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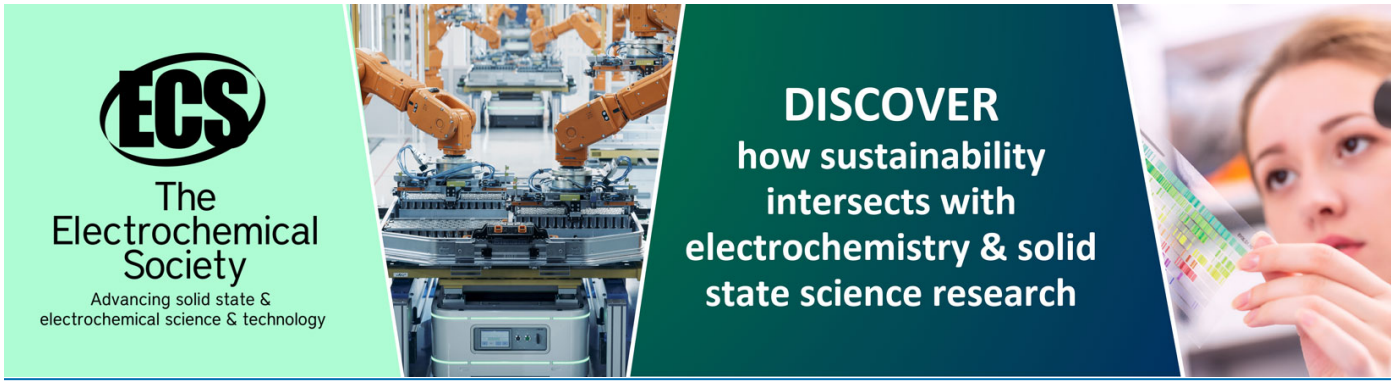

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Pulse Related Changes in Electrical Impedance of Blood Vessels: Physical, Experimental and Modelling Aspects

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Abstract. The paper presents the results of studies directed toward the determination of physical mechanisms and causal factors responsible for variations in the electrical impedance of the cardiovascular system. Experiments were carried out using the original hydrodynamic apparatus modelling different hemodynamic conditions, i.e., a pulsatile flow in a blood vessel of variable diameter, ramified pulmonary blood flows and the function of a cardiac valve. Computer-assisted signal processing techniques provided measurements of the active and capacitive components of the electrical conductivity with an error not exceeding 0.1%. Impedance values were analyzed for different vessel size and geometry, flow rate, temperature, concentration of ionic and dielectric components in some model biological fluids at different frequencies of the probing alternating current. It has been found that bioimpedance oscillations can be mainly attributed to the local modulations of the diameter of blood vessels such as the function of cardiac valves.

1. Introduction

Bioimpedance rheography techniques based on registration of the complex electrical resistance of biological tissues with respect to alternating electric current are used in modern medicine for non-invasive diagnostics of many conditions and disorders of the human body. Current application areas of these methods include: assessment of the cardiovascular system function and structure (rheography and analogous methods); investigation of water metabolism of human body; identification of body fat and musculoskeletal mass; differential diagnosis of diseases of parenchymatous organs (liver, etc.); intraoperative myocardium protection control during open-heart surgery; conductimetric analysis of blood cell composition, and so on. The feasibility of rheographic diagnostics stems from the fact that biological tissues are complex multi-component media with quite different electrical conduction and dielectric properties (Schwan 1956, 1957 [1-2]; Geddes & Baker 1967 [3], Schwan & Foster 1980 [4], Nyboer 1970 [5]). The most pronounced electrically conductive properties are characteristic of extracellular biological fluids composed predominantly of electrolytes; for instance, blood contains a 0.85% NaCl solution and other univalent and bivalent metal salts of a less amount. That is why the impedancemetry methods are suitable for determination of the degree of human organ blood filling and, therefore, to assess the function of the cardiovascular system (Holzer *et al* 1946 [6], Nyboer 1959 [7]).

One of these techniques is thoracic impedance cardiography (rheocardiography), which provides a technically simple and inexpensive method of early diagnostics of hemodynamic disturbances and heart insufficiency. Rheocardiography consists in time monitoring of pulsatile oscillations of impedance of the thorax region during the cardiac cycle (Kubicek *et al* 1970 [8], Penney 1986 [9], Geddes & Baker 1989 [10], Grimnes & Martinsen 2008 [11]). Although rheocardiography has been known for several decades, its clinical utility is still limited because of the ambiguity and difficulty of interpretation of experimental data and also of the high variability of clinical parameters obtained by this method for different patients. The possible reasons for the low reliability of bioimpedance measurements include the dependence of electrical resistivity on the excessive number of biological and physical parameters, the low accuracy of measuring techniques and apparatus, neglecting a contribution of the capacitive component of impedance and, besides, the insufficient theoretical understanding of the mechanisms of electrical conductivity in biological fluids, tissues and blood vessels.

The last circumstance plays a crucial role in generating diagnostic errors in rheocardiography. The idea that bioimpedance changes could be used for measuring variations of blood filling in arterial circulatory vessels was first put forward in the mid 20th century (Holzer *et al* 1946 [6], Nyboer 1959 [7]). Also, the pioneers of the rheocardiography method have hypothesized the fundamental assumption that the relative change in the volume *V* of the conductive liquid is in direct proportion to the relative change in its electrical resistance *R*. The statement was made within the framework of a simplified mathematical model, in which a blood vessel was represented as an electrolytic conductor with fixed length *L* and time-varying cross-sectional area *S*, remaining, however, uniform throughout the whole length of the vessel. In this case the well known physical formulas for the vessel volume $V(t) = L \cdot S(t)$ and its active (ohmic) resistance $R(t) = \rho \cdot L / S(t)$ (where ρ is the specific resistance of the fluid) are indeed applicable and valid, and their time differentiation gives the so-called Nyboer-Bonjer (Nyboer 1959 [7], Bonjer 1950 [12]) equation:

$$\partial V = -V \frac{\partial R}{R} = -\frac{V}{R} \cdot \left(\frac{\partial R}{\partial t} \right) \partial t = -\frac{\rho L^2}{R^2} \cdot \left(\frac{\partial R}{\partial t} \right) \partial t \qquad (1)$$

This expression was used as a physical basis of all the known rheocardiography methods, including the most popular methods suggested by Kubicek-Patterson and Sramek-Bernstein. Kubicek *et al* (1966 [13], 1970 [8]) made a basic assumption that the systolic stroke output V_S (cardiac blood volume ejected from the heart ventricle into the thoracic aorta over a single systolic cycle) fully corresponds to the aortic dilatation volume and proposed a method for its determination via the change of the total thoracic resistance (impedance) *Z*:

$$V_S \equiv \Delta V = -V \frac{\partial Z}{Z_0} = -\frac{V}{Z_0} \cdot \left(\frac{\partial Z}{\partial t} \right) \Delta t = -\frac{\rho_b d^2}{Z_0^2} \cdot \left(\frac{\partial Z}{\partial t} \right)_{\max} T_{LVE} \qquad (2)$$

