro et al., 2020). The resistivity is calculated by considering the current disturbance produced by each particle as independent of each other (Bakonyi, 2021). Resistivity has a proportional relationship to the impedance value. If the resistivity of a biological medium is high, then the impedance of the medium is also high. The shape and orientation factors of the particles can influence the resistivity (Qin et al., 2020).

The impedance value is expressed in a Nyquist graph which has real and imaginary parts, where the resistance value is the real part of the impedance (Z_{real}) and the reactance value of the capacitive or inductive is the imaginary value (Z_{im}) shown in the results of the $_{real}$ Z and $Z_{im\ values}$ in Figure 9. The real part of impedance is influenced by the measured total resistance, namely electrode interface resistance, extracellular fluid resistance and intracellular fluid resistance. The imaginary part of the impedance is influenced by the measured total capacitance, namely the electrode interface capacitance and the cell membrane capacitance (Oswald et al., 2022). The measured value is consistent at 300 Ω to 350 Ω. The resistance value is obtained from the highest real Z value, namely 662 Ω. while the Zimaginer value is 959 Ω which is a representation and the frequency of the reactance is obtained at the Ohms value. By knowing the reactance value and the frequency at which the reactance value is at the highest point, the C value can be calculated using the equation C = 1 $j\omega XC$.

In ischemic stroke, blockages can occur along the arterial blood vessels leading to the brain by the lipid profile. Stroke is caused by abnormalities in the blood lipid profile, 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. Blockage by the lipid profile in the bloodstream causes changes in the shape and size of blood cells. 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 (Swanepoel & Pretorius, 2012). This is a way for cells to adapt so they can pass through narrow surfaces and a way for cells not to die easily. Figure 10 shows the changes in red blood cells (erythrocytes) that occur in each blood sample from an ischemic stroke patient.

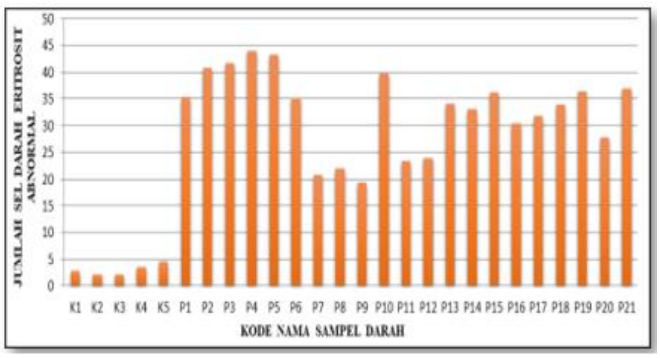


Figure 10. Changes in erythrocytes in blood samples from ischemic stroke patients

In this study, erythrocyte changes were directly proportional to the patient's severity. The results obtained were that the highest erythrocyte changes were in the patient (P4) with a value of 44% and the least erythrocyte changes were in the patient (P9) with a value of 19%. The order of levels of ischemic stroke patients with the highest to lowest erythrocyte changes is P4, P5, P3, P2, P10, P21, P15, P19, P1, P6, P13, P18, P14, P17, P16, P20, P12, P11, P8, P7, P9 can be seen in Figure 10. The more erythrocytes that experience changes, the higher the level of severity in ischemic stroke patients so that the highest level of severity is in patient 4 (P4) and the lowest level of severity is in patient 9 (P9). The control group showed changes in erythrocyte cells that occurred in normal humans were 2% to 5%.

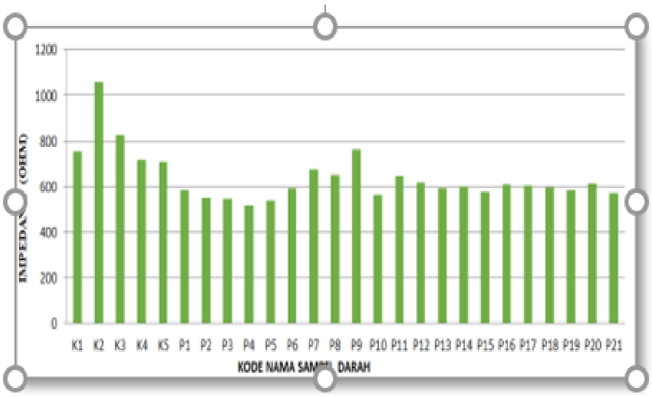


Figure 11. Impedance values in blood samples from ischemic stroke patients

The impedance value of ischemic stroke patients was found to be the highest value of 761 Ω in the patient (P9) and the lowest value of 517 Ω in the patient (P4). The impedance value will be inversely proportional to the patient's severity because the greater the impedance value obtained, the lower the severity level in ischemic stroke patients. This study obtained results in the form of a sequence of patient severity levels based on their impedance values, namely P4, P5, P3, P2, P10, P21, P15, P19, P1, P6, P13, P18, P14, P17, P16, P20, P12, P11, P8, P7, P9. In Figure 11 it can be seen that the control group has a higher impedance value, namely up to 1058 Ω.

