Combinational Bioimpedance and Ultrasonic Diagnostics Method for Prospective Medical Applications

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Abstract. An innovative method of non-invasive combinational bioimpedance and ultrasonic diagnostics of the physiological condition and processes in the superficial tissues of a patient has been developed. The method is based on simultaneous or alternative measurements of the complex electrical resistance and ultrasonic velocity and attenuation coefficient on an arbitrary part of the patient's body. Designs of ultrasonic and bioimpedance diagnostic moduli have been developed and tested. An experimental verification of the developed combinational echo-pulse and transmission ultrasonic and bioimpedance spectroscopy method was carried out on reference solutions and patient's superficial tissues *in-vivo.*

Keywords: Complex electrical resistance · Bioimpedance methods · Ultrasonic diagnostics · Superficial tissues · Diagnostic moduli · Echo-pulse method · Ultrasonic velocity · Attenuation coefficient · Cell membranes · Intracellular fluid

1 Introduction

Methods and devices using electromagnetic fields and ultrasound for diagnostics and therapeutic or aesthetic procedures in target tissues of the patient's body are well known in the art [1–4]. The application of ultrasonic and bioimpedance methods as a valuable diagnostics means in several fields of clinical medicine is now so well established that it can be considered essential to good patient care [2, 3].

Until recently, the main goal of measuring the ultrasonic velocity in biological tissues, in terms of medical applications, was to obtain data that would allow the calibration of echographic imaging systems. Currently, many researchers have concluded that the ultrasonic velocity itself is a very informative specific characteristic of a tissue [2]. Excellent reviews [5−8] are devoted to the analysis of the acoustic characteristics of biological tissues.

Ultrasonic attenuation, that is, the total loss of acoustic energy in biological tissues, is determined by the total action of refraction, reflection, scattering and absorption of ultrasound. In practical applications, data on the change in velocity, acoustic impedance,

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absorption, scattering and attenuation in the tissue volume are used to obtain information about its structure. It should be noted that studies of the attenuation of ultrasonic waves in various biological media and tissues are extremely complex. Thus, it can be stated that the speed of sound is more suitable for the role of a fundamental characteristic of biological tissues than the attenuation coefficient, which to a certain extent depends on variations in the speed of sound. At the same time, relative measurements of the attenuation coefficient are very informative in relation to changes in the structure and composition of biological tissue occurring under the influence of physiological and pathophysiological factors, as well as at therapeutic treatments.

In view of the absence of a generally accepted standard, the measurement system error can be checked by performing ultrasonic measurements on materials whose parameters have already been studied and the measurement results for which are well reproducible. Distilled water and solutions of ethyl alcohol in water are most widely used for control measurements of the ultrasonic velocity.

To date, many different methods for measuring the ultrasonic velocity have been developed, although these methods are often difficult to apply to biological tissues. In fact, methods for measuring various tissues *in vivo* are just beginning to develop [9–11]. Ultrasonic measurements of individual segments and local areas of the body using standard ultrasound methods and transducers are difficult due to deformation and changes in the size of the measured soft tissue [10]. Thus, it can be stated that there is a need for new ultrasound methods for diagnostics of the physiological conditions and processes in the biological tissues of a patient that occur during therapeutic treatment.

Bioimpedance analysis is a contact method for measuring the electrical conductivity of biological tissues, which makes it possible to assess a wide range of morphological and physiological parameters of a body [12–16]. The method is based on measuring the impedance, Z, of the whole body or individual segments of the body using impedance analyzers. Bioimpedance analysis of body composition helps to control the state of lipid, protein and water metabolism of the body and, in this regard, is of interest to physicians of various specialties.

In addition to integral assessments of the bioelectrical parameters of the body, it is possible to study individual segments and local areas of the body. Clinical studies have shown that the impedance parameters of body regions are sensitive indicators of the physiological condition of patients and, in particular, make it possible to predict adverse outcomes in critically ill patients [17].

