

A USAGE OF THE IMPEDANCE METHOD FOR DETECTING CIRCULATORY DISORDERS TO DETERMINE THE DEGREE OF LIMB ISCHEMIA

Valerii Kryvonosov¹, Oleg Avrunin², Serhii Sander³, Volodymyr Pavlov⁴, Liliia Martyniuk¹, Bagashar Zhumazhanov⁵

¹National University of Life and Environmental Sciences of Ukraine, Kyiv, Ukraine, ²Kharkiv National University of Radio Electronics, Kharkiv, Ukraine, ³Vinnitsia National Medical University named after M. I. Pirogov, Vinnitsia, Ukraine, ⁴Vinnitsia National Technical University, Vinnitsia, Ukraine, ⁵Institute of Information and Computing Technologies of the CS MES, Almaty, Kazakhstan

Abstract. New engineering technologies allow the creation of diagnostic devices for predicting the development of acute tissue ischemia of the extremities and determining the residual time until the removal of the tourniquet, and solving these tasks is particularly relevant during military actions. Acute limb ischemia is a sudden critical decrease in perfusion that threatens the viability of the limb. The incidence of this condition is 1.5 cases per 10 000 people per year. Acute ischemia occurs due to the blockage of blood flow in major arteries (embolism, thrombosis, trauma), leading to the cessation of adequate blood supply to metabolically active tissues of the limb, including the skin, muscles, and nerve endings. To address these issues, the article analyzes the changes in the impedance of biological tissue. The introduction and use of the coefficient of relative electrical conductivity, denoted as k , as a diagnostic criterion parameter, are justified. Experimental studies of changes in the coefficient of relative electrical conductivity k were conducted, confirming that the transition from exponential to linear dependencies of the coefficient establishes the degree of viability of the biological cell (tissue) and the moment of occurrence of reperfusion syndrome. It has been established that a deviation of the value of k by 10–15% from its unit value diagnoses the initial process of blood perfusion impairment and the development of ischemic tissue disease. The rate of change of k serves as a criterion for predicting the progression of the disease and as a corrective factor for therapeutic treatment.

Keywords: ischemic tissue disease, perfusion, reperfusion syndrome, tourniquet, transient process, ionization

IMPEDANCYJNA METODA WYKRYWANIA ZABURZEŃ KRAŻENIA KRWI DO OKREŚLENIA STOPNIA NIEDOKRWIENIA KOŃCZYNY

Streszczenie. Nowe technologie inżynierskie umożliwiają tworzenie urządzeń diagnostycznych do przewidywania rozwoju ostrego niedokrwienia tkanek kończyn i określania czasu pozostałego do usunięcia opaski uciskowej. Rozwiązanie tych zadań jest istotne, zwłaszcza podczas operacji wojskowych. Ostre niedokrwienie kończyny to nagłe, krytyczne zmniejszenie perfuzji, które zagraża żywotności kończyny. Częstość występowania tego schorzenia wynosi 1,5 przypadku na 10 000 osób rocznie. Do ostrego niedokrwienia dochodzi w wyniku zablokowania przepływu krwi w głównych tętnicach (zatorowość, zakrzepica, uraz), co prowadzi do ustania odpowiedniego ukrwienia metabolicznie aktywnych tkanek kończyny, w tym skóry, mięśni i zakończeń nerwowych. Aby rozwiązać wybrane problemy, w artykule przedstawiono analizę zmiany impedancji tkanki biologicznej. Uzasadnione jest wprowadzenie i stosowanie współczynnika przewodności elektrycznej względnej k , jako parametru kryterium diagnostycznego. Przeprowadzono eksperymentalne badania zmiany współczynnika względnego przewodnictwa elektrycznego k , które potwierdziły, że przejście zmiany współczynnika względnego przewodnictwa elektrycznego z zależności wykładniczej na liniową będzie determinować stopień żywotności komórki biologicznej (tkanki) i moment wystąpienia zespołu reperfuzyjnego. Ustalono, że odchylenie wartości k o 10–15% od jego wartości jednostkowej świadczy o początkowym procesie zaburzenia perfuzji krwi i rozwoju choroby niedokrwiennej tkanek, a szybkość zmiany jest kryterium do przewidywania rozwoju choroby i czynnika korygującego w postępowaniu terapeutycznym.