Conclusion

This study concluded that the severity of ischemic stroke patients was correlated with the impedance value and the results of calculating the number of cells in the morphological test. The patient's severity is inversely proportional to the impedance value obtained and directly proportional to the number of cell changes obtained on the morphological test. The impedance value becomes lower as the patient's severity level increases. Morphological tests showed that red blood cell changes were increasing and this was directly proportional to the severity of ischemic stroke patients. The severity levels obtained from the Impedance Test and Morphology Test in ischemic stroke patients include P4, P5, P3, P2, P10, P21, P15, P19, P1, P6, P13, P18, P14, P17, P16, P20, P12, P11, P8, P7, P9.

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Author Contributions

Conceptualization, F. N, C. S. W, D. R. S.; methodology, F. N.; validation, C. S. W. and D. R. S.; formal analysis, F. N.; investigation, C. S. W, and D. R. S.; resources, F. N. and C. S. W.; data curation, D. R. S.: writing—original draft preparation, F. N and C. S. W.; writing—review and editing, D. R. S.: visualization, and F. N.and C. S. W. All authors have read and agreed to the published version of the manuscript.

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Conflicts of Interest

The authors declare no conflict of interest.

References

Astashev, M. E., Konchekov, E. M., Kolik, L. V., & Gudkov, S. V. (2022). Electric Impedance Spectroscopy in Trees Condition Analysis: Theory and Experiment. *Sensors*, *22*(21), 8310. https://doi.org/10.3390/s22218310

Bakonyi, I. (2021). Accounting for the resistivity contribution of grain boundaries in metals: Critical analysis of reported experimental and theoretical data for Ni and Cu. *The European Physical Journal Plus*, *136*(4), 410. https://doi.org/10.1140/epjp/s13360-021-01303-4

Cabrera-Peña, J., Brito-Garcia, S. J., Mirza-Rosca, J. C., & Callico, G. M. (2023). Electrical Equivalent Circuit Model Prediction of High-Entropy Alloy Behavior in Aggressive Media. *Metals*, *13*(7), 1204. https://doi.org/10.3390/met13071204

Chowdhury, S. P., Hartmann, A., Gao, X. W., & Borriss, R. (2015). Biocontrol mechanism by root-associated Bacillus amyloliquefaciens FZB42—A review. *Frontiers in Microbiology*, *6*(JUL), 1–11. https://doi.org/10.3389/fmicb.2015.00780

Feigin, V. L., Stark, B. A., Johnson, C. O., Roth, G. A., Bisignano, C., Abady, G. G., Abbasifard, M., Abbasi-Kangevari, M., Abd-Allah, F., Abedi, V., Abualhasan, A., Abu-Rmeileh, N. M., Abushouk, A. I., Adebayo, O. M., Agarwal, G., Agasthi, P., Ahinkorah, B. O., Ahmad, S., Ahmadi, S., … & Murray, C. J. L. (2021). Global, regional, and national burden of stroke and its risk factors, 1990–2019: A systematic analysis for the Global Burden of Disease Study 2019. *The Lancet Neurology*, *20*(10), 795–820. https://doi.org/10.1016/S1474-4422(21)00252-0

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

Kim, H., Zhbanov, A., & Yang, S. (2022). Microfluidic Systems for Blood and Blood Cell Characterization.

Biosensors, *13*(1), 13. https://doi.org/10.3390/bios13010013

Kong, X., Plett, G. L., Trimboli, M. S., Zhang, Z., & Zheng, Y. (2020). An Exact Closed-Form Impedance Model for Porous-Electrode Lithium-Ion Cells. *Journal of The Electrochemical Society*, *167*(1), 013539. https://doi.org/10.1149/1945-7111/ab67c7

Kwon, S., Yang, W., Moon, D., & Kim, K. S. (2020). Biomarkers to quantify cell migration characteristics. *Cancer Cell International*, *20*(1), 217. https://doi.org/10.1186/s12935-020-01312-w

Liao, S., Ye, P., Chen, C., Zhang, J., Xu, L., & Tan, F. (2022). Comparing of Frequency Shift and Impedance Analysis Method Based on QCM Sensor for Measuring the Blood Viscosity. *Sensors*, *22*(10), 3804. https://doi.org/10.3390/s22103804

Liu, Y., Li, D., Qian, J., Di, B., Zhang, G., & Ren, Z. (2021). Electrical impedance spectroscopy (EIS) in plant roots research: A review. *Plant Methods*, *17*(1), 118. https://doi.org/10.1186/s13007-021-00817-3

Meddings, N., Heinrich, M., Overney, F., Lee, J.-S., Ruiz, V., Napolitano, E., Seitz, S., Hinds, G., Raccichini, R., Gaberšček, M., & Park, J. (2020). Application of electrochemical impedance spectroscopy to commercial Li-ion cells: A review. *Journal of Power Sources*, *480*, 228742. https://doi.org/10.1016/j.jpowsour.2020.228742