Options for bioimpedance analysis are classified according to several criteria: the frequency of probing, as well as areas and tactics of measurements. Depending on the set of current frequencies used, bioimpedance methods are classified as single-frequency, dual-frequency or multi-frequency. In the latter case, the method is called bioimpedance spectroscopy. Bioimpedance spectroscopy makes it possible to quantify the state of organs and systems of the body in various diseases, and allows one to monitor and evaluate the effectiveness of physiotherapy and other therapeutic effects.

The main drawback of existing ultrasonic and bioimpedance methods, particularly for superficial tissue diagnostics, is a restricted number of body areas accessed for analysis caused by the complex body shapes and structure, low tissues thickness, low accuracy and reliability of measurements, and inability to use them in the process of

therapeutic procedures [4, 18, 19]. Thus, it can be stated that there is a need for new ultrasonic and bioimpedance methods for diagnostics of the state and physiological processes in the biological tissues of a patient that occur during therapeutic treatment.

In this paper, we propose a new method and universal diagnostic modulus for non-invasive combinational bioimpedance and ultrasonic diagnostics of the physiological condition and processes in the superficial tissues of a patient.

2 Bioimpedance Analysis of the Patient's Superficial Tissues

Measurements of the electrical impedance of reference solutions and superficial tissues of the patient were performed using a measuring setup and a diagnostic module for non-invasive diagnostics of the physiological condition of superficial tissues. The LCR HiTester HIOKI 3532–50 was used for impedance measurements. Data collection and processing was carried out using the PRAP software package [20, 21].

The design of the universal diagnostic module was provided for temporary fixation of the superficial tissue under the study by means of vacuum suction and simultaneous measurement of its electrical impedance. The measuring probe was designed as a vacuum cup connected to a vacuum system, in the case of which the central and ring measuring electrodes and connecting cables were mounted (Fig. 1).

(a) (b)

Fig. 1 Diagnostic module for bioimpedance study of the physiological condition of superficial tissues (a) and experimental configuration for vacuum fixation of tissue (b) used to measure electrical impedance *in vivo*

The central and ring metal electrodes of the measuring probe were connected to the input connectors of the impedance analyzer. Impedance scanning was carried out in the frequency range from 1 kHz to 5 MHz. Before performing measurements on the superficial tissues of the patient in vivo, the diagnostic transducer was calibrated using reference solutions of ethyl alcohol and aqueous NaCl solutions. To do this, the diagnostic probe was placed in a chemical vessel filled with reference solutions. Figure 2 shows the impedance spectra of standard solutions.

The difference between the impedance spectra of ethyl alcohol and NaCl aqueous solutions is due to different mechanisms of ionic conduction and electrode/solution contact capacitance. Ethyl alcohol, like distilled water, is close to a classical dielectric

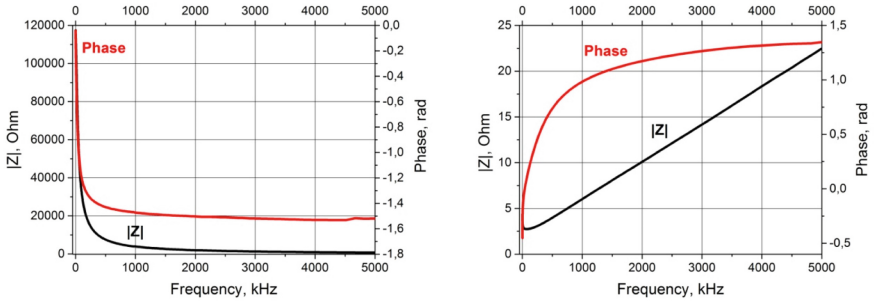


Fig. 2 Impedance spectra of standard solutions: (a) ethyl alcohol; (b) NaCl aqueous solution (50 g/450 ml)

solution, while electrolyte solutions have an ionic type of conductivity, which leads to an increase in impedance with frequency in the result of a decrease in ions mobility.