Słowa kluczowe: choroba niedokrwienne tkanek, perfuzja, zespół reperfuzyjny, staza hemostatyczna, proces przejściowy, jonizacja

Introduction

The primary cause of death in trauma cases remains hemorrhage. The frequency of injuries to major vessels in modern military conflicts reaches 7.5–9.0% [3, 14]. Consequently, it is essential to address temporary hemostasis during the pre-hospital stage, leading to an increasing use of tourniquets [4, 5, 15]. Experimental studies [6, 17] have demonstrated that tourniquets can induce systemic changes. The application of a tourniquet (artificial limb ischemia) leads to the development of paraneuronal necrosis and reperfusion injuries not only in skeletal muscles but also in vital organs, such as the brain, heart, lungs, and kidneys. The most severe consequence of restoring arterial blood flow is reperfusion syndrome [27, 10].

According to [9, 19], the time a tourniquet can be applied depends on the patient's individual characteristics, environmental temperature, type of injury, and other factors, and can vary from 1 to 6 hours. The decision of when to remove the tourniquet is subject to the physician's judgment.

Disorders of blood circulation are also associated with a range of conditions, such as arterial and venous congestion (hyperemia), ischemia, blood stasis, thrombosis, disseminated intravascular coagulation (DIC) syndrome, embolism, infarction, bleeding, hemorrhage, diabetes mellitus, and others [11]. Currently, the frequency of blood circulation disorders is 1.5% per 10,000 people per year. Limb injuries resulting from occupational and domestic

activities remain the leading cause of fatal outcomes and injuries among working-age individuals.

Blood circulation disorders lead to the development of necrosis and paraneuronal necrosis preceding necrobiosis. Acidosis occurs in tissues, and hyperkalemia develops [20].

Figure 1 illustrates the consequences of acute limb ischemia development.

Timely diagnosis of the initial process of tissue necrosis formation allows not only predicting the development of the disease but also adjusting the course of therapeutic treatment at early stages, thereby postponing surgical intervention and disability of the patient. In the case of hemostasis with a tourniquet, it helps determine the time remaining before the tourniquet is removed [3, 15, 25].

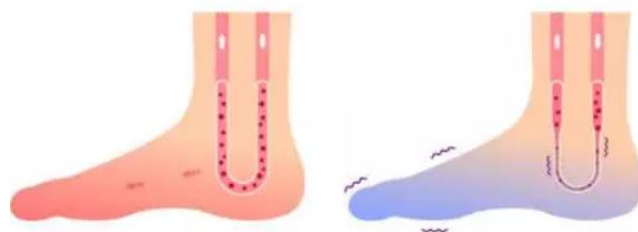


Fig. 1. Consequence of acute limb ischemia

1. Materials and methods of research

The main methods for diagnosing the development of ischemia in biological tissue during stationary research include differential diagnosis, ultrasound duplex scanning of lower limb vessels, computed tomographic angiography, magnetic resonance angiography, and digital subtraction angiography [14]. These methods require complex and expensive equipment, and they are typically used to refine the diagnosis and determine the extent of the disease. They are not cost-effective and may require a significant amount of time for diagnosis.

Electrical research methods on processes occurring in living organisms have been extensively studied [13, 17, 21] and widely applied. Many studies have focused on the effects of alternating, high-frequency currents on biological tissue.

For instance, in study [3, 9, 22], the influence of variable-frequency electric current on the electrical conductivity of skeletal muscles was investigated. The results presented in [19, 25] demonstrated changes in the electrical conductivity of biological structures under the influence of pulsed electric current in various frequency ranges. In [20, 28], methods of bioelectrical impedance were explored for non-invasive health monitoring using high-frequency alternating currents.

These research findings contribute to the understanding and application of electrical methods in the study and assessment of biological tissues and their responses to different electrical stimuli.