The fundamental assumptions in formula (1) are as follows. The specific resistance of blood ρ_b is considered to be constant and equal to the average value 150 Ohm·m (Schwan 1956 [1]). The ohmic resistance R of the blood-containing tissue (aorta) is replaced by the thoracic impedance Z, and the contribution of the possible capacitive component of the alternating current is thus neglected. The base value of the bioimpedance Z_0 in the formula denominator is averaged over a cardiac cycle and is also assumed to be invariable, and the inter-electrode distance d substitutes the aorta length L. Based on this method, the duration of blood expulsion from the left ventricle T_{LVE} and the maximum rate of impedance variation over the cardiac cycle can be determined by analyzing the shape of the rheographic curve (impedance time profile). With the alternative rheocardiography method developed by Sramek (1981 [14]), the initial blood volume V in aorta is calculated using additional anthropomorphic measurements (the patient's height *P* and the empirical correction factor δ suggested by Bernstein (1986 [15]) and related to human body types) as:

$$V_S = -\frac{V}{Z_0}\left(\frac{\partial Z}{\partial t}\right)_{\max} T_{LVE} = -\frac{\delta}{4.25}\frac{(0.17\cdot P)^3}{Z_0}\cdot\left(\frac{\partial Z}{\partial t}\right)_{\max} T_{LVE} \qquad (3)$$

Rheocardiography methods used in present-day clinical practice are normally modifications or combinations of these two basic methods. However, from the physical point of view the methodology described above have some principal shortcomings. The main problem is that the patient data collected during actual diagnostics procedures are in rather rough agreement with parameters necessary for correct mathematical calculations of the stroke output. Thus, Kubarev & Borisov (2008 [16]) have pointed out that the formulas used are valid only for homogeneous cylindrical conductors of arbitrary cross-section and only in the case when the cross-section varies simultaneously and uniformly over the entire length of the conductor in such a way that it always remains cylindrical. However, these formulas are currently applied without sufficient justifications to rheography studies of the thorax with all its contents. It is quite evident that the replacement of the ohmic resistance of the aorta in equations (2-3) by the impedance of the entire thorax region (i.e., by the resistance related to the capacitive conductivity of soft tissues and skin around the aorta, the shape of the tested region, the material and location of electrodes, and the quality of the electrode/skin contact) yields the value that is not equal or, at best, is only proportional to the desired value of the real stroke volume. Thus, for practical calculations based on rheocardiography data there is a need for correction factors, which can be determined solely by comparing with the results obtained by other clinical diagnostic techniques. Generally, these factors correspond to the mean value defined for some control group of patients and, therefore, may prove to be inefficient and incorrect for each individual person. Thus, medical examiners have obtained by rheocardiography only the averaged statistical relationships between the impedance pulsatile oscillations and the magnitude of stroke output, whereas the exact measurements of real stroke output cannot be obtained in such a way. For people with cardiovascular abnormalities, the efficiency of determination of the stroke output on the basis of the rheogram is more doubtful.

Over the past years many researchers have expressed serious doubts about the validity of the fundamental concepts of the existing rheocardiography method from the viewpoint of not only physics but of physiology as well. Since the human body consists of many components with different electrical and geometrical characteristics, we cannot exactly define the path that an electric current takes through the body and cannot be absolutely certain that the observed change in the recorded impedance waveform is caused only by the ejection of a systolic stroke volume into the thoracic aorta. Actually, when the average volume of the entire human aorta is about 90 cm^3, and the maximum possible increase of its cross-section area is ~20% (Westerhof *et al* 1969 [17]), the aorta can accommodate additionally no more than ~20 cm^3 of blood, which is only a small fraction of the normal stroke output (~75 cm^3). At the same time, in reality the amplitude of pulsatile fluctuations of thoracic impedance during the cardiac cycle is normally equal, in absolute value, to ~0.2–0.5 Ohm and, thus, does not exceed 0.5% of the impedance basic magnitude. The aforesaid allows us to conclude that the assumption that the aorta is the most significant source of the rheographic signal is not justified.

For instance, Sakamoto *et al* (1979 [18]) examined the origins of impedance cardiographic signals using the original geometrical model of a thorax, which allowed them to evaluate a contribution of each component of the vascular system to changes in blood volume during a systole: vena cava from right atrium (+20%), right ventricle (–30%), pulmonary artery and lungs (+60%), pulmonary vein and left atrium (+20%), left ventricle (–30%), aorta and thoracic musculature (+60%). Faes *et al* (1979 [19]) pointed to the absence of satisfactory solutions to the so-called "outflow" problem, which lies in the fact that the amount of blood pumped by the heart into the aorta is not in fact proportional to its extension, because a much portion of the cardiac output is further delivered through the aorta into the ramified vascular system. Therefore, the volumetric expansion of the aorta determined from impedance measurements must be much less than the real value of the systolic stroke volume V_S.

Patterson (2010 [20]) reviewed various preceding publications, in which an attempt was made to determine the physiological origin of impedance modulation, and drew the conclusion that there is still no clear evidence to support the assumption that the aortic volume pulsation is the source of a signal.

In 1995 Wang & Patterson [21] started to develop a computer electrical model of the human thorax using the finite-element method. At present, the model contains 3.8 million of basic elements with sizes 1.5×1.5×5 mm. A certain value of specific resistance that corresponds to the average resistance of a particular internal organ obtained using the X-ray data of a realistic human thorax was assigned to every unit volume. By this procedure, the conductivity for all elements in each horizontal cross-section can be calculated. Summing up the obtained values with respect to all slices, one can evaluate the percentage contribution of various thorax organs and regions to the total impedance measurement. The obtained results show that the contribution from the skeletal muscle is dominated, and the contribution from the aorta is small (less than 1%), while the contributions from other arterial and venous vessels of the upper thorax are twice as much as that of the aorta. Similar results were found using the 212 000 tetrahedral element model of the thorax (Lewandowska *et al* 2010 [22]). The model was based on the data obtained from X-ray examination of a 68-year-old man. The authors evaluated the conductivity of the aorta not exceeding 3.2%. Hence, significant distortions in the impedance cardiography waveform, leading to errors in the determination of the stroke volume, can be ascribed to the contributions from other organs.

From the above reasoning it is clear that insufficient accuracy of the traditional rheocardiography methodologies generates a need in the experimental determination of physical mechanisms driving variations in the electrical conductivity of human tissues (Mishlanov *et al* 2010 [23]). The aim of the present paper is to identify most influential parameters on the biological impedance value and to study the main physical mechanisms responsible for changes in the electrical conductivity of model biological fluids in relation to the probing alternating current characteristics (frequency, voltage, current strength), the hydrodynamic parameters of the flow (flow rate and velocity, pressure fluctuation amplitude and frequency), the shape and geometrical sizes of the blood vessel, the temperature and composition of tested electrolytes, and the concentration of ionic and dielectric components in these electrolytes.