Figure 3 shows the impedance and dielectric spectra of the patient's superficial tissues (abdominal region) *in vivo*. The active resistance of the surface tissue decreases with increasing frequency. At relatively low frequencies, this is due to a decrease in the reactance of the dielectric partitions and an increasing penetration of current into the intracellular space. Parallel capacitance also decreases with increasing frequency. At different frequencies, different mechanisms of relaxation operate, that is, a decrease in the polarization of dielectrics with an increase in the frequency of the alternating electric field. At frequencies from fractions of a hertz to units of kilohertz, the decrease in the value of ε_p is due to various effects occurring on the surface and in the channels of cell membranes and in intracellular structures. In the range from tens of kilohertz to 5 MHz, the Maxwell–Wagner effect affects, which consists in a decrease with increasing frequency of the effective permittivity of a multilayer dielectric with the layers having different dielectric permittivity. Moreover, at these frequencies the polarizability of large protein molecules gradually decreases.

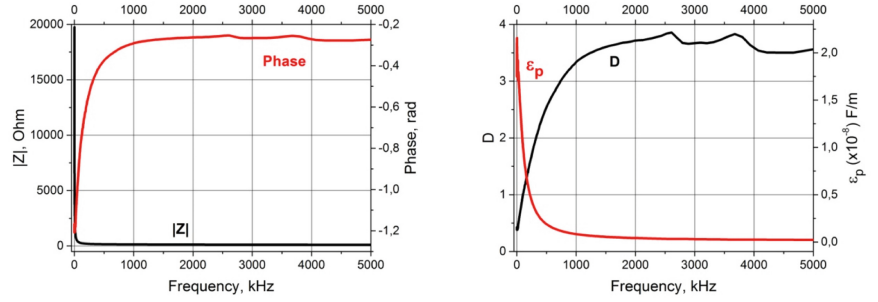


Fig. 3 Impedance (a) and dielectric (b) spectra of the patient's superficial tissues (abdominal region) *in vivo*

When analyzing the obtained dependences, it should be noted that the electrical impedance of biological tissues Z has two components: active R and reactance X, related by the relationship: $Z^2 = R^2 + X^2$. The material substrate of the active resistance R in a biological object is liquids (cellular and extracellular), which have an ionic mechanism of conduction. The substrate of reactance X (the dielectric component of the impedance) is cell membranes. It should also be noted that there is a capacitive component of the impedance associated with the contact of the electrodes and the structure of the superficial tissues.

Since vacuum fixation of superficial tissues is used for measurements of impedance spectra *in vivo* (Fig. 1), it is of interest to study transient processes in the studied tissues under the action of vacuum suction. The impedance of the superficial tissues has been found to decrease with time, and the dependence is exponential. The change in impedance is due to the gradual influx of blood and lymph to the area of the superficial tissue under study, caused by vacuum suction.

Thus, it can be stated that the complex impedance of biological tissues, determined for a given electric current frequency, can changes significantly under the influence of physiological and pathophysiological factors. In addition, the impedance spectrum of biological tissue changes drastically during therapeutic treatment, reflecting the modification of the structure and composition of the tissue (lysis of adipose tissue, necrosis, coagulation, and blood supply, changes in the content of intercellular and intracellular fluid) [18].

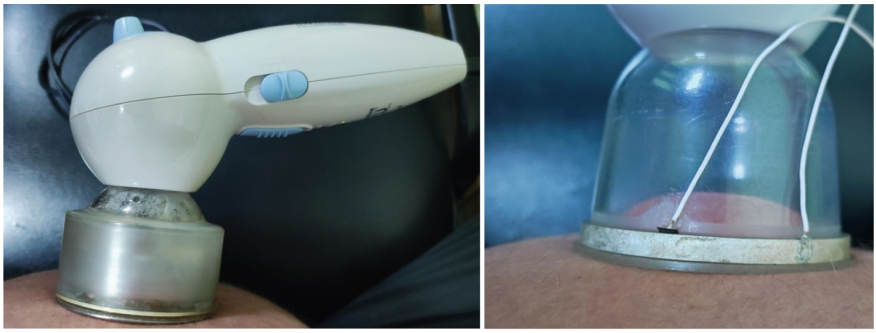
This makes it possible to use the developed method of bioimpedance spectroscopy and a diagnostic module for quantitative assessment of the physiological condition of the patient's superficial tissues at various diseases, as well as to monitor and evaluate the effectiveness of physiotherapy and other therapeutic treatments.

