ПРИМЕНЕНИЕ БИОИМЕНДАНСНОЙ СПЕКТРОСКОПИИ В ЛУЧЕВОЙ ТЕРАПИИ

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APPLICATION OF BIOIMPEDANCE SPECTROSCOPY IN RADIATION THERAPY

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Annotation. *Cancer cells exhibit altered local dielectric properties compared to normal cells because of the difference in shape, size and orientation. These properties are measurable as a difference in electrical conductance using electrical impedance spectroscopy. Electrical impedance is one of the most often used parameters for characterizing material properties, especially in biomedical applications. The electrical parameters of the tissues could be used to distinguish the tissue's status. Changes in electrical properties at different frequency rate reveal that there exist differences between conductivity of non-irradiated and irradiated tissues.*

Radiation therapy is a reliable method in the treatment of malignancies. However, the radiation affects both healthy tissue and tumor. It damages the parenchymal and vascular tissue. The value of radiation damage is dependent on dose and has a latency period, which is determined by the type of tissues. Studies have shown that in the irradiated skin changes are observed in the conductivity and dielectric constant. The dependence of the complex conductivity of the frequency is determined by the charging capacity of cell membranes and the relaxation of protein dipoles. These properties can be very sensitive in the case of a tissue damage progress. The use of bioimpedance spectroscopy for assessment of tissue damage after irradiation is perspective method for planning secondary irradiation sessions.

Measuring the impedance of living tissues in vivo presents certain difficulties. First, it depends on what parameters may vary for each patient. Living tissues are heterogeneous material, but to date there is enough accumulated datal for an understanding of the conducting properties of tissues [2,3]. The electric impedance has two components: active (ohmic) and reactive (capacitive) resistance. The first of these reflects the extracellular space, the second - the structure, limited to a biological membrane, i.e. cells. The range of frequencies used for the study of biological objects, ranging from 1 kHz to 1.3 MHz. At low frequencies (less than 50 kHz) electric current passes mainly through the intercellular fluid. By increasing the frequency of the current total electrical resistance of the tissues is reduced. This is due to capacitive properties of cell membranes. The purpose of this study was to evaluate the feasibility of electrical bioimpedance spectroscopy for measurement of damaged tissues after irradiation.

The model device for measuring complex impedance of the tissues in the frequency range 100 Hz – 1 MHz has been developed at the Department of Applied Physics, Tomsk Polytechnic University.

The selected microcontroller is ATmega-16 (Atmel Corporation), which performs analog-digital conversion, and calculates the impedance value and stores it in the memory EEPROM. The software is written in assembly language and C ++ Builder. Voltage drop across the measured tissue and reference resistor is fed to the phase detector. The phase detector outputs a voltage proportional to the amplitude and phase. AD8302 as an amplitude-phase detector is used. In our work we use 4-wire circuit, in order to improve the accuracy of resistance measurement. The method allows to reduce the error arising in the case of contact between the tissues and the electrodes. This means that the resistance of the leads and existing contacts is completely excluded from the measuring circuit. In addition four-wire circuit measuring helps to eliminate much of the random and systematic errors. The electrodes were fabricated on a printed circuit board with two parallel plates. The electrodes were polished using a sponge and then cleaned with an alcohol swab.

For calibration of the device a simple RC circuit is used, which consists of two resistors and a capacitor, as shown in Fig. 1.

