Application of Electroimpedance Spirometry for Clinical Assessment of Respiratory Function Indices

A L Zuev1,2, a, N N Shakirov1, A I Sudakov1 and V Ju Mishlanov3

1 Institute of Continuous Media Mechanics, Perm Federal Research Center of Ural Branch of Russian Academy of Sciences, Perm, Russia
2 Perm National Research Polytechnic University, Perm, Russia
3 Acad. Wagner Perm State Medical University, Perm, Russia

E-mail: *zal@icmm.ru

Abstract. A practical method of studying the dynamics of respiratory function associated with the registration of the electrical impedance of conductive biological fluids exhaled by the patient is described. In the model measuring cell, the physical causes and relationships in the conductivity of the air flow, saturated with an electrolytic fluid aerosol created by an ultrasonic nebulizer have been investigated experimentally. The design of a new electrical impedance spirometer in the form of a mouthpiece with electrical sensors, filled with a porous medium impregnated with electrolyte, through which the patient breathes, is developed and tested. To register fluctuations in the magnitude of the impedance modulus, an original hardware and software complex is used, made on the basis of a high-speed analog-to-digital converter. Based on electrical impedance analysis data, the methods are proposed for quantitative assessment of the basic spirometric medical indicators characterizing the state and functioning of the patient’s breathing apparatus, such as respiration rate, entry and expiration rate, exhaled air volume, amount and concentration of exhaled lung fluid.

1. Introduction

Over the past decades, bioimpedance methods of medical analysis, based on the registration of changes in the complex electrical resistance (impedance) of biological media to alternating current, have been increasingly and successfully used in clinical practice for the diagnosis of diseases of internal organs. The advantages of bioimpedance methods for instrumental research of the human body are their non-invasiveness, relative ease of use, as well as their exceptional low cost, which does not require expensive reagents and equipment. The areas of their modern application are the study of the state of the cardiovascular system (rheocardiography and similar techniques) [1-8], the study of the tissue composition of the human body (assessment of the ratio of fat, musculoskeletal and water masses) [9-10]; analysis of the molecular composition of biological fluids [11], conductometric method for counting blood cells [12-13] and many others. In these geographical methods, the objects of measurements were biological tissues and liquids having some conductive properties (such as, for example, blood). However, until recently, no attempt was made to apply electrical impedance techniques to assess the condition and viability of non-conductive organs such as the respiratory tract and lung tissue of patients.

A group of physicians from Perm State Medical University under the leadership of the head of the Department of Propedeutics of Internal Diseases, professor V. Ju. Mishlanov, was the first to suggest using impedance measurements for the diagnosis of respiratory diseases. To achieve this goal, the researchers proposed an original key idea, which consists in the preliminary saturation of the patient's airways using an ultrasonic nebulizer inhaler with a suspension of the smallest drops of a conductive liquid – 0.9% sodium chloride (NaCl) solution [14]. In the experiments, one of the measuring electrodes was installed in the inhaler mouthpiece, and the second electrode was located on the chest skin. It was assumed that the exhaled aerosol has electrical conductive properties, and it is due to the movement of charged dispersed particles that the electrical circuit in the inhaler mouthpiece closes. Such ionization
of particles could arise in a nebulizer during random collisions (friction) of particles with each other or with surrounding surfaces during aeration of a solution of a conducting liquid with ultrasonic waves. The application of the new impedance method for clinical spirometry was reported at the Annual Congresses of the European Respiratory Society (Barcelona 2013, Amsterdam 2015) and aroused great interest among pulmonologists and specialists in functional medical diagnostics. The obtained preliminary results of clinical studies revealed a significant difference in the mean modular value of the electrical impedance between the groups of patients with various disorders of the respiratory function and the group of practically healthy individuals [15]. Thus, a marked growth in the impedance magnitude was found for patients with bronchial asthma in comparison with control group. The method is also able to detect early pneumonia signs; it shows approximately 90% sensitivity when compared with conventional spirometry. In some cases (e.g. in the case of allergic inflammation of the respiratory tract), the sensitivity of the method exceeds that of the common spirometry by 30%, which makes it possible to diagnose bronchial asthma in the patients who had no yet clinically significant symptoms of this disease [15-16]. The authors made an assumption that the reason for the recorded changes in impedance is a decrease in the rate and volume of the air flow exhaled by the patient during the respiratory cycle. It is just the strength of the respiratory muscles, determined by the rate of air flow exhaled by the patient during the respiratory cycle, that is one of the most important indicators of the medical assessment of the respiratory system. So, a decrease in the rate of this flow is a typical sign of impaired ventilation in bronchial asthma and diseases of the lung parenchyma.