3 Ultrasound Diagnostics of the Patient's Superficial Tissues

The propagation velocity and attenuation of ultrasonic waves in reference solutions and superficial tissues were measured using transmission and echo-pulse ultrasonic methods. The measuring setup included a LeCroy Wave Surfer 422 digital oscilloscope, a Panametrics (Olympus) 5077 PR pulse generator/receiver, and a developed ultrasound diagnostic module.

The design of the ultrasonic diagnostic module was provided for temporary fixation of the superficial tissue under the study by means of vacuum suction and simultaneous measurement of the velocity and attenuation of ultrasonic waves. The diagnostic module was designed as a plastic cup connected to the vacuum system, in the body of which a cylindrical ultrasonic transducer was mounted, which is a piezoceramic ring with an outer diameter of 64 mm, a thickness of 2 mm and a height of 5 mm, made of PZT piezoceramics [22, 23], and connecting cables (Fig. 4). The ultrasonic transducer was connected to the input connectors of the pulse generator/receiver.

Before performing measurements on the superficial tissues of the patient in vivo, the diagnostic transducer was calibrated using a reference solution (distilled water). To do this, the transducer was placed in a heated chemical vessel filled with distilled water and equipped with a thermocouple for temperature control. An excitation pulse with a

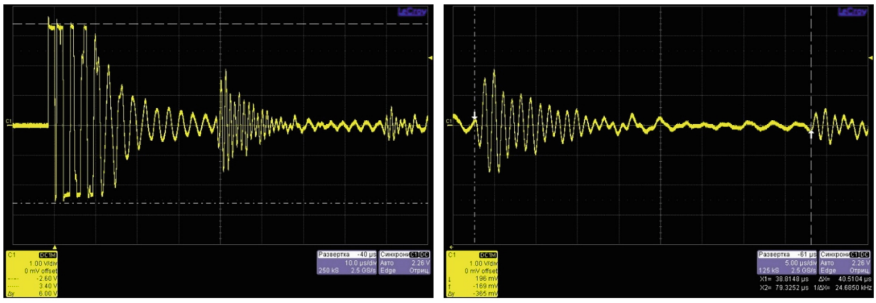


(a) (b)

Fig. 4 Ultrasonic diagnostic module for examining and monitoring the physiological condition of superficial tissues (a) and illustration of vacuum fixation of the tissue inside a cylindrical ultrasonic transducer (b) used to measure the velocity and attenuation of ultrasound *in vivo*

duration equal to a half-cycle of the resonant frequency of 1 MHz was applied from a pulse generator/receiver to a cylindrical piezoelectric transducer, and the transmission and serial echo signals, received by the same transducer, were recorded by a digital oscilloscope.

Examples of oscillograms obtained when measuring the ultrasonic velocity and attenuation by the transmission and echo-pulse methods at a frequency of 1 MHz in distilled water are shown in Fig. 5.



(a) (b)

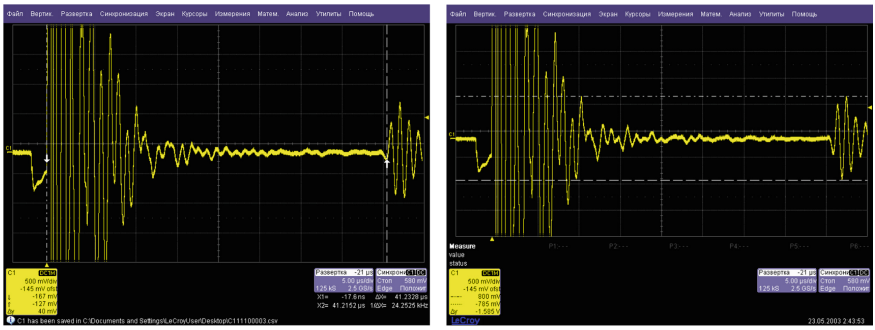
Fig. 5 Oscillograms of the excitation, transmission and echo pulses when measuring the attenuation (a) and the ultrasonic velocity (b), obtained in distilled water at a frequency of 1 MHz at room temperature

The measured values of the ultrasonic velocity in distilled water at different temperatures are given in Table 1. The results obtained are in good agreement with the literature data [2, 4].