It should be noted that the utilization of changes in the electrical conductivity of biological tissues during the transitional period of ionization as an informative diagnostic criterion is not sufficiently studied in well-known scientific sources. As known, parane-crisis is manifested by alterations in the cytoplasm properties, shifting the reaction of cystazoa and the nucleus to the acidic side, release of potassium ions and phosphates from the cell, accumulation of sodium and chloride ions, increased colloid viscosity, nuclear compaction, enhanced sorption properties, and

overall changes in the electrolyte composition of biological tissues [8, 21, 30]. When applying a constant voltage to biological tissue, the main mechanism characterizing the flow of direct electric current at the initial moment is ionic conductivity. In study [6, 20, 28], it has been proven that the development of portable and cost-effective devices for studying the impedance changes in biological tissues has become significant at the present time.

The change in the property state of biological tissue during the development of necrosis correlates with changes in electrical conductivity. Therefore, by measuring the constant time of ionization during the transitional process of impedance change in biological tissue, it is possible to use it as an informative criterion for diagnosing ischemia. The duration of the transitional process of ionization in biological tissue, under the influence of direct current, does not exceed two minutes, which allows for a shorter diagnostic time and the development of cost-effective diagnostic devices.

Research objective: To justify the selection of a criterion diagnostic parameter describing changes in the properties of biological tissue (BT) under the influence of direct current voltage and formulate criteria for determining the critical state of BT properties. To develop a method for rapid diagnosis of changes in BT properties during ischemia development.

2. Model experiment

An electric method was applied – invasive measurement of the impedance of biological tissue (BT) using a constant voltage of 5 V. Sexually mature guinea pigs – males weighing 500–600 g were used for the study. The experiments were conducted under anesthesia, using thiopental sodium 10 mg/ml – 3-4 ml. Anesthesia was administered 30 minutes before the start of the experiment. During the 2-hour procedure,

premedication was administered, consisting of diphenhydramine 1% – 0.3 ml and analgin 50% – 0.3 ml.

To assess the changes in BT impedance during circulatory disturbances, a subcutaneous ligature was applied to the right hind paw at the level of the hip joint. Tightening the ligature simulated the situation of applying a tourniquet. Measurements were taken simultaneously in areas with the tourniquet and without it [9, 10].

The research complied with the provisions of Article 26 of the Law of Ukraine No. 3447-VI dated October 16, 2012, "On the Protection of Animals from Cruelty" [1, 7, 15], and the requirements of the European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes [6, 15].

The needle electrodes used for measuring the impedance of biological tissue were placed in identical locations on each limb, with the needles oriented along the direction of the muscle tissue.

The experiments were conducted in the Photonics Laboratory of Vinnytsia National Technical University. Fig. 2 shows the laboratory setup for measuring the electrical conductivity of biological tissue.

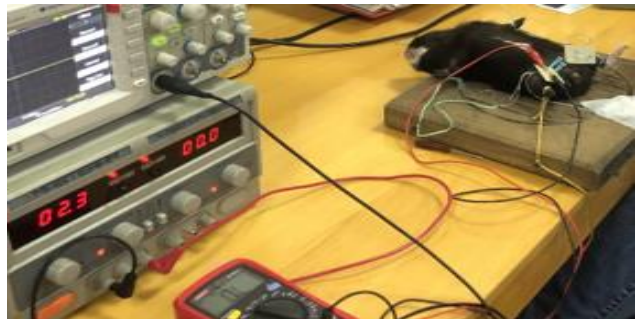


Fig. 2. Laboratory setup for measuring the impedance of BT

Medical needles with step-by-step distance adjustment were used as sensors for impedance measurements using the invasive method. The step adjustment was set at 1 cm. Fig. 3 presents the block diagram of the connection of the equipment for impedance measurements of biological tissue.