The present research was undertaken with the aim of a thorough study of physical and biophysical processes underlying the proposed electrical impedance spirometric technique, and its further development and improvement for the diagnosis of respiratory diseases. Thus, one of the drawbacks of the previously used bipolar circuit for measuring electrical impedance was the location of the electrode on the patient's chest, which led to a high degree of uncertainty in the pathways of electric current through the human body and seriously complicated the interpretation of the obtained results. In particular, it is required to develop a new type of electrical impedance spirometric sensor, which allows one to estimate the physical parameters of the expiratory and inspiratory flows of the air exhaled and inhaled by the patient. This would make it possible to estimate by the magnitude of electrical resistance the main parameters of spiropgraphy, such as: respiratory rate, volume, inhalation and exhalation velocity and to analyze the state of muscle activity of the patient's lungs and tissues.

2. Results of model experiments

2.1. Experimental apparatus and technique

A model electromechanical setup was created for the experimental study of the electrical conductivity of aerosol electrolyte particles flow in the channel when probing with an alternating electric current in a wide frequency range. The setup consisted of a conductive aerosol generator (nebulizer), an experimental measuring cell, and a hardware-software complex for measuring the modulus and phase angle of impedance [16]. The design of the measuring cell and electrodes was specially selected to be identical to that used earlier in clinical studies of patient respiration by the method of electrical impedance spirometry [15]. In our experiment, two silver chloride (AgCl) electrodes 25 mm long and 8 mm wide were placed inside a polystyrene tube 8 cm long and 10 mm in diameter. The electrodes were located inside the cell at a distance of 3 mm from each other in the same plane near the inner wall of the tube. The medical ultrasonic inhaler Omron NE-U17 was used for aerosols creation. For this purpose, the reservoir of the inhaler was filled with a 10% solution of sodium chloride (NaCl) or calcium chloride (CaCl2) with a volume of 50 ml. As a result of exposure of the liquid to ultrasonic vibrations with different intensities of nebulization (spraying), an aerosol with an average particle size of ~ 4-6 microns is formed in the inhaler. The nebulization power of the inhaler could be varied (ten different levels from 1 to 10 are possible). The air flow carrying the aerosol out of the reservoir is created by the ventilator of the inhaler, and the air flow rate could vary from 0 to 17 l/min (the eleven levels from 0 to 10 are adjustable).

The registration of the impedance value fluctuations was carried out using a designed portable hardware-software complex connected to a personal computer (laptop) through the USB port [16]. The ability to quickly and objectively obtain large amounts of experimental data is very important and relevant for the development of the clinical application of impedance measurement in medical practice. The developed and assembled original high-precision electrical measuring equipment made it possible
to significantly increase the accuracy of measurements of the modulus and phase angle of the impedance at alternating current. An alternating current of a wide frequency range (20 Hz – 100 kHz) and an amplitude value of a sinusoidal voltage (up to 10 V) was created by a generator of sinusoidal oscillations G3-106. The measured signal (the value of the electric current in the measuring cell) was recorded by the TERMODAT 13E1 device, developed by the instrument-making enterprise OOO NPP "Control Systems" (Perm) specifically for recording signals from industrial thermocouples and resistance thermometers, then it was digitized and transmitted to a computer. The device made it possible to reliably record both sufficiently large values of the electrical resistance itself (from 1 kΩ to 100 MΩ), and very weak (not exceeding 0.1-1%) changes in it. The measurement error was no more than 5% at low resistances up to 100 kΩ and no more than 10% at high resistances above 100 kΩ. The computer program can continuously receive data in real time from 4 channels with a measurement period of 0.2 sec, record them to a text file and, at the end of the data reception process, view them in the form of graphs of the signal amplitude versus time.