Mukai, M., & Oka, T. (2018). Mechanism and management of cancer-associated thrombosis. *Journal of Cardiology*, *72*(2), 89–93. https://doi.org/10.1016/j.jjcc.2018.02.011

Oswald, S., Riewald, F., & Gasteiger, H. A. (2022). Novel Method for Monitoring the Electrochemical Capacitance by In Situ Impedance Spectroscopy as Indicator for Particle Cracking of Nickel-Rich NCMs: Part III. Development of a Simplified Measurement Setup. *Journal of the Electrochemical Society*, *169*(4), 040552. https://doi.org/10.1149/1945-7111/ac67b3

Patil, S., Rossi, R., Jabrah, D., & Doyle, K. (2022). Detection, Diagnosis and Treatment of Acute Ischemic Stroke: Current and Future Perspectives. *Frontiers in Medical Technology*, *4*, 748949. https://doi.org/10.3389/fmedt.2022.748949

Pedro, B. G., Marcôndes, D. W. C., & Bertemes-Filho, P. (2020). Analytical model for blood glucose detection using electrical impedance spectroscopy. *Sensors (Switzerland)*, *20*(23), 1–11. https://doi.org/10.3390/s20236928

Pedro, B., Marcôndes, D., & Bertemes-Filho, P. (2020). Analytical Model for Blood Glucose Detection Using Electrical Impedance Spectroscopy. *Sensors*, *20*(23), 6928. https://doi.org/10.3390/s20236928

Pîslaru-Dănescu, L., Zărnescu, G.-C., Telipan, G., & Stoica, V. (2022). Design and Manufacturing of Equipment for Investigation of Low Frequency Bioimpedance. *Micromachines*, *13*(11), 1858. https://doi.org/10.3390/mi13111858

Qin, P., Liu, Y., Song, Z., Ma, F., Wang, Y., Zhang, X., Miao, C., & Dong, X. (2020). An Electrical Resistivity Method of Characterizing Hydromechanical and Structural Properties of Compacted Loess During Constant Rate of Strain Compression. *Sensors*, *20*(17), 4783. https://doi.org/10.3390/s20174783

Rahman, S., Azam, B., Khan, S. U., Awais, M., Ali, I., & Ul Hussen Khan, R. J. (2021). Automatic identification of abnormal blood smear images using color and morphology variation of RBCS and central pallor. *Computerized Medical Imaging and Graphics*, *87*, 101813. https://doi.org/10.1016/j.compmedimag.2020.101813

Santoso, D. R., Pitaloka, B., Widodo, C. S., & Juswono, U. P. (2020). Low-Cost, Compact, and Rapid Bio-Impedance Spectrometer with Real-Time Bode and Nyquist Plots. *Applied Sciences*, *10*(3), 878. https://doi.org/10.3390/app10030878

Serrano-Finetti, E., Castillo, E., Alejos, S., & León Hilario, L. M. (2023). Toward noninvasive monitoring of plant leaf water content by electrical impedance spectroscopy. *Computers and Electronics in Agriculture*, *210*, 107907. https://doi.org/10.1016/j.compag.2023.107907

Seyoum, M., Enawgaw, B., & Melku, M. (2018). Human blood platelets and viruses: Defense mechanism and role in the removal of viral pathogens. *Thrombosis Journal*, *16*(1), 16. https://doi.org/10.1186/s12959-018-0170-8

Swanepoel, A. C., & Pretorius, E. (2012). Scanning electron microscopy analysis of erythrocytes in thromboembolic ischemic stroke. *International Journal of Laboratory Hematology*, *34*(2), 185–191. https://doi.org/10.1111/j.1751-553X.2011.01379.x

Urbanowicz, T., Michalak, M., Marzec, E., Komosa, A., Filipiak, K. J., Olasińska-Wiśniewska, A., Witkowska, A., Rodzki, M., Tykarski, A., & Jemielity, M. (2023). Coronary Artery Disease and Inflammatory Activation Interfere with Peripheral Tissue Electrical Impedance Spectroscopy Characteristics—Initial Report. *International Journal of Environmental Research and Public Health*, *20*(3), 2745. https://doi.org/10.3390/ijerph20032745

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

Yang, L., Liu, W., Chen, R., Zhang, G., Li, W., Fu, F., & Dong, X. (2017). In Vivo Bioimpedance Spectroscopy Characterization of Healthy, Hemorrhagic and Ischemic Rabbit Brain within 10 Hz–1 MHz. *Sensors*, *17*(4), 791. https://doi.org/10.3390/s17040791

Yokoyama, Y., Tanaka, A., & Tagawa, Y. (2022). Droplet impact of blood and blood simulants on a solid surface: Effect of the deformability of red blood cells and the elasticity of plasma. *Forensic Science International*, *331*, 111138. https://doi.org/10.1016/j.forsciint.2021.111138