Development of an electrode unit for a bioimpedance spectrometry device

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Abstract. An electrode unit of a bioimpedance spectrometry device has been developed. This device measures the resistance of biological tissues for specified frequencies of electric current. The device is capable of evaluating the condition of organs and tissues of biological structures in case of breast cancer, as well as in case of various external influences. It differs from all existing devices of bioimpedance spectrometry by the fact that it has small dimensions, is able to change the frequencies of probing current and at the same time to fix impedance values. The electrode unit has a hemispherical shape and to obtain more accurate impedance data each electrode is equipped with a spring which is fixed on a dielectric hemisphere. The purpose of the research is to study breast cancer using the developed electrode unit of the bioimpedance spectrometry device. Patients with malignant neoplasms of the breast were examined with the use of the bioimpedance spectrometry device. The study of impedance data obtained from the patients with and without breast cancer showed that the impedance of the breast affected by cancer lies within 13...20 ohms, depending on the current frequency. That is, the electrical impedance of the affected patient's breast decreases by up to 13.6 percent. The analysis showed that the developed bioimpedance spectrometry device allows to diagnose cancerous diseases.

1. Introduction
Numerous methods of studying the tissue of biological structures for cancer diseases, such as ultrasound scanning, radionuclide diagnostics, magnetic resonance imaging, X-ray mammography, cannot be applied for long-term monitoring of patients with cancer. Analysis of high-tech methods of cancer diagnostics revealed that due to the high cost of equipment and procedures, complexity and duration of the session, high radiation dose, the listed methods are applicable for short-term monitoring of the state of internal organs of patients.

Practice shows that to monitor the condition of patients with cancer a long-term monitoring of affected tissues and organs should be performed. When monitoring it is necessary to observe the following conditions: simplicity of measurements, safety of the procedure, low invasiveness. These conditions fully correspond to the bioimpedance spectrometry. Tissue testing consists of determination of biological structures tissue resistance, subsequent processing of signals obtained from electrodes placed on the examined area of the patient. For the fixed current frequency, the electrical resistance of the studied area of the patient varies depending on the degree of damage of the living tissue and its pathological condition.
In all kinds of diseases the electrical conductivity of biological structures tissues is different. Electrical conductivity of lungs changes depending on the level of their filling with air, kidneys on the level of their filling with blood, blood itself on the amount of proteins in it, the electrical conductivity of muscle fibers varies and changes depending on the strength of their contraction, lymph on the amount of electrolytes in it. Electrical conductivity of tissues of biological structures changes due to the presence of a tumor in the affected area, as well as due to the presence of a variety of ischemia, edema and other tissue lesions. Due to the variety of electrical conductivity levels of tissues of biological structures, the possibility to use bioimpedance imaging to identify the areas of lesions and the physical state of internal organs, peripheral tissues and other systems of the body has arisen.

It has been found that the electrical conductivity of the cell and its internal resistance in the presence of viruses have different values, and the higher their concentration in the cell is, the more obvious is the difference between the values of electrical conductivity and internal resistance of a viral cell and a healthy one. The electric internal resistance of the cell is of lower value when the concentration of viruses in the cell increases. The normal electrical resistance of a healthy human cell without viruses is approximately 4 ohms. When the concentration of viruses exceeds 223...227 in a cell, it becomes cancerous or malignant, and the electrical resistance of this cell is less than that of a healthy cell. A healthy human cell becomes cancerous, with the increase of cell division, and the intracellular electrical resistance passing the threshold value.

The possibility of using bioimpedance measurement to differentiate between healthy and tumor tissue has been determined experimentally [1]. Assessment of impedance of the stomach affected by a malignant tumor demonstrated a statistically significant difference between the affected tissues and healthy ones [2]. When benign or malignant tumors develop in mammary and thyroid glands we managed to reveal statistically significant changes of indices [3].

Currently, diagnostic bioimpedance spectrometry devices that record the resistance values of biological tissues for specified frequencies of electric current have become widespread. The devices mainly have an identical layout containing a data processing unit or ADC, an alternator, a switching unit, current electrodes, and potential electrodes [4,5]. These bioimpedance spectrometry devices are designed to determine the water balance of the human body and the condition of organs and tissues of biological structures during their diseases.

Bioimpedance spectrometry devices are designed to diagnose the extent of damage to biological peripheral tissues. Damage can be frostbite, burns and drug damage. In addition, the devices are used for the numerical assessment of the state of the internal systems of the body and organs with pathological changes [6,7,8,9,10].