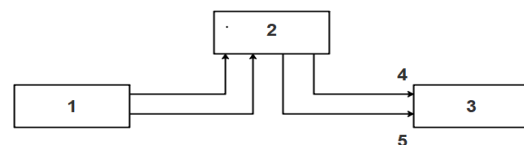


Fig. 3. Block diagram of the connection of equipment for impedance measurements of biological tissue, where indicated: 1 – DC voltage control unit; 2 – two-channel oscilloscope; 3 – biological object; 4 and 5 sensors for invasive conductivity measurement

For the analysis of the transient process, a mathematical model of biological tissue based on the corrected electrical equivalent circuit [12, 18, 24] was applied, which is presented in Fig. 4a and 4b. The equivalent circuit diagram (Fig. 4a), corresponds to the physico-chemical processes under the applied tourniquet, while the circuit in Fig. 4b corresponds to the investigation of healthy tissue.

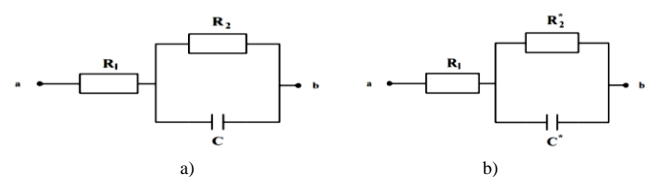


Fig. 4. Electrical equivalent circuits of biological tissue: a) without tourniquet, b) with applied tourniquet, where R_1 is the active resistance in the intercellular space, R_2 and R_2^* are the active resistances of tissue cells with and without the tourniquet, respectively, C and C^* are the capacitive components of cells characterizing the process of ionization in biological tissue, respectively

Table 1. Results of the study of impedance changes over time depending on the distance between the needle electrodes

$\frac{s}{L}$ [kΩ/mm]	0	10	20	30	40	50	60	70	80	90	100	110	120
10	1.30	2.78	3.76	4.32	4.85	5.17	5.37	5.46	5.6	5.7	5.71	5.72	5.73
30	1.65	3.16	4.10	4.65	5.16	5.42	5.67	5.86	5.99	6.13	6.34	6.34	6.42
50	1.90	3.49	4.33	4.92	5.25	5.60	5.93	6.13	6.25	6.45	6.58	6.65	6.65

The mathematical model describing the change in resistance for the circuit (Fig. 4b) is as follows

$$Z = R_1 + R_2(1 - e^{-\frac{t}{\tau_1}}) \quad (1)$$

where $\tau_1 = C \cdot R_2$ the time constant of the ionization process for biological tissue without the applied tourniquet. Note that $R = \rho_0 \frac{L}{S}$, where ρ_0 – the specific resistance of tissue, L – the distance between the electrodes, S – the cross-sectional area, in this case, is constant.

To study the influence of the sensitivity of changes in the impedance of biological tissue on the distance between the electrodes for invasive measurements, the data obtained are presented in table 1.

Fig. 5 it shows the graphs of changes in the impedance of biological tissue during the transitional period, depending on the distance L between the needle electrodes, obtained experimentally. The investigated biological object was not harmed after the completion of the experiments.

The analysis of the curves (Fig. 5), indicates that the distance between the detector needles does not alter the nature of the transient process but only affects the sensitivity.

As known from studies [8, 9, 11], muscles contain potassium, sodium, calcium, magnesium, fluorine, and trace amounts of copper, manganese, zinc, cobalt, arsenic, and others. Among the anions, phosphoric and hydrochloric acids are found in the highest quantities. Muscles are characterized by a high content of potassium, phosphorus, and sulfur, and the primary component of the biological tissue (BT) environment is blood, which consists of electrolyte solutions. For instance, plasma contains 0.32% NaCa, with concentrations of Na⁺ ions at 142 mmol/L and K⁺ ions at 5 mmol/L. Electric current represents the directed movement of positive and negative ions and is determined according to [12] as:

$$j_+ = q_+ \cdot n_+ \cdot v_+ \text{ and } j_- = q_- \cdot n_- \cdot v_- \quad (2)$$

where q_+ – the positive charge carrier, q_- – the negative charge carrier; n_+ , n_- – the amount of positively and negatively charged ions; v_+ , v_- – the concentration of positively and negatively charged ions, respectively.