2.2. Measurements and observations

The results of the carried out model experiments revealed the inconsistency of the initial assumption about the conductivity of the blown aerosol flow. Under normal conditions, the ionization of aerosol particles in the Omron NE-17U nebulizer does not occur. The smallest droplets of a conductive liquid that form an aerosol do not have their own electric charge, are separated from each other by air spaces and are not in electrical contact. As a result, the aerosol of a conducting liquid behaves like a neutral non-conducting medium with a very high ohmic resistance of the order of hundreds and thousands of MΩ. Therefore, the flow of aerosol particles by itself cannot be the cause of the closure of the electrical circuit in the inhaler mouthpiece. Further experiments showed that the reason for the appearance of an electric current in the inhaler mouthpiece was the formation on its inner surface of a thin conductive film of condensed liquid, which is deposited on the wall of the tube when an aerosol flow is pumped through it and through which the electrical circuit between the electrodes was closed. It was found that the thickness of the resulting liquid film depends on the blowing time, flow rate and nebulization power. For this reason, the value of the electrical resistance created by the condensed film can indeed serve as a certain parameter characterizing the patient's respiratory activity obtained in the impedance spirometry method. With further condensation of the electrolyte over time on the walls of the tube and an increase in the thickness of its liquid film, the value of the active resistance decreases.

In the experiments, we studied the temporal changes in the active conductivity (impedance modulus) caused by condensation on the inner surface of the measuring cell of a thin film of a conductive liquid at frequencies of 20 and 100 Hz at different values of the velocity \( V \) and the level of spray power \( W \). Thus, figure 1 represents the dependences of the impedance modulus \( |Z| \) on the aerosol blowing time of a 10\% NaCl solution. The resulting relationships show that after switching the nebulizer, which generated a flow of drops of a conductive salt solution, the values of the electric current in the measuring cell at first remained equal to zero. At that moment the resistance value recorded by the measuring device was infinitely large, which corresponded to the upper measurement limit of the device of 100 MΩ. However, after a certain period of time, depending on the aerosol pumping rate and atomization power, a sudden appearance of an electric current starts and, accordingly, a monotonic decrease in the values of electrical resistance is observed. The lines 1-3 on the graph correspond to pumping levels \( V = 2, 5, 10 \) at the identical maximum spraying power \( W = 10 \). The lower the flow rate, the longer it takes for the condensate film to form on the inside of the tube.
Over time, the resistance value decreases monotonically and approaches a certain asymptotic value corresponding to the resistance of a steady-state liquid film of a certain thickness. This dimensionally stable film, obviously, corresponds to the establishment of equilibrium between the processes of condensation and evaporation of the conductive liquid. In this case, the resistance values, related to the equilibrium film thickness, seem to be quite close, which suggests that the thickness of the final film does not strongly depend on the flow rate. On the contrary, similar resistance values obtained at the same flow rate \( V = 10 \), but different levels of nebulization power \( W = 2, 5, 10 \) (see figure 2) demonstrate a monotonic increase in conductivity (proportionately to the thickness of the formed film) from the concentration of conductive particles in the stream. In this graph, time is counted from the moment an electric current occurs in the cell. In general, it can be concluded that the value of the arising electrical resistance is most dependent on the time interval from the moment the aerosol flow starts pumping.

The dependence of the time of occurrence of the electric current, counted from the moment of the beginning of the pumping of the flow of aerosol particles, on the level of the flow rate \( V \) is shown on the graph figure 3. This experiments were carried out with only one fixed nebulization power corresponding to a maximum value level \( W = 10 \). This is due to the fact that at a lower powers of particle spraying, the nature of the relationships remains just the same, however, the time intervals themselves increase very strongly (up to tens of minutes). The steady-state conductivity values (inverse to the active resistance) corresponding to the equilibrium film thickness are shown in figure 4. As can be seen from the graph, the conductivity of the film approximately increases with an increase in the flow rate according to a law close to linear, although the errors of each specific implementation turn out to be
large enough, reaching 50 and more percents. The reason for such a large scatter of data was due to the very poor repeatability of experiments due to the unpredictable shaking of the tube by the aerosol stream, which led to the disruption of the equilibrium of the film and its runoff to the bottom in the form of separate drops of unequal thickness. The location of the tube itself (horizontally, with an upward slope, with a downward slope), the angle of this slope, and the location of the electrodes (in the upper part of the tube, in the middle of the side wall, in the lower part of the tube) also has a great influence. In order to avoid dependence on these geometrical parameters, in further experiments the tube was placed strictly horizontally, and the electrodes were located from below (at the bottom of the tube), where the thickness of the formed adsorbed electrolyte film turns out to be maximum due to its draining down the walls.