These apparatuses use a small number of probing current frequencies, which reduces the information content of the indices. A small number of electrodes and their division into current and potential electrodes are a big disadvantage of these devices, they do not allow obtaining the necessary indices in full and do not provide the required accuracy of measurements. The considered disadvantages of the apparatuses do not allow their widespread use in medical institutions.

To eliminate the above disadvantages of bioimpedance spectrometry devices, we propose a device that measures the resistance of biological tissues for given frequencies of electric current designed for long-term monitoring of patients with cancer.

2. Methods and materials
The ESSUTM is working on a bioimpedance spectrometry apparatus. The apparatus is capable of generating three different probing current frequencies to increase the number of impedance data and informative indicators. The apparatus includes information display, electrodes, generator, power supply unit, detector, stabilizer, microcontroller and filter [11].

The 6 watt pine unit of the machine produces a 12 volt DC voltage. The voltage is unstabilized and is stabilized by two analog IC’s. The first analog LM3175 chip is an unregulated stabilizer with an output voltage of 5 volts, which feeds all circuits of the machine except the oscillator repeater. The second
analog LM7805 is a regulated stabilizer with an output voltage of 10 volts, which feeds the oscillator repeater.

The bioimpedance spectrometry diagnostic procedure begins with the positioning of the electrodes on the patient's body. A voltage is applied to the current electrodes, resulting in a potential on the measuring electrodes, from which the voltage is fed to the phase shift fixation unit or detector consisting of a diode, a resistor and a capacitor.

The phase shift detection unit outputs pulses of the same length as the phase shift and runs on a microcircuit, which is four logical elements. The pulses are then converted to DC voltage with a resistor and a capacitor.

The current electrodes receive a voltage of up to 10 volts from an oscillator, which contains a master oscillator, running on a 4011 microcircuit. This chip contains a microcontroller and amplifiers. The inputs of the master oscillator are combined to amplify the input meander, so we get an inverter. The voltage from the oscillator is also fed to a measuring circuit consisting of a diode, a resistor and a capacitor. This circuit converts the pulses into a direct current for the microcontroller, which records the magnitude of the signal applied to the current electrodes.

Functions of the microcontroller using the built-in analog-digital converter of the bioimpedance spectrometry device: 1 - records the signal value and calculates the impedance value for display; 2 - digitizes the values of the measuring electrodes from the phase shift fixation unit; 3 - forms a sequence of pulses with a frequency of 0.5 and with frequencies of 200, 100, 50 kHz.

We are working on the creation of an electrode block of the bioimpedance spectrometry apparatus for diagnosing the female breast for neoplasms, which consists of eight disposable chlorosilver electrodes placed at an equal distance from the center of the hemisphere, with four electric electrodes located along the vertical and horizontal axis of the dielectric hemisphere, and the remaining electrodes placed at 45 degrees between the horizontal and vertical axes. Such a form of execution of the electrode unit allows to ensure its sufficient ergonomics of the female mammary gland. At the same time, the necessary structural rigidity is provided, which allows a reliable spatial fixation of electrodes, the possible errors of measurement results due to mutual spatial displacement of electrodes during installation of the electrode block on the mammary gland are reduced. Installation of 8 electrodes along the vertical and horizontal axes and at 450 to these axes allows to determine more precisely the location of a neoplasm in the breast.

Such shape of the electrode unit (figure 1) allows to estimate asymmetry of voltage drops distribution pattern on the mammary gland surface not only when installing electrodes on the level of the gland base, but also on the levels of its several sections parallel to the surface of the woman's chest. Such installation of electrodes promotes increase of detection of a neoplasm location in mammary glands.
In addition, each electrode has a plug to which springs of a certain length are soldered, and these in turn are attached to a dielectric hemisphere. The plug allows quick removal and installation of the electrodes. The springs allow the electrodes to be pressed against the female breast from all sides with equal force and thus reduce impedance error. In addition, the electrode unit is held on the female breast, evenly distributing electrode pressure in all areas of the female breast, and capturing impedance from all electrodes without error.

Each electrode has a wire attached to it that connects to a commutator to sense the electrical impedance. The commutator allows you to switch to different diametrically arranged electrodes and to read the electrical impedance from two diametrically opposite electrodes.

Electrode block is placed on the right breast (figure 2), potential appears on the measuring electrodes of the block after electric current is fed to them from generator, generated voltage is analyzed by phase shift fixation block, other blocks of the device (detector, microcontroller, ADC) conduct further data processing, processing results are displayed on the device display. The display shows the impedance values.

The bioimpedance spectrometry apparatus was used in breast cancer research. A group of volunteers at the age of 45 years with a diagnosis of breast cancer was organized for the research.

