Low-intensity
UHF-VHF therapy device
BIOL

A brief description of the principles of operation of the device and the effectiveness of electromagnetic radiation therapy

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Studies of the influence of electromagnetic fields (EMF) on living organisms have been conducted since the middle of the last century. As a result, it has been established that EMFs can affect biochemical reactions and the behavior of charged molecules near membranes (Barnes, 1992), namely: create electric fields in conductors, affect moving charge carriers, change the diffusion rate through membranes, distort bond angles, which influences the binding of proteins and the synthesis of macromolecules, etc.

Research in molecular biology has made it possible to detect the presence of endogenous bioelectric signals, as well as to determine their sources and influence on embryogenesis, regeneration and neoplasms formation. **Ion flows and voltage gradients** generated by ion channels and pumps **are key regulators of cell proliferation, migration, and differentiation** (Levin, 2003). Ion channels are pore-forming proteins that allow or prevent the flow of ions across membranes (Sherwood et al., 2005; Hille, 2001).

The uneven distribution of several **key ions**[1] between the intracellular and extracellular fluids and their selective flow across the plasma membrane determines the electrical properties of the membrane (Panagopoulos et al., 2002; Pall, 2013). **All living cells have a membrane potential**, hence transmembrane voltage gradients (V_{mem}) determine polarity between charges located on different sides of the membrane. (Sherwood et al., 2005). The interior of the cell being slightly more negative than the fluid surrounding the cell when the cell is electrically at rest. Charges are separated across the plasma membrane and each time, when the V_{mem} value differs from 0 mV, in the positive or negative direction, the membrane is in a state of polarization. And this value is directly proportional to the number of positive and negative charges separated by the membrane. In other words, changes in V_{mem} cause changes in the ions flow across the membrane. **Exposure to an exogenous electromagnetic field (EMF), which frequencies resonate with endogenous EMF, can be a trigger and causes changes in membrane permeability** (Funk et al., 2009), and therefore affect the opening and closing of ion channels and ions flow across membrane (Sherwood et al., 2005; Panagopoulos et al., 2002; Pall, 2013). V_{mem}-associated changes have also been shown to regulate proliferation in precursor cells, stem cells, and regenerating systems (Sarah Sundelacruz et al., 2009), as well as the effectiveness of Killer T cells - cytotoxic T lymphocytes, CTLs (Jesse A et.al, 2019).

Other studies have shown that **transmembrane voltage gradients** were specific signals for key metabolic processes in regenerative wound healing (Hotary and Robinson, 1992; Levin, 2007; Nuccitelli, 2003). These signals determine the migration path of cells, forming voltage gradients between the intracellular and extracellular environment (Funk and Monsees, 2006).

Voltage gradients are localized DC electric fields that turn on and off at different stages of development (McGaig et al., 2005). They spread into the extracellular space, as well as into the cytoplasm of one or more cells connected by gap junctions (Funk et al., 2009). These gradients can penetrate the cell membrane, into the cytoplasm, and even the membrane of the cell nucleus through signal transmission, while the EMF signal is received through receptors on the cell surface, and then processed by G-proteins that bind the receptors to effectors such as ion channels (Ermakov et al. others, 2012). These signaling processes are known to have a correlation between the presence of EMF gradients and the cellular response (Funk and Monsees, 2006; Sundelacruz et al., 2013).

These particular features were taken into account during the device BIOL designing, and the frequency ranges of meter and decimetre waves were chosen.

In addition to the frequencies used, the signal shape is important. Back in 1993, it was found that a sinusoidal waveform, which creates coherent fields, has a stimulating effect on the immune system (Adey, 1993). In this case, repetitive signals must be generated regularly and must be present for a certain minimum period of time (Litovitz et al., 1993). This resonant coherence is the key to producing larger effects with low thresholds (Panagopoulos et al., 2002). **Our own findings have shown that a triangular signal is more efficient than a sinusoidal one, due to the uniform distribution of the carrier frequency over the spectrum. Therefore, such a waveform is used in BIOL**.