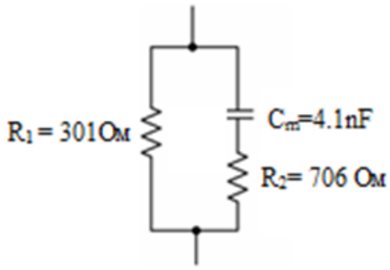

Figure 1. The model RC circuit

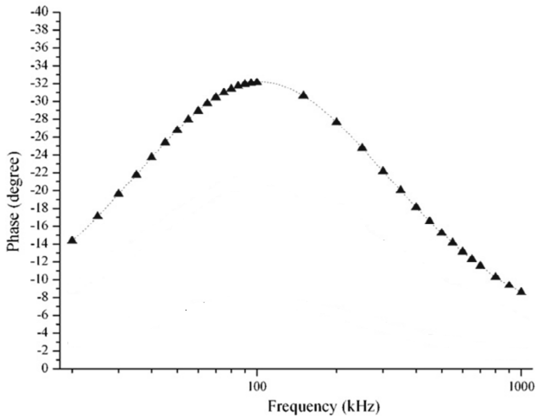

Figure 2. The magnitude-frequency characteristic of the RC circuit

We made the assumption, that the extra-cellular liquid and intra-cellular liquid act like resistors and the cell membrane like a capacitor in biological tissues [4]. The RC circuit has a characteristic frequency f_c, at which phase θ reaches its peak θ_p.

The mathematical calculation indicates f_c= 100 kHz and θ_p= -32,6°. The measurement of the calibration circuit characteristics was performed by using the model device. Each sweep-frequency measurement collects impedance data at 30 frequency points. The result at each frequency point is averaged by sampling 50 samples, which makes the random errors negligible. The results are presented in Fig. 2.

As can be seen from the graph, the phase has maximum at frequency value 100 kHz. This result coincides with the calculated data. It implies that the instrument can measure the complex resistance of tissue in the frequency range 100 Hz –1 MHz.

The next test of the device was made by measuring the real and imaginary parts for the hand of a healthy person. The results are shown in Figure 3.

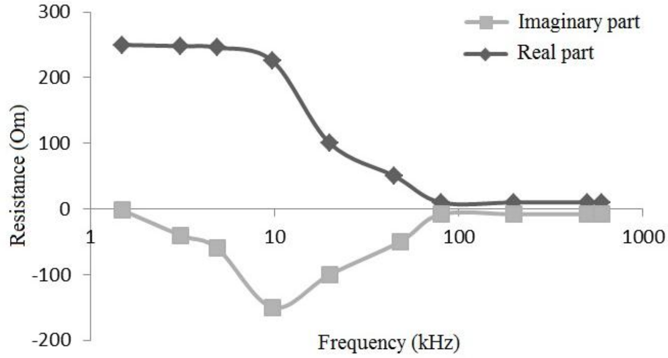

Figure 3. The value of the real and imaginary parts of the impedance for the hand of a healthy person

The measured results of the real and imaginary part of a healthy person coincide with the literature data[2].

The changes in the electrical properties of irradiated tissue have been measured in patients with breast cancer. The phase angle change was measured twice with an interval of 3 days at a frequency 110 kHz. The first measurement was made prior to irradiation, and the second immediately after irradiation in a cyclotron with a dose of 1.6 Gy of neutrons, third - after 3 days. The graph shows that the value of the phase angle after exposure differs considerably from the original. It can be seen that the second irradiation resulted in greater destruction of tumor cells, leading to a decrease in the phase angle.

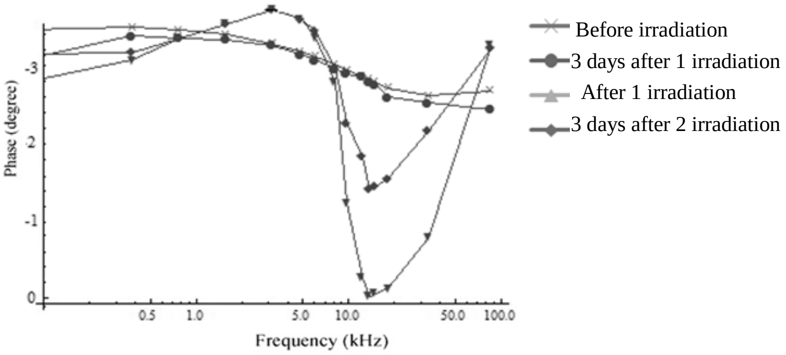

Figure .4. The phase-frequency dependence for the irradiated and non-irradiated tissues .

The value of the phase angle reflects the relative contributions of the fluid (resistance) and cell membranes (impedance) in the human body. Decrease value of the phase angle involves cell death or violation of their integrity, while its growth is associated with an increase in the number of intact cell membranes

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