Impedance measurements by bioimpedance spectrometry device were carried out in a therapeutic office. Relative position of the device and the patient were fixed, the electrode unit was equally held to the breast for studies in the same conditions. Sources of interference and distortion were excluded at the place of measurements.
Figure 2. Electrode unit on the right chest.

3. Results and discussion
Patient №1, a 45 years old woman, 166 cm tall, 68 kg of weight with cancer diagnosis "Breast cancer of the right breast". The tumor is 2.4 by 2.8 centimeters in size in the lower node of the right breast. Data were obtained from the mammography machine. Table 1 shows the average impedance data at 200, 100, and 50 kHz.

| Impedance                                | Frequency     |
|------------------------------------------|---------------|
|                                          | 200 kHz | 100 kHz | 50 kHz  |
| Impedance of the affected mammary gland, Ohm | 123     | 171     | 192     |
| Impedance of unaffected mammary gland, Ohm  | 142     | 188     | 205     |

Table 1. Average impedance data of patient №1.

Patient № 2, a 43 years old woman, 172 cm tall, 75 kg of weight with right breast cancer. The tumor is 3.2 by 2.4 centimeters in the upper-left quadrant of the right breast. Data were obtained from the mammography machine. Table 2 shows the average impedance data at 200, 100, and 50 kHz.

| Impedance                                | Frequency     |
|------------------------------------------|---------------|
|                                          | 200 kHz | 100 kHz | 50 kHz  |
| Impedance of the affected mammary gland, Ohm | 121     | 164     | 182     |
| Impedance of unaffected mammary gland, Ohm  | 140     | 181     | 202     |

Table 2. Average impedance data of patient №2.

The created device of bioimpedance spectrometry with an electrode unit is capable of generating pulses with a duty cycle of 0.5 and with frequencies from 0 to 200 kHz, with several harmonic components. The device implements technologies capable of analyzing impedance and probing current data, which contributes to increasing informativeness of bioimpedance diagnostics and accuracy of measurements.
Real-time assessment of impedance data when a probing current is applied to the human body provides the ability to monitor phase and amplitude spectra, which provides diagnostic data on the patient's tissue condition for a long time while in the studied area.

The device under development performs parallel measurement by four channels, one of them can be used as a current source, the rest perform the role of sensors. The use of given number of electrodes and variety of their mutual positioning makes it possible to diagnose the affected areas of biological tissue, which state is out of the norm.

Impedance values of healthy tissues and tissues affected by a cancerous tumor differ significantly. This fact is explained by the fact that functional activity of malignant tumor is higher than functional activity of healthy tissue. Active development and enlargement of a cancerous tumor leads to enlargement of blood vessels by means of vessels ingrowth into the tumor.

Hemorrhages and necroses appear in the area where the malignant neoplasm is located. This phenomenon appears as a result of destruction of biological tissues, in turn, free ions are released and intracellular membranes disintegrate and go out into intercellular areas. Heterogeneity of affected tissues and impedance data differ significantly compared to healthy homogeneous tissues.

Analyzing impedance data taken from different sections of homogeneous healthy tissue we did not find significant differences in impedance data. Healthy tissue is marked by the uniformity of impedance values in all sections and is a distinctive feature compared to the affected tissue.

Thus tissue impedance decreases and tissue conductivity increases. As a result the bioimpedance spectrometry device registers lower impedance values of the affected tissue.

Thus, affected tissue with cancerous tumor differs significantly from healthy tissue in terms of bioimpedance values.

As a result of our work we created an algorithm for finding neoplasms using bioimpedance spectrometry, which is able to distinguish healthy tissue from affected tissue. The apparatus measures and analyzes impedance of healthy biological tissue and impedance of cancerous tumor at all three generated frequencies - 200 kHz, 100 kHz and 50 kHz. The results are displayed on the screen of the device.

The data obtained in the course of research will allow to determine the scope of the upcoming cancerous tumor removal operation. Thus, the bioimpedance spectrometry method can be used to diagnose cancerous diseases.

4. Conclusion
The electrode unit of the bioimpedance spectrometry apparatus for diagnosing the disease of the examined area of the patient was developed. The apparatus performs parallel impedance measurement through several channels generating in a wide range of probing current frequencies. Studies were performed on patients with breast cancer.

Studies showed that impedance of healthy breasts is higher than impedance of breasts with cancer at all generated frequencies and impedance difference was 13...20 ohms. As a percentage, the impedance of breasts with disease fell within 6.4...13.6%.

Thus, the developed bioimpedance spectrometry device carries out diagnostics of oncological diseases. It can be used for constant monitoring of cancer diseases dynamics in medical institutions, in oncological clinics

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