Nevertheless, the presence of such a large number of random factors (including wall wettability, surface and aerosol temperatures, design, geometric dimensions and location of the mouthpiece and electrodes, inclination, accidental shaking and vibrations, etc.), affecting the time of the onset of liquid film formation, thus has a much more decisive effect on the magnitude of the electrical impedance than the studied effect of the aerosol flow velocity, which turns out to be negligible in comparison with it. The random spread (error) of impedance measurement also turns out to be very large and reaches tens of percent. The results obtained did not allow us to consider the proposed impedance method for diagnosing the function of external respiration as sufficiently reliable, accurate and informative from a physical point of view and to recommend it for further use in a clinical setting. The task of the study was to develop a more reliable and valid method of impedance spirometry and to create a design for an electrical impedance spirometric sensor based on the use of another physical principles.

3. Electrical impedance spirometer

3.1. Physical principle of electrical impedance spirometry

In connection with the revealed significant shortcomings of the previously used technique, the purpose of the study was to develop a more accurate and reliable method of impedance spirometry and to create a design for an electrical impedance spirometer based on the use of other physical principles. The main task is to change the design of the used breathing mouthpiece in such a way that the electrical circuit between the electrodes is closed not by a poorly controlled film of electrolytic liquid deposited on the walls of the mouthpiece, but by some conductive medium with well controlled and experimentally repeatable properties, the conductivity of which would depend on the speed of exhaled/inhaled air flow. Based on the results of test experiments, we proposed to use a porous medium impregnated with an electrolytic liquid (solutions of sodium chloride NaCl or calcium chloride CaCl₂ of various concentrations) as the working medium of the spirometer. A patent of Russian Federation was obtained for the proposed design of the electrical impedance spirometer [17].

In the experiments, the porous medium has a form a foam rubber cylinder 10 mm in diameter and 10 mm in length, placed in the tube of the spirometer mouthpiece. The measuring electrodes were located along the perimeter of the cylinder. The pores of the foam rubber was filled with a conductive solution and form conductive tracks inside the foam cylinder that contact the sensor electrodes and thus closed the electrical circuit inside the sensor. The value of the electrical resistance of such a circuit is determined by the concentration of the electrolyte solution and can be selected in such a way as to lie in the most convenient selected range from 1 to 100 kΩ. When the patient breathes through the mouthpiece, the inhaled/exhaled air flows freely through the foam cylinder. During breathing, these conductive paths either become denser (when exhalating) or partially evaporate (when inhaled), thereby periodically changing the value of the electrical impedance. The difference in the recorded values of the electrical impedance between the phases of inspiration and expiration makes it possible to assess the strength of the patient's respiratory function, and the period of its change – the respiratory frequency.

The tests carried out have shown that even in the case when the foam rubber is not impregnated with an electrolyte solution, nevertheless, there is also a significant difference between the impedance values during patients inhalation and exhalation. These changes occur only due to some natural conductivity of the exhaled by a person lung fluid, containing an aqueous solution of some organic salts and lung surfactants. The air exhaled by a person, passing through the foam rubber cylinder, leaves on it traces of these exhaled gases and biological fluids in the form of vapor. During exhalation impedance decreases due to the condensation of vapors on the foam rubber, while during inhalation the impedance increases due to evaporation and escape of vapors from the foam rubber. Of course, the values of the electrical impedance themselves in the absence of impregnation with an electrolytic solution turn out to be
significantly (1-2 orders of magnitude) larger. Without impregnation, the average impedance value reaches 60-80 kΩ (figure 5) and gradually decreasing over time due to the accumulation of biological conductive liquids in the foam. In the presence of impregnation with a 0.9% NaCl solution, the amplitude of impedance fluctuations significantly decreases to the level of 3-5 kΩ (figure 6), however, on the contrary, then gradually increases as the conductive solution impregnating the foam rubber evaporates. However, decreasing the impedance value (which means an increase in the flowing electric current) significantly improves the accuracy and stability of electrical impedance measurements.