The total current will be equal to:

$$G = j_+ + j_- = q_+ \cdot n_+ \cdot v_+ + q_- \cdot n_- \cdot v_- \quad (3)$$

Expression (18) indicates that the electrical conductivity of biological tissue is proportional to n_+ , n_- – the quantity of positively and negatively charged ions, and v_+ , v_- – the concentration of positively and negatively charged ions, respectively.

The speed of ordered ion movement is directly proportional to E_{ion} , which is caused by the displacement of free charged ions under the influence of the electric field of the source and is determined as:

$$V = g \cdot E_{ion} \quad (4)$$

where g – the coefficient of proportionality of the carrier mobility.

The specific electrical conductivity δ for the electrolyte will be expressed as follows:

$$\delta = \frac{1}{Z} = b_+ \cdot n_+ \cdot v_+ + b_- \cdot n_- \cdot v_- + b \cdot n \cdot v \quad (5)$$

The input impedance of the biological tissue for the circuit (Fig. 4b) with a limited number of ions, obtained by performing similar calculations as for the circuit (Fig. 4a), is determined by the following expression:

$$Z_{inp4}^* = R_1 + R_2^*(1 - e^{-\frac{t}{\tau^*}}) \quad (6)$$

where τ^* – the time constant of the ionization process for the biological object with a reduced number of ions is equal to: $\tau^* = C^* R_2^*$

The analysis of expressions (3), (4), and (5) shows that the time constant of the ionization process $\tau^* = C^* R_2^*$ is directly proportional to the number of charged ions, their concentration in the biological tissue, the level of electric field intensity E_{ion} , and the composition of salts in the biological tissue. It remains a constant value characterizing the flow of this process.

The specific electrical conductivity δ^* for the electrolyte is expressed as:

$$\delta^* = \frac{1}{Z^*} = b_+ \cdot (n_+ - \Delta n) \cdot v_+ + b_- \cdot (n_- - \Delta n) \cdot v_- + b \cdot (n - \Delta n) \cdot v \quad (7)$$

where $\Delta n = (n_+ - n_+^*) -$ the number of charged particles that did not enter the biological tissue due to perfusion.

Due to the increase in Δn , the following inequality is obviously satisfied:

$$Z^* < Z; \quad \tau_2 < \tau_1 \quad (8)$$

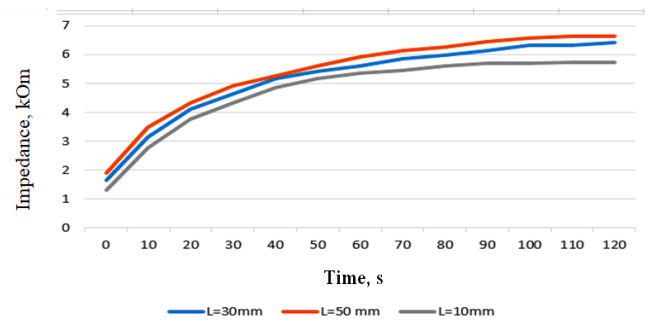


Fig. 5. Dependency of impedance change $R = f(t)$ on the distance between the electrodes: $L = 1$ cm, $L = 3$ cm and $L = 5$ cm

3. Experimental results

Confirmation of expression (8) is provided by the presented results of measuring the change in tissue impedance at two extremities in identical locations. Fig. 6 shows the graph of tissue impedance variation over time during the cessation of blood circulation.

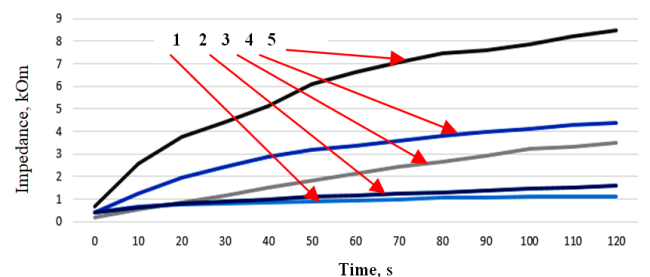


Fig. 6. Graph of tissue impedance change over time during the application of a tourniquet (1 – R,kOm (0.5 time), 2 – R,kOm (1.1 time), 3 – R,kOm (2.5 time), 4 – R,kOm (3.0 time), 5 – R,kOm (without tourniquet))

Fig. 7 shows the graph of changes in the ionization time constant with respect to the tourniquet application time.

