SUPPRESSION OF MALIGNANT NEOPLASMS IN BIOLOGICAL STRUCTURES BY METHOD OF IMMUNE THERAPY

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An approach to solve a problem of reducing the zone of malignant tumors in biological structures is proposed. The method is based on the combined effect of permanent magnetic and electric fields on the vascular endothelium of the blood stream in biological structures in order to enhance the immune response in the body. Monitoring of the state of the area under treatment is carried out by resonant diagnostics in the UHF band.

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INTRODUCTION

One of the main problem in oncology remains metastasis, which consists in the fact that cancer cells migrating through the blood and lymphatic system give rise to new tumor formations in various biological tissues [1, 2]. Cancer arises from the weakening of the immune system, and the key to recovery is an increase in the body's immune response. Tumor regression is possible as a result of proliferation suppression and induction enhancement of the tumor cells apoptosis due to modification of T-lymphocytes and increase in the transparency of endothelial membranes of the blood vessels. The most characteristic changes on the side of the body's immune system are changes in the spectrum of immunoglobulins and cytokine activity. To establish the prognostic factors of the disease, an international TNM system [3] is used in combination with the Gleason scale and a PSA level in the blood. The TNM system describes the stages of development and spread of malignant tumors and takes into account the following factors: category T – the main (most extensive) tumor, category N – whether the tumor was spreading to the nearest (pelvic) lymph nodes, category M – absence or presence of metastases (whether neoplasms spread on other organs).

The tumor grades definition is established by the histological analysis of the biological material. In general tumors are graded between I and IV, depending on the amount of abnormality. For example, the Gleason scoring system is used to grade prostate cancer. The higher the Gleason score is, the more aggressive the malignant tumor tissue is. The Gleason score is based on biopsy samples taken from the prostate. Hormone therapy, designed to reduce the level of individual hormones, works only in cases of hormone-sensitive tumors, blocking the receptors of cancer cells and reducing their ability to use hormones. Oncocells are classified as medium – or low-grade. They are found to have the loss of microscopic hairs to communicate with other cells and the environment.

Thus, for example, diagnosis of the prostate G3T3N1M0, established due to a high level of the oncoprotein, a protein of a specific antigen PSA, presence in the blood means that the tumor begins to spread beyond the prostate gland, including nearby (pelvic) lymph nodes. However, no metastases in distant (not pelvic) lymph nodes neither in other organs are found. Benign tumors spread inside, while malignant tumors – TNM out-side of the body. When the metastases exit the prostate capsule, they get picked up and are carried by the of blood flow throughout the whole body. In this situation, the most acceptable treatment would be immune therapy. According to the TNM qualification system, transition from hormonal to immune therapy occurs with an increase in the M. to increase the antitumor immunity, immunomodulators are used.

1. MAIN BIOLOGICAL STRUCTURES

Proteins Interleukin-33 in cancer cells, T-lymphocytes of the immune system, T-immunocytes as modified T-lymphocytes, transparent endothelial membranes of the blood vessels. Biological structures increase efficiency of detection of genome disorders in the biological cells by the helpers, and efficiency of malignant tumors destruction by the cytoimmune therapy, and, for the system of reproduction, by the hormone replacement therapy. The goal of hormone therapy in oncology is to reduce the hormone content in the blood, which stimulates tumor growth, to a minimum, or to block the binding of the hormone to receptors in the tumor cells. In order to monitor the course of the disease, tumor markers are being used. With help of the tumor markers metastasis can be detected often more than 6 months before the clinical manifestation of the relapses. State of the reproduction system is determined the level of change in the PSA tumor marker and in the testosterone hormone (estrogen). Testosterone gets converted into dihydrotestosterone, which in turn increases the synthesis of PSA and stimulates tumor growth. In order to preserve the human reproductive system, and to suppress the metastases, the thymus – immunocytes ensured by the transparency of the endothelium are introduced. At a small level of lymphocytes (a) and weak transparency of the endothelium, the immune response does not occur (Fig. 1).