2. Materials and methods

2.1. Experimental apparatus and technique

Experimental studies were carried out using the original hydrodynamic apparatus intended for simulation of hemodynamics of the cardiovascular system, i.e., a pulsatile flow in a blood vessel of variable diameter, the ramified pulmonary blood flows and the function of a cardiac valve. Biological fluids different in their crystalloid and ionic compositions were investigated: NaCl, $CaCl_2$, protein and dextran solutions such as physiologic saline (0.9% NaCl), polyglukin (0.9% NaCl + 6% dextran) and rheopolyglukin (0.9% NaCl + 10% dextran), blood plasma and whole blood. A sample vessel (a cell for measurements) was a glass or flexible polymer tube with nichrome electrodes inside. Electrolytic solutions were transported through the measuring cell by a precision peristaltic pump drive Heidolph PD–5101. The pump flow rate varied from 0 to 200 ml/min.

2.2. Electrical measurements

The electrical conductivity of electrolytic solutions was determined using the developed equipment. The electrical meter unit of the setup was used to record the modulus and the phase shift angle of impedance in a wide range of probing alternating current frequencies. It included a sinusoidal voltage generator, an interface unit and a 2-channel analog-digital converter SIGMA–ZET 210 connected to a USB-2 computer port. The signal produced by the sinusoidal voltage generator of current frequency of 20 Hz – 100 kHz and amplitude of 2 mkA – 1 mA was delivered to the input of the interface unit, which generated two resistance signals: reference and measured. This made it possible to measure a resistance values within the wide range from 20 Ohm to 100 kOhm irrespective of feed voltage amplitude. One of the half-bridges of the interface unit contained reference resistors, which were used to calculate the value of an input electric current. The arm of the second half-bridge involved the measurement cell, whose electrodes delivered the sounding signal and removed the measured resistance signal (bipolar connection circuit). The reference and measured signals from the interface

unit were fed to the analog-digital converter inputs, quantized and transferred to the computer to store as a data file. The measuring time was fixed and equal to 0.8 s. The specific computer program was applied to calculate the total resistance at every time moment and the phase shift between the reference and measurement signals. Since the summary frequency of discretization of the analog-digital converter SIGMA–ZET 210 was equal to 500 kHz, then the number of the obtained experimental points at each input channel amounted to 200 000. Such a considerable number of calculations (and, consequently, an essential decrease in the sum of the root-mean-square deviation of the measured resistance from the average value) provided high-accuracy measurements in a wide range of frequencies, currents and phase shifts of the input signal. Taking into account computer corrections (based on the results of normalization test measurements) yielded a measurement error not exceeding 0.1%. If it is necessary, the accuracy of measurements can be improved by applying more complicated and advanced filtration, fluctuation smoothing and statistic data processing algorithms.

3. Results and discussion

3.1. Dispersion relationships of fluid conductivity

Measurements of the modulus and phase shift angle of the conducting fluid impedance were performed in the cylindrical glass tubes of various length L (6.8, 18.2, 20.5, 22.0 cm) and inner diameter D (3.48, 6.85, 8.82 mm). The experiments allowed us to determine the dependence of the specific resistance of the fluid ρ on the flow rate, temperature and ionic concentration at different electric current frequencies. It has been found that the frequency (dispersion) dependence of impedance manifests itself most strongly. In the general case, the resistivity values, which are maximal in the low frequency range due to polarization and electrolysis effects, monotonically decrease with increasing frequency and, when the frequency reaches 10 kHz, they become almost equal for all examined fluids (figure 1*a* and figure 2*a*). At the same time, at these high frequencies the phase angle φ, whose tangent characterizes the ratio between the capacitive and active components of impedance, approaches zero as well (figure 1*b* and figure 2*b*). Thus, at frequencies higher than 10 kHz, the total resistance of electrolytic solutions is caused basically by the active (ohmic) conductivity mechanism so that the reactive (capacitive) conductivity of the fluid can be justifiably neglected. However, this conclusion certainly is not relevant to a clinic medical situation observed during examination of the human thorax by impedancemetry, when an alternating electric current flows not only through the aorta filled with blood but also through the surrounding soft tissues, which, on the contrary, have a significant capacitive conductance at high frequencies (the so-called two-compartment model (Baker *et al* 1971 [24], Geddes & Baker 1989 [10]). Under these conditions, one should take into account the capacitive conductance of soft tissues as well.

As it is known from physical electrochemistry, the basic conductivity of electrolytic solutions is produced by the directional transport of dissociated ions. For direct current, the electric current strength reaches its maximum value at the moment when the potential difference arises. Later, when the free ions reach the electrodes, the electric current decreases monotonically to zero. The charge relaxation time depends on the geometrical size of the liquid conductor and is usually equal to $\sim 10^{1}$ s. Such a relaxation effect reduces considerably in the case when the alternating current with a short period of oscillation is applied. This provides a decrease in the solution resistance with increasing probing current frequency, as is readily seen in the graphs in figure 2*a* and figure 3*a*.

In biological fluids, containing such dielectric components as organic and protein molecules, cells, membranes, etc., there takes place an additional macrostructural polarization. The positive and negative ions flow under the action of the external electrostatic field in the opposite directions and reach the surface of ion-impermeable objects, where their accumulation provides additional dipole moments (Frank-Kamenetskii & Sedunov 1963 [25]). The relaxation time of macrostructural polarization is equal to $\sim 10^{-3}$–10^{-8} s. The role of polarization of this type in biological objects is more important compared to other types of polarization. Hence, the specific resistance of blood containing both the blood formed elements and the mixtures of protein, fat and saccharides has been found to be considerably higher than the resistivity of physiological solutions (see figure 2*a)*.

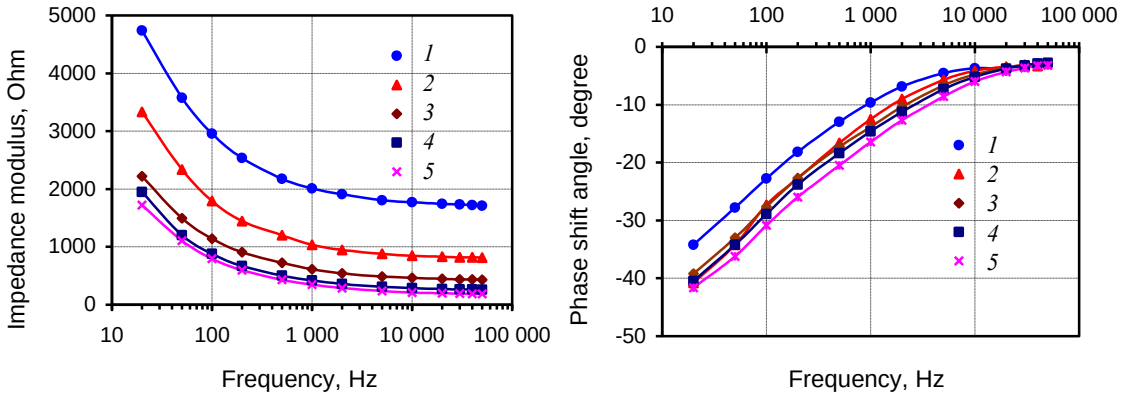

Figure 1. Impedance modulus (a) and phase shift angle (b) as a function of frequency for aqueous NaCl solutions of different concentration: *1* – 0.9%, *2* – 2%, *3* – 4%, *4* – 7%, *5* – 10%.