The obtained relationship confirms that changes in the ionization time constant can be one of the diagnostic criteria for changes in the properties of biological tissue [16, 23, 26].

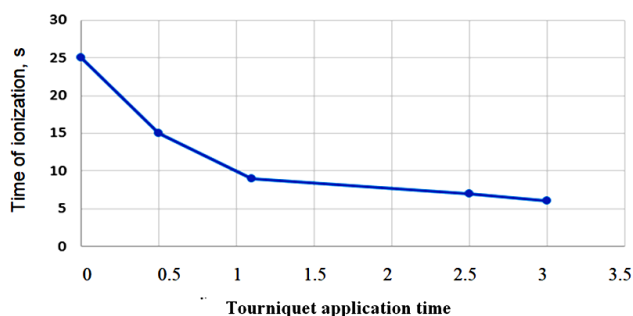


Fig. 7. Graph of changes in the ionization time constant as a function of tourniquet application time

The investigation of individual characteristics of impedance changes was conducted on four objects. Fig. 8 presents the graph of impedance variations for each specimen.

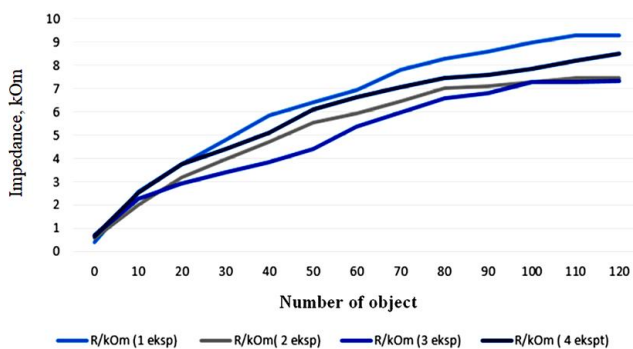


Fig. 8. Graph of impedance changes in biological tissue for four specimens

The analysis of the dependencies $R=f(t)$ (Fig. 8), indicates that the variation in impedance values depends on the individual properties of the investigated specimens and ranges from 10% to 20%. In order to exclude individual human characteristics and determine diagnostic criteria for ischemia development that are independent of many uncertain factors, a diagnostic method has been developed as follows [2, 29, 30].

1. Electrodes are placed in pairs on corresponding areas of each limb.
2. Simultaneously measure the change in impedance of each limb segment.
3. The coefficient of relative impedance change is determined as follows: $k = \frac{Z^*}{Z}$, where Z^* – are the impedances of the biological tissue in the segments of the limb with and without the tourniquet applied, respectively. In cases of conditions such as diabetes or limb injury, the healthy limb is taken as the baseline value.

Fig. 9. The graphs of the coefficients of relative impedance change are presented as a function of the duration of tourniquet application.

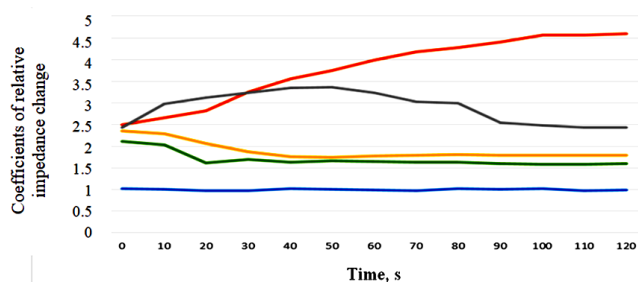


Fig. 9. Graphs of changes in the coefficients of relative impedance change as a function of the duration of tourniquet application

Analysis of the graphs, shown (Fig. 8), depicting changes in the relative impedance coefficient $k=f(t)$ over time, allows for the establishment of criteria for assessing the condition and development of ischemia in biological tissue.