### 3.2. Electrical impedance research

A prototype of a portable hardware-software complex based on a high-speed analog-to-digital converter (ADC) and connected to a personal computer (laptop) was created for the examination of patients in clinical conditions. The used electrical circuit is presented in figure 7, which shows a block diagram of an apparatus consisting of a sensor 1 connected to a measuring half-bridge 3, which, together with a reference half-bridge 4, is connected to a broadband frequency generator 2. Fluctuations in the magnitude of the impedance modulus and phase angle at low-power alternating electric current are registered by a hardware-software complex based on a ADC converter 5 and a personal computer 6 [18].

![Figure 7. Block diagram of the apparatus: 1 – sensor, 2 – frequency generator, 3 – measuring half-bridge, 4 – reference half-bridge, 5 – high-speed ADC, 6 – computer.](image)

The developed software of the device allows carrying out a series of experiments with predetermined parameters specified in the control text file, processing the obtained data and displaying them in graphical form. To carry out measurements, the operator needs to specify the necessary parameters on the monitor screen (software control panel of the complex): set the measurement time (up to 8 minutes),
the frequency of the probing current (10-30000 Hz), the amplitude of the voltage of the probing current (10-10000 mV). Also, before starting measurements, the operator can prepare the sensor in the mouthpiece – moisten the foam rubber cylinder with an electrically conductive solution to achieve the required range of electrical impedance values. After the patient makes several test breaths through the mouthpiece, the breathing process is recorded, during which a graph of the changes in the impedance value over time is displayed on the screen (figure 8). The program analyzes the data obtained and, using the points of this graph, calculates the parameters of spirography and muscle activity of the lungs. Such important spirometric indicators of external respiration function as respiration rate, entry and expiratory flow rates, and expired air volume are assessed. Thanks to continuous time monitoring it will also be possible by the shape of the signal of the inhalation-exhalation curve (the rate of its rise/fall) to track changes in the dynamics of respiration in patients with various diseases of the pulmonary system and to assess the state of muscle activity of the lungs. At the end of the experiment, data reception will be stopped automatically and the spirometry indicators are displayed on the screen in the form of tables and graphs.

4. Conclusion
An experimental model electromechanical setup has been created to study the electrical conductivity of a flow of aerosol particles of electrolytes in a channel when probing with an alternating electric current in a wide frequency range. The conductivity of an air flow with aerosol particles of a 10% solution of sodium chloride and calcium chloride was experimentally measured as a function of the flow rate and the intensity of particle spraying. The physical mechanisms and regularities of the occurrence of electrical conductivity in the experimental cell when an electrolytic liquid aerosol flow is blown through it are revealed. It was found that the cause of the appearance of an electric current was the deposition of a thin conductive film of condensed liquid on the inner surface of the inhaler mouthpiece when an aerosol flow was pumped through it. The temporal changes in the impedance modulus of the condensed liquid film of the conducting liquid are studied, and the dependence of the impedance change on the flow velocity is revealed and analyzed. It is shown that the thickness and electrical conductivity of such a film in a random and unpredictable manner depends on a large number of different factors. This does not allow the use of such a technique of electrical impedance spirometry in clinical practice with a sufficient degree of accuracy.

The original design of a new electrical impedance spirometer in the form of a mouthpiece with sensors filled with a porous medium impregnated with electrolyte through which the patient breathes has been proposed, developed and tested. The advantages of the proposed new method in comparison with the previously used are: significant (up to 30% of the signal level) sensitivity of the electrical impedance from the spirometric parameters of inspirationexpiration; improving the measurement accuracy by reducing the overall level of the impedance value and increasing the measured current; the ability to view the dynamics of the inhalation/exhalation process, calculate the parameters of spirography and analyze the state of muscle activity of the lungs and tissues of the patient in the current time directly during the measurement. The developed automated portable device for high-precision measurement of the impedance modulus in biological media in a wide frequency range, connected to a computer (laptop), significantly reduces the measurement and data processing time. The ability to quickly and objectively obtain large amounts of experimental data is very important and relevant for the development of the clinical application of impedance measurement in clinical medical practice.