Table 1 Ultrasonic velocity in distilled water measured at various temperatures

Water temperature (°C)	Ultrasound velocity (m/s)
50	1564.5
45	1555.2
40	1509.4
35	1500.0
20	1474.9

Measurements of velocity and attenuation of ultrasonic waves in superficial tissues *in vivo* were performed on various parts of the patient's body using a pre-calibrated diagnostic transducer. Examples of oscillograms obtained by measuring the ultrasonic velocity and attenuation in the abdominal region of the patient's body are shown in Fig. 6.



(a) (b)

Fig. 6 Oscillograms of the excitation and transmission pulses obtained by measuring the ultrasonic velocity (a) and attenuation (b) at a frequency of 1 MHz in the abdominal region of the patient's body *in vivo*

The measured values of the ultrasonic velocity in the superficial tissues of the patient at various temperatures are shown in Table 2.

Table 2 Ultrasonic velocity in the patient's superficial tissues, measured in different parts of the body at two fixed temperatures

Body temperature (°C)	Ultrasonic velocity (m/s) (abdominal region)	Ultrasonic velocity (m/s) (thigh)
36	1447.9	1449.6
40	1438.0	1439.7

The body was heated through a transparent transducer cup with an infrared heater. The body surface temperature was monitored by a built-in thermocouple. It should be noted that in the used configuration of the diagnostic transducer, the ultrasonic wave is completely localized in the surface layer of 10 mm thickness, that is, in the skin and subcutaneous adipose tissue. The ultrasonic velocity in adipose tissue is less than in water and is characterized by a negative temperature coefficient, which is in good agreement with the literature data [2, 3].

It is not possible to measure the absolute value of attenuation using the developed diagnostic module, since in this configuration the main contribution to the measured attenuation (1.46 dB/cm) is made by the divergence of the acoustic beam and reflections in the transducer case, but not by the attenuation in the medium (0.002 dB/cm for water on 1 MHz). However, any changes in body temperature, as well as the condition of its structural components, lead to recorded changes in the speed of sound and in the relative attenuation of the ultrasonic wave. In addition, the velocity and attenuation of ultrasound in biological tissue change dramatically during therapeutic treatment, reflecting physiological processes and modification of the structure and composition of the tissue (lysis of adipose tissue, dehydration, necrosis, coagulation, blood supply) [3, 4].

Finally, both designs of ultrasonic and bioimpedance diagnostic moduli have been combine in one universal modulus for combinational diagnostics of superficial tissues shown in Fig. 7.

Fig. 7 Universal diagnostic modulus for combinational diagnostics of superficial tissues

This makes it possible to use the developed method and universal diagnostic modulus for combinational non-invasive diagnostics and monitoring of the physiological condition of the patient's superficial tissues at various diseases, as well as to monitor and evaluate the efficiency of physiotherapy and other therapeutic treatments.

4 Conclusions

In this paper, we have developed an innovative method and universal diagnostic modulus for non-invasive combinational diagnostics of the physiological condition and processes

in the superficial tissues of a patient. The method is based on simultaneous or alternative measurements of the complex electrical resistance and ultrasonic velocity and attenuation coefficient on an arbitrary part of the patient's body. An experimental verification of the developed combinational echo-pulse and transmission ultrasonic and bioimpedance spectroscopy method was carried out on reference solutions and patient's superficial tissues *in-vivo*. The results of the experiments confirmed the high accuracy and applicability of the developed methods and designs for non-invasive diagnostics of the physiological condition of the patient's superficial tissues and permanent control of the treatment procedures.

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