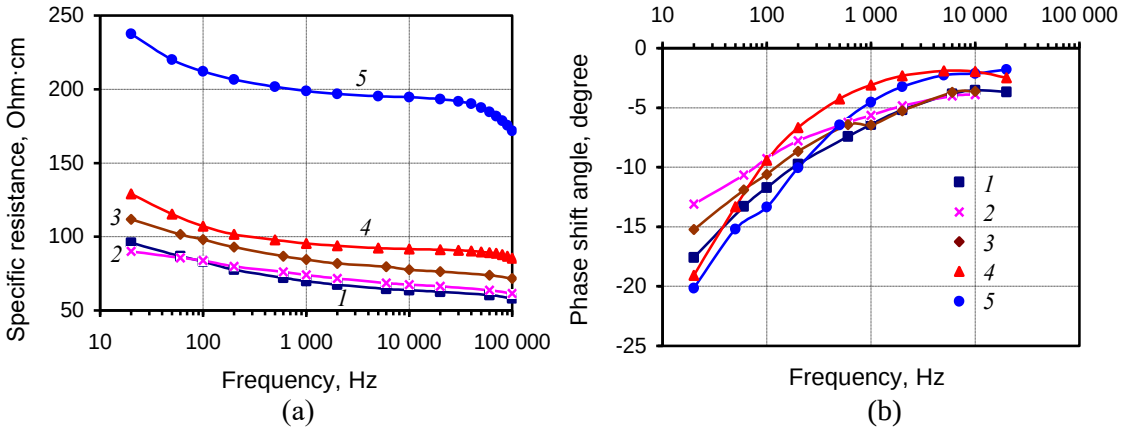

Figure 2. Specific resistance (a) and phase shift angle (b) as a function of frequency for different fluids: *1* – 0.9% NaCl solution, *2* – polyglukin, *3* – rheopolyglukin, *4* – blood plasma, *5* – whole blood.

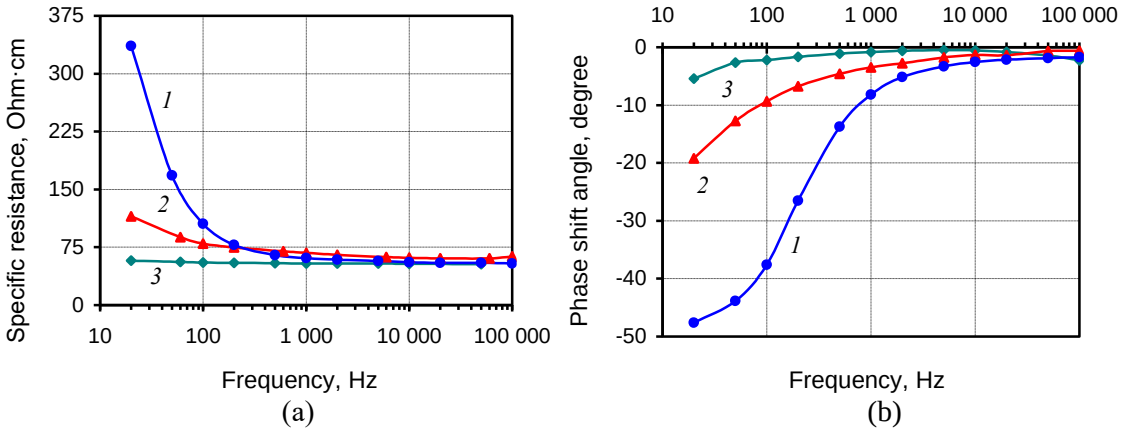

Figure 3. Influence of the electrode material on the frequency dependence of specific resistance (a) and phase shift angle (b) in 0.9% NaCl solution: *1* – aluminium, *2* – Ni-Cr alloy, *3* – chromium.

At low frequencies, an additional contribution to the capacitive component of impedance is introduced by electrolytic (concentration) polarization caused by the inhomogeneity of ion concentration near electrodes and dependent, in turn, on the state of the electrodes surface and their chemical composition and properties. Figure 3 illustrates how the material of the electrodes immersed into the tested fluid influences the resistivity and phase shift measurements obtained in the experiments with 0.9% sodium chloride solution (NaCl). The electrodes, made of aluminium, nichrome alloy and chromium-plated brass, were tested. The graphs show that at low-frequency range the impedance values measured with the aid of aluminium electrodes are significantly higher then the values obtained using the electrodes made of chromium and Ni-Cr alloy. However, after the frequency reaching ~2000 Hz, the influence of the electrode material becomes insignificant for this solution.

3.2. Influence of different parameters

The experiments have also indicated that the specific resistance of the electrolytic fluids depends considerably on the temperature T and concentration of charged ions. In particular, the specific resistance values show the straightline temperature dependence. Thus, when variation in temperature is 1 degree Celsius (from 36 to 37°C), the specific resistance of blood plasma reduces from 53.2 to 52.0 Ohm·cm (the percentage change of 2.4%). For reference, the thermal resistivity coefficient $\partial Z / \partial T$ of the NaCl 0.9% solution has been found to be nearly two times lower, and thus its conductivity changes by 1.4% only (figure 4). Change in the specific resistance caused by increasing concentration of NaCl ions in water fits the hyperbolic approximation. This means that the specific conductivity j of the solution (quantity reciprocal to the specific resistance ρ) is in direct proportion to its concentration (figure 5*a*), which corresponds to theoretical fundamentals (Robinson & Stokes 1959 [26]). After adding into NaCl 0.9% solution the accessory bivalent calcium chloride ions ($CaCl_2$ 10% solution), the curve that illustrates the specific resistance of such a multi-component electrolyte acquires a more complex character, although the specific conductivity still increases linearly with increasing concentration of ions (figure 5*b*).

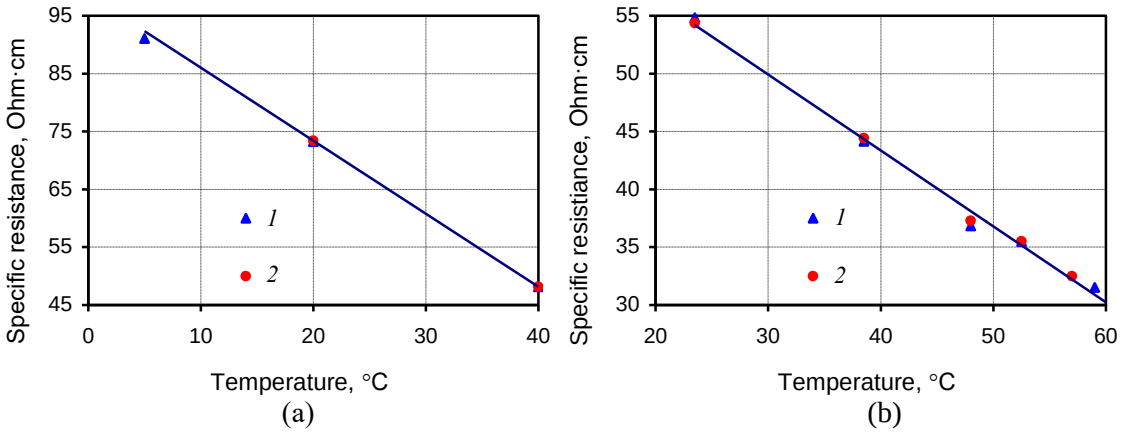

Figure 4. Temperature dependence of the specific resistance of blood plasma (a) and 0.9% NaCl solution (b) at frequencies: *1* – 5 kHz, *2* – 50 kHz.