- the graph of the changes in $k(0)$ for the investigation of two healthy limbs shows that the relative impedance coefficient remains within the range of 1 ± 0.05 , fluctuating within 0.5% (the instrument's accuracy error). The value of $k(0)=1 \pm 0.05$ indicates an equal (healthy) state of the biological tissue.
- the graph of changes in $k(1)$ during a 0.5-hour perfusion stop follows an exponential pattern, indicating the absence of biological changes in the tissue and its ability to recover.
- the coefficient $k(1.1)$, corresponding to a 1.1-hour perfusion stop, changes according to a quadratic-decreasing law, characterizing the transition of the biological tissue from viable to the initial stages of tissue necrosis.
- the coefficients $k(2.5)$ and $k(3.0)$ obtained after a perfusion stop of 2.5 and 3.0 hours or more show minimal changes, indicating irreversible processes of tissue necrosis and the manifestation of the reperfusion effect.

On Fig. 10 graphs of changes in the impedance of BT after releasing the tourniquet are presented. The tourniquet was applied for 2.5 hours, and measurements were taken after its removal at 10 and 30 minutes.

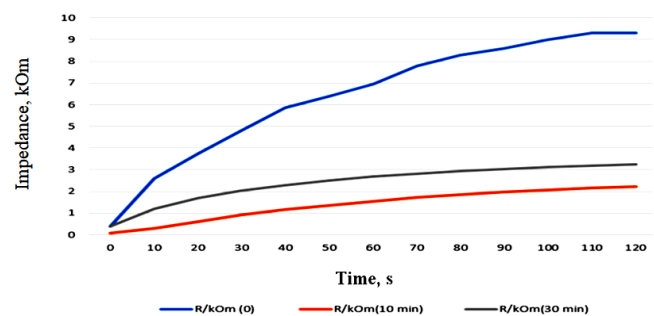


Fig. 10. Graphs of changes in the impedance of biological tissue after releasing the tourniquet

The analysis of the graphs (Fig. 10), provides grounds to consider that for the investigated biological object, the initial stage of cell necrosis and the onset of reperfusion syndrome are observed when blood perfusion is disrupted for more than 1.0 hour. The cessation of blood perfusion for 2.5 hours and more led to irreversible tissue necrosis processes. Tissue impedance practically does not recover and requires additional medical intervention.

4. Conclusions

Determining the remaining time until critical changes in the properties of biological tissue during the application of a tourniquet is not always possible in field conditions, considering the complexity of using existing stationary devices. Conducting rapid diagnosis of limb ischemia requires fast and cost-effective diagnostic tools, especially in the surgeon's office.

The study of the transient ionization process, which lasts up to 2 minutes, has shown that to avoid discrepancies related to individual patient characteristics, it is advisable to use the k -coefficients of relative impedance changes in biological tissue.

Based on the results of the study of the transient ionization process, a method for detecting changes in the properties of biological tissue during impaired blood circulation has been developed. The duration of the transient process is between 100 s and 120 s, allowing for rapid diagnosis of ischemia in the muscle

tissue of the patient's extremities. The method is based on comparing two simultaneously obtained integrated functions of healthy and affected tissues and analyzing the relative coefficient – k , which is determined by the formula: $k = \left(1 - \frac{S_{ex}}{S_{ex}^*}\right) \cdot 100\%$, where S_{ex} – the result of integrating the function $Z=f(t)$ without the application of a blood occlusion cuff is denoted as S_{ex} , and the result of integrating the function $Z=f(t)$ with the application of a blood occlusion cuff is denoted as S_{ex}^* . According to the data presented in Fig. 8, if the relative coefficient – k falls within the range of $0 \pm 0.05\%$, it indicates unchanged properties of biological tissues in both extremities. When the relative coefficient varies between 0.05% and 1, it suggests changes in the properties of biological tissues in both extremities. If the value of k is 0.5 or lower, it indicates the presence of irreversible processes in the development of ischemia in the muscle tissue.