Note 1: In most cells, sodium (Na^+) and chlorine (Cl^-) ions dominate outside the plasma membrane, while potassium ions (K^+) and organic molecules such as anions (A^-) dominate inside.

Depending on the EMF parameters ("what field is used for therapy") and the target biological process ("what are we treating"), either stimulation/activation of biochemical processes or inhibition/suppression can occur. And considering the effect of EMF on biochemical reactions and the behavior of charged molecules near cell membranes, **the increase in the effectiveness of the medication treatment in combination with BIOL therapy becomes explicable** (noted in practice).

By changing the permeability of the cell membrane using EMF, we increase the possibility of the formation of an immunological synapse between an infected or oncological cell and cytotoxic T-lymphocytes, which allows the latter to efficiently release perforins[2] and granzymes[3] into the affected cells. Perforin molecules are embedded in cell membranes and form pores through which granzymes enter, stimulating the death of affected cells (along the path of apoptosis, a regulated process of programmed cell death).

Our own studies and experiments with the device BIOL have been started in 2007. Initially, the biological activity of the electromagnetic radiation of the medical device BIOL was tested at the Department of Genetics and Cytology of Kharkiv National University named after V.N. Karazin using the cytobiophysical method (2008). The effect of EMF on buccal epithelial cells in vitro was studied at different exposure times on donors/volunteers. The normalizing effect on the bioenergetic properties of the cell nuclei of native human epithelial cells was reliably established, which made it possible to draw conclusions about the healing effect of EMF radiation.

In 2009, the device BIOL was clinically tested at the Kyiv Regional Hospital No.2 for patients aged 17-94 with the following diseases: intercostal neuralgia, osteochondrosis, rhinolaryngitis, rhinosinusitis, osteoarthritis, rhinitis. The results showed an improvement in physical condition in 80% of patients (a 40% decrease in pain syndrome and a 20% decrease in the clinical manifestations of diseases of the upper respiratory tract) and no changes in the course of the disease were observed in 20% of patients.

In 2009, the device BIOL has been used as part of the complex therapy for 128 patients of the spa and rehabilitation center "Ukraine" (Simferopol, Crimea) suffered from hypertension of the II-III degree (of which 125 had a concomitant diagnosis - chronic coronary heart disease (CHD) and 3 had angina pectoris and conditions after arriving cerebral circulation disorders). A reliable effect was obtained after the therapy, confirmed by hemodynamic parameters and laboratory studies. More than 50% of patients noted a significant improvement in well-being, a decrease in the number of angina attacks and enhancing the action of medications (nitrates were applied, like cardiket, nitroglycerin, isoket).

In 2011, in several research centers in Europe, the BIOL device was used for patients (21) with the following diseases: prostate adenoma, breast cancer (with and without metastases), lung and colon tumors (adenocarcinoma), and squamous cell carcinoma of the larynx. All patients noted an improvement in the quality of life and a significant reduction in pain. In 4 patients, the tumor state remained unchanged (did not improve and did not progress). For other 17 patients a decrease in tumor size by an average of 15% (10-18%) was observed, and in patients with metastases - a decrease in the degree of metastasis (in one of the patients, the metastases disappeared).

In 2017-2018, BIOL was used in Taiwan for 3 patients with nasopharyngeal carcinoma, ankylosing spondylitis and colorectal cancer. After a year, all patients showed regression of the disease (according to CT data) and improved quality of life.

Note 2: Activated killer T cells kill cells with a foreign antigen, to which they have a receptor, by inserting perforins into their membranes (proteins that form a wide, non-closing hole in the membrane) and injecting toxins inside (granzymes).