In contrast to the above factors, no appreciable dependence of the impedance on the fluid flow velocity was revealed during the experiments with 0.9% NaCl, rheopolyglukin and polyglukin solutions placed in the glass tube L = 22 cm long and of diameter D = 6.85 mm. In the polymer tube with elastic walls (L = 23 cm, D = 5.55 mm) at the rotational speed of the pump rotor increasing from 0 to 120 rpm (which corresponds to the flow rate up to 200 ml/min), a slight decrease (at most 0.5%) in the electrical resistance of the solutions (figure 6*a*) occurs. However, in the tube ten times longer (L = 233 cm), the corresponding resistance decrease has already amounted to 5% (figure 6*b*), i.e., the

observed difference in the solution conductivity has appeared to be proportional to the length of the conductive vessel. This is probably caused by a slight increase in the diameter of the elastic tube (and, consequently, in its cross-section), which is brought about by higher pressure drop during the pump operation. Because of this extension of the tube diameter, the resistance decreases with the growth of tube length. To confirm this supposition and evaluate the probable influence of the vessel necking on the impedance value, we have carried out a new series of experiments.

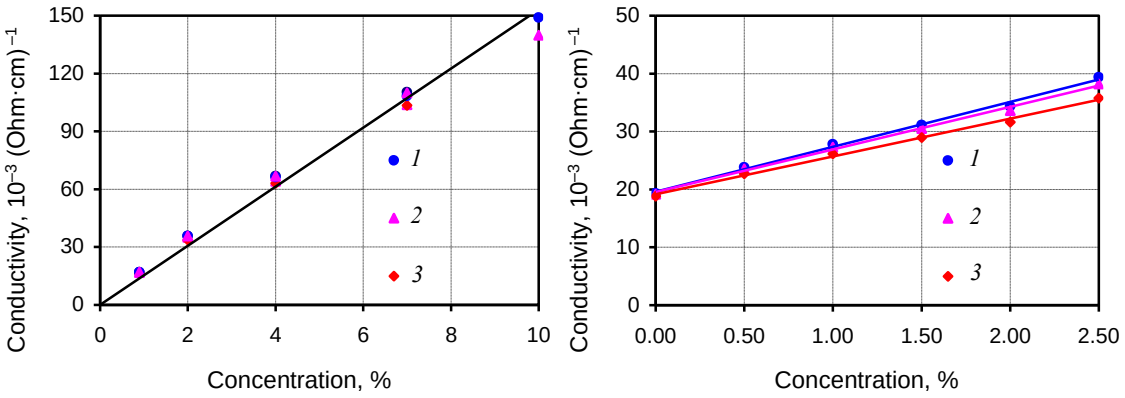

Figure 5. Specific conductivity versus concentration of the NaCl (a) and $CaCl_2$ (b) solutions at frequencies: *1* – 5 kHz, *2* – 50 kHz, *3* – 100 kHz.

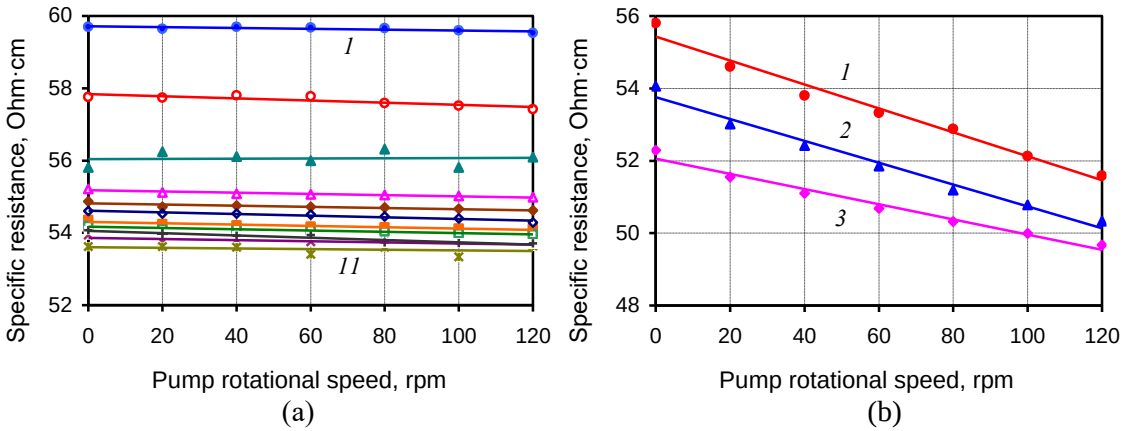

Figure 6. Changes in the specific resistance of 0.9% NaCl solution with various flow rates in the short tube of length L = 23 cm (a) at frequencies 10, 20, 50, 100, 200, 500 Hz, 1, 2, 5, 10, 50 kHz (lines *1*–*11*) and in the long tube of length L = 233 cm (b) at frequencies 100 Hz (*1*), 1 kHz (*2*), 10 kHz (*3*).

3.3. Modulation of the cross-sectional area

Experimental studies have revealed a new and much more powerful origin of conductivity variation, which can be attributed to heterogenous changes in the cross-sectional area of a blood vessel. Indeed, any cross-clamping of the local part of an extensive electrolytic conductor leads to an infinite increase of its electrical resistance, even though the volume of electrolyte remains nearly constant. Figure 7 shows the time dependence of the impedance signal of 0.9% NaCl solution in the deformed tube with flexible walls located between the guide rollers of the peristaltic pump so that they partially squeeze the tube. Even when the deformation of the tube produced by the circulating roller was rather weak, the much more significant periodic impedance fluctuations, synchronous with the pump rotational

speed, were observed. The higher the compression, the larger is the amplitude of impedance fluctuation. It can amount hundreds and thousands percents of the initial basic impedance of the undistorted tube and approaches an infinite value in the case of complete cross-clamping of the tube. Thin lines in the graphs correspond to theoretical computation for the electrical resistance of the solution subject to harmonic modulation of the tube diameter between the moving rollers. Calculations were based on the analysis of the mechanical model of rollers shifting. A good fit between the measured results and the calculated data proves that the reduction in the tube area exerts a major impact on the impedance value.