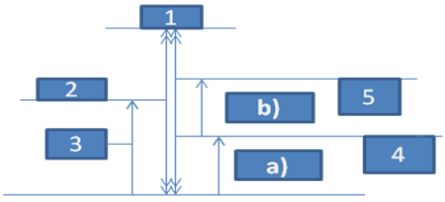

Fig. 1. Scheme of suppression of malignant formations in biological structures by method of the immune therapy: 1 – Transparent endothelium; 2 – Stage of neoplasm; 3 – Stages of TNM; 4 – T-Lymphocytes; 5 – T-Immunocytes; a) – weakened immune system; b) – immune system strengthened by thymus – immunocytes and transparent endothelium in the blood vessels

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Transparency of the endothelium ensures the passage of the immune defense components from the channel of blood movement into the biological structures. Reducing the transparency of the endothelial membranes of the blood vessels leads to an increase in the malignancy of the biological structures at the existing levels of lymphocytes of the immune system, which, in turn, leads to increase in lethality. For proper treatment of education, it is important to establish the right stage of their development, the size of the tumor, its spread to other organs (presence of metastases), and the aggressiveness (malignancy) of the cells.

The most effective method with respect to influence on suppression of metastases is a combined approach – transparency of the endothelium of blood vessels, immunotherapy and / or hormone therapy for hormone-dependent type of cancer.

2. PROCESS OF EDUCATING TRANSPARENT ENDOTHELES BY METHOD OF CAPILLARY CLEANING FOR IMMUNE THERAPY

Changing the inner surface of the colloidal structure of the capillary endothelium, leading to Loosening of the adhesions between their cells, holes are created for the passage of T- lymphocytes from the blood into the tissue spaces. The effect of transverse E and H-fields on the cleaning of the inner surface of a vessel with a large layer of sediment filled with an electrolyte from sodium chloride was investigated. The process of purification of the walls of the vessel [4] occurs due to knocking out of its surface toxins by accelerated ions of electrolyte in the applied electromagnetic field when creating the Lorentz force F = q (E + [V × B]) in the E ⊥ B-field geometry. When changing the direction of the vessels, it is necessary to take into account that the Factor [V × B] = |V| |B| sinα, where α is the angle between the vectors V and B.

When an ion moves in a circle, the centripetal force $F_c = MV^2 / R$ is equal to the Lorentz force.

The radius of the cyclotron rotation with frequency ώ = q B / M, and the period of revolution T = 2πM / q B has a value of $R_{cycle} = \frac{E}{qB^2} M = \frac{\nu}{qB} M = \frac{\sqrt{2M\varepsilon_{kin}}}{qB}$. Velocity of the positive ion in the solution is $\nu = \frac{qF}{6\pi\eta r} E = bFE$, where F = 96496 Cal / mol – is the Faraday constant. Magnitude of the ion velocity in the electric field of the electrolyte determines the radius movement of ion to the wall of the vessel as $R = \frac{\nu}{qB} M$, where B, q, V, ε_{kin}, M, ή are the magnetic field induction, charge, velocity, energy, ion mass and solution density, respectively. The value of should be sufficient for the breakdown the covalent interatomic bonds by ions, and $R_{ckl} \geq R_{vessel}$. At the magnetic induction level of B = 78 Oe the vessel gets cleaned, and the solid substance from its walls precipitates into a strongly diluted aqueous NaCl salt solution, following the scheme as shown in Fig. 2.

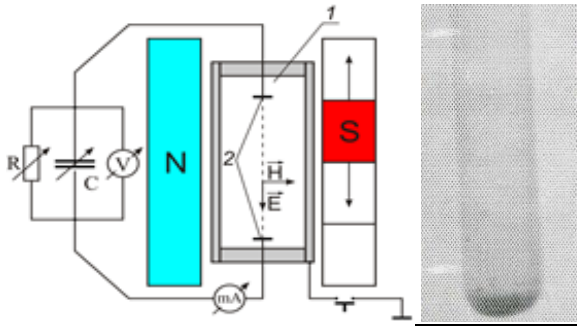

Fig. 2. Scheme of purification of the inner surface of a vessel by accelerated ions in crossed E ⊥ H-fields

Observation of the cleaning process of the vessel's inner walls (2) is performed by the magnitude of the current in the voltage supply circuit to the electrodes (1) of the electrolyte while a transverse magnetic field is applied to the vessel.