Note 3: Granzymes are serine proteases released by cytoplasmic granules of cytotoxic T cells and natural killer cells (NK). They induce programmed cell death (apoptosis) in the target cell, thereby eliminating cells that have become cancerous or infected with viruses or bacteria. Granzymes also kill bacteria and inhibit viral replication. In NK cells and T cells, granzymes are packed in cytotoxic granules with perforin.

A bit of physics to understand the processes of interaction between EMF and a biological object.

To further describe the biological aspects of the interaction of electromagnetic waves with the body and to understand the processes occurring in cells under its influence, we will not describe the electromagnetic field's parameters emitted by the BIOL since this affects the technical aspects of this device design.

When discussing either endogenous or exogenous fields' cellular influences, it is important to indicate definitions and terms. Here, the term "electromagnetic field" is used to summarize the entire field, which includes "electrical", "magnetic", and combined "electromagnetic". Electric field (EF) includes current, which can be direct (DC) or alternating (AC). Electric current units are measured in amperes (A). The electrical potential difference is measured in volts (V).

We will not describe here Faraday's law of induction and Maxwell's equation, which explain the occurrence of electromotive force (EMF). Only recall that the higher the oscillation frequency, the stronger the electric (EF) and magnetic (MF) fields are mutually related.

Unlike a membrane, cytoplasm or fluids in the extracellular space do not contain free electrons for charge transfer, so the current is carried by charged ions such as Na^+, K^+ и Ca^{2+}. A solution's resistivity can be measured and is usually around 100 Ohm (Ω) (Funk et al., 2009). If there is a voltage difference between any two points in the conductive medium, the current will flow. This voltage difference per unit distance is EF. Considering the size of the cell and the thickness of the cell membrane (~ 10 nm) with a difference of 0.1 V, this corresponds to a field strength of ~ 70 V / m, which means that the potential inside the cell is 70 mV less than the potential outside due to the negative charge on the inner surface of the cell membrane and a positive charge on the outer surface. Since the cell's diameter is much larger than the thickness of the membrane, it is reasonable to ignore the curvature of the cell and treat it as a charged capacitor with a capacitance of about 2 μF per cm^2 of membrane area (Hille, 1992). Variations of different ion concentrations on both sides of the membrane can lead to a new voltage across the membrane of 70 to 80 mV. With a negative charge on the intracellular side of the membrane and a positive charge on the extracellular side, the cell membrane is best modelled as a parallel plate capacitor. This voltage difference prevents weaker EFs from entering a cell. By adding a magnetic component (MF), EMF is able to penetrate the cell membrane (Otter et al., 1998).

MF influences cell behavior by the following: by applying force to moving charge carriers such as ions; by creating electric fields in conductive substances; by changing the rate of diffusion across membranes (Ikehara et al., 1998); and by distortion of bond angles, which affects the binding of the protein structure and, consequently, the synthesis of macromolecules (Barnothy, 1969). Unlike EF, which is protected by the high dielectric properties of the cell membrane, magnetic gradients penetrate deeper through the layers of living tissue (Funk and Monsees, 2006), acting directly on the cell organelles. Impulse exposure to EMF causes an increase and decrease in ion flows, due to which the membrane potential is changed and it leads to hyperpolarization of its potential (Alberts et al., 2002).

It is generally known that an induced membrane potential of 1 μV can be detected in 10 ms with less than 10^8 ion channels; therefore, a strong EMF is not required. According to several authors, the EMF intensity of picoTesla - nanoTesla is effective at the appropriate resonance depending on the charge and mass of the target molecules (Jacobson, 1994; Jacobson, Yamanashi, 1995; Persinger, 2006; Persinger, Koren, 2007; Sandyk, 1996).

According to the "Protocol for measuring EMF levels that are generated by the medical device BIOL" dated 02/18/2009, issued by the Scientific Research Institute of Occupational Hygiene and Occupational Diseases of the Ministry of Health of Ukraine, the total EMF levels do not exceed the maximum permissible levels and are at their maximum 1.98 V/m at a distance of 2.8 meters from the device.

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