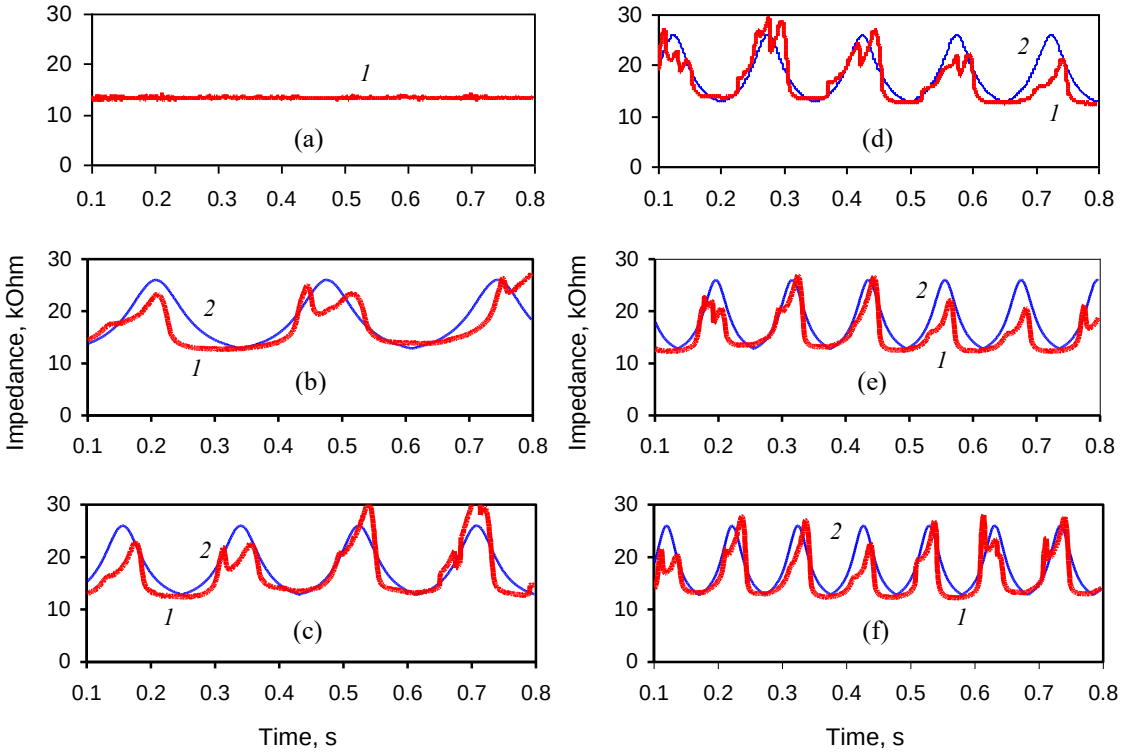

Figure 7. Time variation of the impedance modulus in 0.9 % NaCl solution in the strongly compressed tube at pump rotational speed 0 (a), 20 (b), 40 (c), 60 (d), 80 (e), 100 (f) rpm. Alternating current frequency is 20 kHz; *1* – experiment, *2* – calculations.

Further investigation included the study of a flexible tube, whose part equal to 1/8 of its length was progressively flattened between the clamping jaws. The liquid volume expelled from the tube by squeezing was measured through determining the rising fluid level in a special graduated capillary. The obtained experimental data on impedance modulus for various degrees of compression allowed us to determine the values of conductivity of vessel at different frequencies of the alternating current (figure 8*a*) and variations in the tube area (figure 8*b*). The relations between the parameters describing the relative variations in conductivity, volume and cross-sectional area of the cylindrical vessel for various proportions of the pinched and undistorted sections on the tube length are shown in figures 9*a* and 9*b*. As one can see, the direct proportionality between $\Delta J / J$ and $\Delta V / V$ (or $\Delta S / S$) quantities, postulated by the classical rheocardiography methods, can only be satisfied when the ratio of the pinched part l of the vessel to its whole length L is close to unity. The deviation from the straight line grows significantly with the decrease of l/L and may lead to serious errors in determination of ΔV assuming a spatially non-uniform extension or reduction of the blood vessel diameter. On the other hand, the relations presented in figure 9*b* can be used for evaluation of sectional area changes ΔS in vascular organs through the indications of the bioimpedance magnitude.

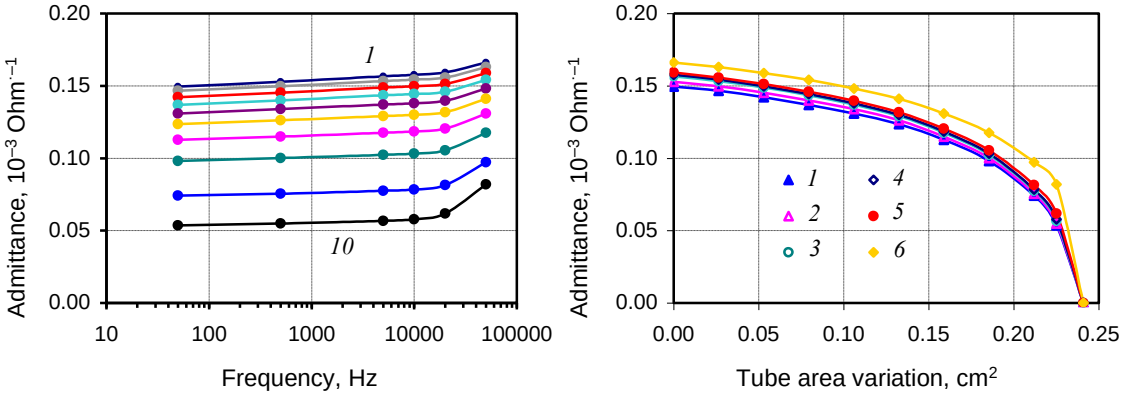

Figure 8. Variations of conductivity of a squeezed tube filled with 0.9% NaCl solution versus alternating current frequency (a) for the values of the expelled volume 0, 0.11, 0.22, 0.33, 0.43, 0.54, 0.65, 0.76, 0.87, 0.92 cm^3 (lines *1–10*) and versus tube area reduction (b) at frequencies 50, 500 Hz, 5, 10, 20, 50 kHz (points *1–6*).

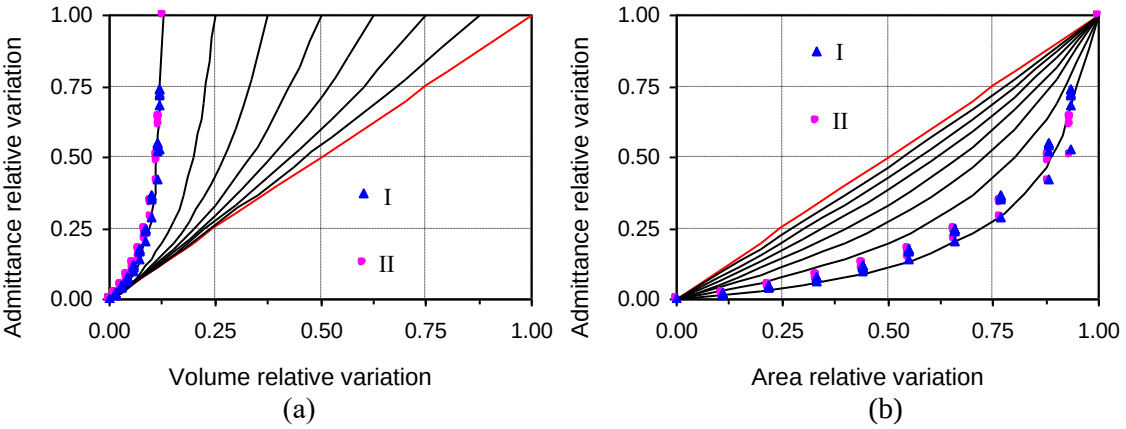

Figure 9. Relative variation of admittance versus relative variations of volume (a) and cross-sectional area (b) in the solutions of reopolyglukin (I) and NaCl (II). *l*/*L*: 8/8 (*1*), 7/8 (*2*), 6/8 (*3*), 5/8 (*4*), 4/8 (*5*), 3/8 (*6*), 2/8 (*7*), 1/8 (*8*).