It should be noted that the changes in the coefficient k according to an exponential law during the transitional process confirm the viability of biological tissue, allowing the avoidance of reperfusion syndrome after the removal of the blood occlusion cuff. On the other hand, changes in the relative electrical resistance coefficient k according to a linear law during the transitional process are associated with irreversible cell necrosis. Deviations in the value of the relative electrical resistance coefficient k by 5–8% from the unit value diagnose the initial stages of blood perfusion disruption and the development of ischemic tissue disease. The development of reperfusion syndrome is observed in the investigated biological objects when the perfusion is disturbed for more than 1 hour, and disruptions of perfusion exceeding 2.5 hours lead to irreversible changes in the properties of the biological tissue.

It has also been established that simultaneous measurements of impedance changes in two identical segments of limbs reveal the time constant of ionization as a critical parameter in studying the development of ischemia.

The prospects of the study – Advances in rapid diagnostic methods based on data obtained from transient processes of ionization in biological tissue require further research in conjunction with results from tissue property changes obtained through biopsy. This will allow the development of prediction methods for the development of ischemia and help determine the timing of surgical interventions and adjust the course of medical treatment.

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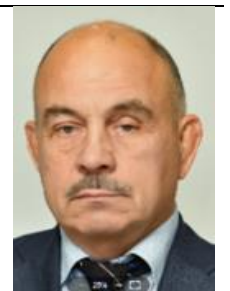
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D.Sc. Valerii Kryvonosov
e-mail: yhtverf007@ukr.net

Doctor of Technical Sciences, professor, National University of Life and Environmental Sciences of Ukraine.

Field of scientific interests are connected with the method of diagnostics of control and management of electrical complexes.

<http://orcid.org/0000-0002-8219-021X>



D.Sc. Oleg Avrunin

e-mail: oleh.avrunin@nure.ua

Doctor of Technical Sciences, professor, Head of Biomedical Engineering Department, Kharkiv National University of Radio Electronics, Ukraine. Scientific supervisor of research work on research of theoretical and technical principles of diagnostics, assessment and correction of medical and social human conditions. Invited Professor in Gottfried Wilhelm Leibniz Universität Hannover (Germany) and Harbin Engineering University (China).



<http://orcid.org/0000-0002-6312-687X>

Ph.D. Sergii Sander

e-mail: sanderserg@gmail.com

Candidate of Medical Sciences, associate professor of the department of surgery of medical faculty No2 Vinnytsya National Medical University named after M. I. Pirogov. Field of scientific interests: diagnosis, prognosis and treatment of limb ischemia.



<http://orcid.org/0000-0003-1667-6198>

M.Sc. Volodymyr Pavlov

e-mail: machinehead6926@gmail.com

Scientific researcher Vinnytsia National Technical University.

Scientific direction: biomedical information optoelectronic and laser technologies for diagnostics and physiotherapy influence.

Deals with issues of improving the distribution of optical radiation theory in biological objects, particularly through the use of electro-optical systems, and the development of intelligent biomedical optoelectronic diagnostic systems.



<http://orcid.org/0000-0002-0717-7082>

M.Sc. Liliia Martyniuk

e-mail: martyniuklilia@nubip.edu.ua

Senior lecturer of the Department of Electrical Supply named after V. M. Synkova of Education and research institute of Energetics, Automatics and Energy saving National University of Life and Environmental Sciences of Ukraine.



<http://orcid.org/0009-0007-3852-5610>

Ph.D. Bagashar Zhumazhanov

e-mail: bagasharj@mail.ru

Senior researcher of the Institute of Information and Computing Technologies of the CS MES RK, associate professor.

Graduated from the Faculty of Physics and Mathematics of the Abai Almaty State University with a degree in Computer Science and Mathematics. Master's degree in "Information Systems". In 2011 he defended his thesis for the degree of Candidate of Technical Sciences. Associate professor of the OP "Digital Engineering and Data Analysis".



<http://orcid.org/0000-0002-5035-9076>