Further development of the proposed method of impedance spirometry requires a detailed theoretical (analytical and numerical) study of changes in the conductivity of a porous medium, partially filled with an electrolytic liquid and blown by an air flow, in order to identify the mathematical regularities of impedance parameters from specific various physical factors (flow rate, flow rate of blown air, concentration electrolyte, coefficient of porosity of the medium) and will be the subject of further research on this topic.

Acknowledgments
The work was carried out under the Ministry of Education and Science of Russia program (topic No. 121031700169-1) and with the financial support of the RFBR grant No. 20-415-596008.
References

[1] 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. 170 724-732.

[2] Sakamoto K, Muto K, Kanai H and Lizuaka L 1979 Problems of the impedance cardiography MBEC 17 697-709.

[3] Pushkar Yu T 1981 Study of regional blood circulation and central hemodynamics using rheographic methods (Moscow: Medicine) (in Russian).

[4] Geddes L A and Baker L E 1989 Principles of applied biomedical instrumentation (New York: Wiley) 591-639.

[5] Ronkin M A, Ivanov L B 1997 Rheography in clinical practice (Moscow: MBN) (in Russian).

[6] Grimnes S and Martinsen O G 2008 Bioimpedance and bioelectricity basics2 ed. (Amsterdam: Elsevier Science & Technology Books).

[7] Patterson R P 2010 Impedance cardiography: What is the source of the signal? J. Phys.: Conf. Ser. 224(1) 012118.

[8] Mansouri S, Alhadidi T, Chabchoub S and Salah R 2018 Impedance cardiography: recent applications and developments Biomedical Research 29(19).

[9] Nikolaev D V, Smirnov A V, Bobrinskaya I G and Rudnev S G 2009 Bioimpedance analysis of human body composition (Moscow: Nautka) (in Russian).

[10] Tsvetkov A A 2010 Bioimpedance methods for monitoring systemic hemodynamics (Moscow: Slovo) (in Russian).

[11] Pepechitelev E P and Philist S A 2011 Methods and models for identification of biomaterials based on analysis of multifrequency impedance Bulletin of the South-West State University. Series management, computer technology, informatics. Medical instrumentation 1 74-80 (in Russian).

[12] Malakhov M V, Nikolaev D V, Smirnov A V, Melnikov A A and Vikulov A D 2011 Assessment of hematological and biochemical parameters of blood by the method of bioimpedance spectroscopy Clinical laboratory diagnostics 1 20-23 (in Russian).

[13] Zhao T X, Jacobson B 1997 Quantitative correlations among fibrinogen concentration, sedimentation rate and electrical impedance of blood Medical & Biological Engineering & Computing 5 181-184.

[14] Mishlanov V Ju 2011 Investigation of the function of external respiration by measuring the electrical impedance of the lungs and airways at various frequencies of the probing alternating current Vestnik sovremennoy klinicheskoy meditsiny 4(4) 24-28 (in Russian).

[15] Mishlanov V Ju, Zuev A L, Ustyantseva T L, Mishlanov Ya V and Savkin V V 2013 Respiratory function study by electrical impedance spirometry: experimental and clinical parallels Russian physiological journal im. I.M. Sechenova 99(12) 1425-1434 (in Russian).

[16] Zuev A L, Mishlanov Ya V and Polyakov V B 2018 Experimental study of changes in the electrical impedance of air channels saturated with an aerosol of an electrolyte solution Bulletin of the South-West State University, Series management, computer technology, informatics. Medical instrumentation 8(1) 41-53 (in Russian).

[17] Zuev A L, Sudakov A I and Shakirov N V 2019 Method of impedance spirometry for studying the dynamics of human respiratory function and a hardware-software complex for its implementation RF patent for invention № 2682936 from 22.03.2019 (in Russian).

[18] Zuev A L, Mishlanov V Ju, Sudakov A I and Shakirov N V 2019 Automated instrumentation complex for measuring electrical impedance of biological media Bulletin of the South-West State University, Series management, computer technology, informatics. Medical instrumentation 9(2) 6-21 (in Russian).