3.4. Modelling of cardiac and pulmonary blood flows

The experimental findings described above demonstrate that bioimpedance variations, registered in cardiologic practice, can correspond to the local modulation of the cross-section of blood vessel diameter. Thus, the semilunar cardiac valves, which periodically blocked the great vessels (aorta and pulmonary trunk) escaped from the heart ventricles, are able to exert more decisive effects on the thoracic bioimpedance amplitude. To check this supposition, a hemodynamic model of the heart left (aortic) ventricle with a cardiac valve was constructed and verified. The model was a 200 ml working chamber made from a rubber bulb with an opening in its neck. The chamber was connected to a peristaltic pump with the aid of a flexible tube. The bulb neck was attached to a spring-loaded ball valve of inner diameter 5 mm, which models the operation of the aortic valve, The rubber bulb was placed into a closed vessel (container) filled with water. A special volumetric capillary tube attached to the vessel was used to determine the bulk of the tested fluid (0.9% NaCl solution), delivered by the pump into the rubber bulb when the valve was in the close state. After achieving sufficient pressure, the valve opened and some amount of liquid left the bulb. As the pressure was thereby reduced, the valve closed again, and the cyclic process representing the systolic and diastolic phases of heart

activity rerun. The frequency of cycles was defined by the operating velocity of the pump and related to the force of the spring inside the valve.

During these cyclic tests, the electrical resistance of the conductive fluid in different parts of the experimental setup was measured. The paired electrodes were placed in the bottom and neck parts of the bulb and also inside the input and output connecting pipes of the heart valve model. This allowed us to estimate impedance variations caused by the modulation of the bulb cross-section and the operation of the valve. The performed experiments have convincingly shown that the maximum effect on the impedance magnitude is exerted by the local change in the conductor diameter, created by the periodic opening and closing of the valve. For example, at alternating current frequency 50 MHz, voltage 1 V and rotational speed of the peristaltic pump 100 rpm (which provided the eigenfrequency of valve operation near 10 Hz) the amplitude of impedance oscillations inside the valve amounted to ~600 Ohm, which was 70% of its base impedance 850 Ohm for the valve in the open state (figure 10*a*). At the same time, the average impedance contribution of the fluid, filling the undistorted rubber bulb that represented the left heart ventricle, was equal to ~50 Ohm only. The change in its resistance, observed in the case of a 50 ml volume increase of the bulb (25% of its initial 200 ml volume), yields only 2 Ohm, which amounted to ~4% of the bulb impedance value and at most 0.2% of the summary impedance of both the valve and the bulb (figure 10*b*).

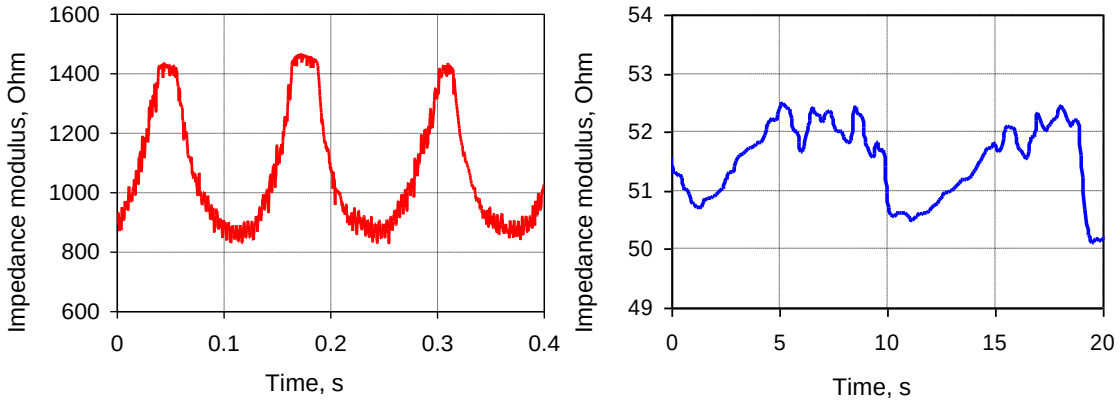

Figure 10. Time variations of the impedance modulus in 0.9 % NaCl solution for the models of aortic valve (a) and heart ventricle (b).

One more experiment was performed to examine the influence of hydrodynamic conditions, modelling the ramified pulmonary blood flow, on impedance changes in model biological fluids. A pulmonary model was composed of 6 identical soft polymer tubes, each of length 25.6 cm and diameter 8.0 mm. The tubes were joined in parallel using two metal union connecting pipes attached in turn to the peristaltic pump by flexible tubes. In the experiment, over the period the fluid passed through the model, these 6 tubes were subjected to cross-clamping one after another, in turn. The electrodes mounted in the connecting pipes recorded thus the joint resistance of different number of electrolytic conductors (at most 6) connected in parallel, whereas the sum of cross-sectional areas of these conductors was a multiple of the cross-sectional area of a single tube.

The tests executed with 0.9% NaCl solution at alternating current frequency 50 MHz revealed that the electrical resistance of the ramified system of tubes increased progressively with increasing number of closed tubes (figure 11*a*), because the fluid conductivity was in direct proportion to the summary amount of the cross-sectional areas of the tubes (figure 11*b*). The obtained results indicate that in the vascular system of lungs, where the total cross-sectional area of blood vessels is ten and hundred times larger than that of the pulmonary artery, the ohmic (active) resistance must be essentially smaller than that of the rest of tissues of human organism.

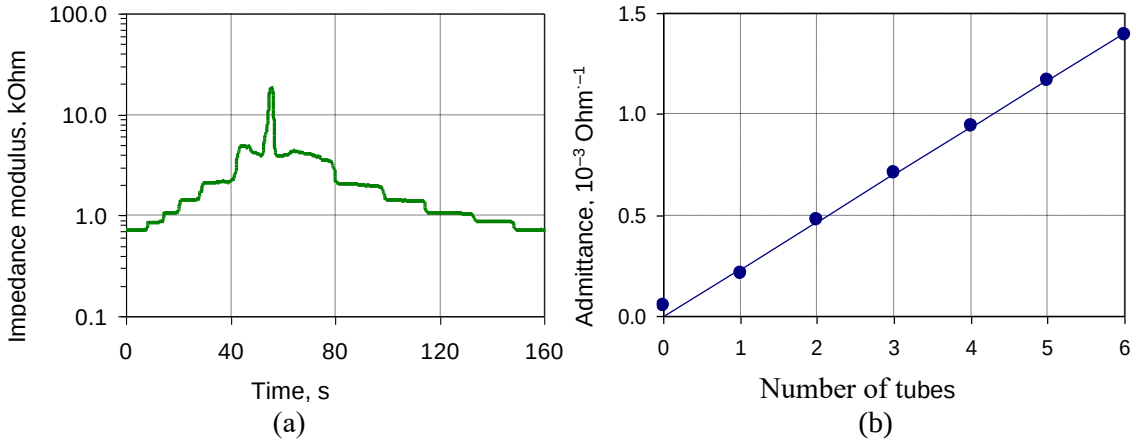

Figure 11. Impedance modulus (a) and admittance (b) in 0.9 % NaCl solution at various numbers of non-clamped open tubes in the model of a ramified pulmonary blood flow.

4. Conclusion

The analysis of publications on rheocardiography methods [27] shows that despite the fact that these techniques are known for more than 50 years there has been no proper understanding of a real physical cause of variations in the thoracic impedance, and that the reliability of determination of the stroke volume and cardiac output by these methods remains so poor that they cannot be recommended for a broad use in clinical practice. In the present work, various physical mechanisms responsible for changes in the electrical impedance of the model solutions of biological fluids were investigated experimentally, and their possible contribution to the amplitude of the signal was quantitatively estimated. It has been found that the conductivity of a blood vessel is most strongly affected by a local change in its cross sectional area – the effect not previously considered by classical rheography, where changes in the biological impedance are attributed solely to an expansion of the volume of blood ejected from the left ventricle into the thoracic aorta during the systolic cycle. However, bioimpedance changes observed in patients can be caused by modulations of not only the volume, but also the form of conductive biological tissues. Heart valve structures that produce local changes in the cross-section of the bloodstream may have a more significant impact on the magnitude of bioelectric impedance. This supposition should be verified in clinical trials, which can provide a good basis for bioelectrical impedancemetry analysis of the geometric forms of cardiac chambers and great vessels.

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References

[1] Schwan H P 1956 Electrical properties measured with alternating currents: body tissues *Handbook of Biological Data* ed W S Spector (Philadelphia: W B Saunders Co)

[2] Schwan H P 1957 Electrical properties of tissues and cell suspensions *Advanced Physics in Medicine and Biology* **5** 147-209

[3] Geddes L A and Baker L E 1967 The specific resistance of biological material – a compendium of data for the biomedical engineer and physiologist *Med. Biol. Eng.* **5** 271-93

[4] Schwan H P and Foster K R 1980 RF-field interactions with biological systems: Electrical properties and biophysical mechanisms *Proc. IEEE* 68(1) 104-13

[5] Nyboer J 1970 Electrorheometric properties of tissues and fluids *Ann. N.Y. Acad. Sci.* **170** 410-20

[6] Holzer W, Polzer R and Marco A 1946 *Rheokardiography. A method of circulation's investigation and diagnosis in circular motion* (Vienna: Wilhelm Maudrich) (English transl.)
[7] Nyboer J 1959 *Electrical impedance plethysmography: The electrical resistive measure of the blood pulse volume* (Illinois: Thomas Springfield)
[8] Kubicek W G, Patterson R P, Mattison R H and Witsoe D A 1970 Impedance cardiography as a noninvasive method of monitoring of cardiac function and other parameters of the cardiovascular system *Ann. N.Y. Acad. Sci.* **170** 724-32
[9] Penney B C 1986 Theory and cardiac applications of electrical impedance measurements *CRC Crit. Rev. Bioeng.* **13** 227-81
[10] Geddes L A and Baker L E 1989 *Principles of Applied Biomedical Instrumentation* (New York: Wiley) 591-639
[11] Grimnes S and Martinsen O G 2008 *Bioimpedance and bioelectricity basics 2 ed.* (Amsterdam: Elsevier Science & Technology Books)
[12] Bonjer F 1950 *Circulationderzock door Impedantiemeting* (Groningen) 146
[13] Kubicek W G, Karnegis J N, Patterson R P, Mattison R H and Witsoe D A 1966 Development and evolution of an impedance cardiac output system *Aerospace Med.* **37**(12) 1208-12
[14] Sramek B B 1981 Noninvasive technique for measurement of cardiac output by means of electrical impedance *Proc. 5th Int. Conf. on Electrical Bioimpedance (Tokyo, Japan, 1981)* 38-41
[15] Bernstein D P 1986 A new stroke volume equation for thoracic electrical bioimpedance: theory and rationale *Crit. Care Med.* **14(**10) 904-09
[16] Kubarev A M and Borisov V I 2008 Pulsation of blood in arterial system and its influence on the body electric resistance *Nizhegorodsky Medical J.* **4** 35-41 (in Russian)
[17] Westerhof N, Bosman F, De Vries C J and Noordergraaf A 1969 Analog study of the human systemic arterial tree *J. Biomechanics* **2**(2) 121-43
[18] Sakamoto K, Muto K, Kanai H and Lizuka L 1979 Problems of the impedance cardiography *MBEC* **17** 697-709
[19] Faes Th J C, Kerkkamp H J J, Hoetink A E and Heethaar R M 2001 The unsolved outflow problem in impedance cardiography *Proc. 11th Int. Conf. on Electrical Bio-Impedance (Oslo, Norway, 2001*) 527-30
[20] Patterson R P 2010 Impedance cardiography: What is the source of the signal? *J. Phys.: Conf. Ser*. **224**(1) 012118
[21] Wang L and Patterson R P 1995 Multiple sources of the impedance cardiogram based on 3-D finite difference human thorax models *IEEE Trans. BME* 42(2) 141-48
[22] Lewandowska M, Wtorek J, Bujnowski A and Mierzejewski L 2010 Monitoring of CRT by means of impedance multiple measurements – simulation studies *J. Phys.: Conf. Ser.* **224**(1) 012097
[23] Zuev A L, Mishlanov V Yu, Sudakov A I and Shakirov N V 2010 Experimental modelling of rheographic diagnostics of biological fluids *Russian J. of Biomechanics* **14**(3) 64-74
[24] Baker L E, Judy W V, Geddes L E, Langley F M and Hill D W 1971 The measurement of cardiac output by means of electric impedance *Cardiovasc. Res. Cent. Bull.* **9**(4) 135-45
[25] Frank-Kamenetskii D A and Sedunov B I 1963 Dielectric constants of biological objects *Sov. Phys. Usp.* **6** 279-93
[26] Robinson R A and Stokes R H 1959 *Electrolyte Solutions* (London: Butterworths scientific publications)
[27] Mansouri S, Alhadidi T, Chabchoub S and Salah R 2018 Impedance cardiography: recent applications and developments *Biomedical Research* **29**(19)