3. BIOLOGICAL OBJECT IN A MICROWAVE-RESONATOR

A device has been designed and manufactured (Fig. 3), in which a biological object can be located to study an effect of transverse E and H-fields and action of the microwave field in the UHF band range on its organism.

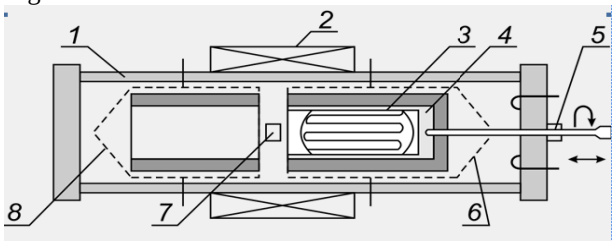

Fig. 3. Scheme of combined effect of permanent electromagnetic fields on a biological object, combined with resonant radio frequency diagnostics: 1 – volumetric microwave resonator operating in the UHF band; 2 – magnets; 3 – biological object; 4 – transport cell of the biological object; 5 – mechanism of displacement and rotation of the biological object; 6, 8 – screen with a gap to protect the bio-object from radiation; 7 – symmetrical electrodes

The screen of the biological object acting as a radiation reflector is made of copper foil with holes 5 mm in diameter and a thickness much larger than the skin layer. The gap in the screen is necessary for penetrating the RF radiation into the investigated object and electrodes to the living organism. To determine the efficiency of the screen without the established gap, the resonance frequencies and quality factors of the transport cell (item 4) with water have been measured as a substitute for blood and without it. Minor changes in resonant frequencies (Δ ~ 0.587 MHz) and Q-factors indicate the effectiveness of the selected protective screen. As penetration of the UHF radiation increases through the gap in the screen, the difference Δ of the resonance frequencies and Q-factors will increase. In order to eliminate parasitic self-excitation of the communication elements, when introducing RF power into the resonator, it is necessary to regulate the depth of their immersion.

4. NUMERICAL REALIZATION

From the theory of small perturbations, it follows that the change in the resonance frequency of the resonator depends on the amount of stored energy when the sample material is introduced into it, and is valid for any form of the resonator. Under the condition that the volume of the inserted dielectric is much smaller than the volume of the resonator, and does not affect the distribution of the electric field in it, then for ε = 1 (the resonator is filled with air), we obtain the equation

$$\frac{\delta f_o}{f_0} = \frac{2(\varepsilon - 1)V_\varepsilon}{V}. \quad (1)$$

To determine the permittivity of the medium, we obtain

$$\varepsilon = 1 + 0.5\frac{V}{V_\varepsilon}\frac{\delta f_0}{f_0}, \quad (2)$$

where V is the volume of the resonator, $V_\in$ is the volume of the sample. The Q factor is determined by the formula $Q = f_0 / \Delta f$, where f_0 is the resonance frequency of the resonator, $\Delta f = f_1 - f_2$, f_1, f_2 is the frequency at the half power level of the resonant frequency.

As an indication of the E and H – fields influence on the body, the dielectric constants of the localized site of the organism are used, measured by the resonance method in a rectangular resonator with dimensions of 300×280×2 mm, and determined by the formula

$$\varepsilon = 1 + 0.5\,(f_0 - f_1)\,V / f_0\,V\varepsilon, \quad (3)$$

where f_0, f_1, is the resonant frequency of the resonator without and with a dielectric body respectively; V_ε, V are the volumes of the dielectric and resonator respectively. The biological object is placed into a metal screen with a gap through which high-frequency radiation is introduced into the structure of the object. Because it is practically impossible to determine directly the local volume of the object enclosed into the metal screen, its magnitude is determined indirectly. Since the blood contains up to ~ 80% of water, and its molecules, being polar, provide enhanced relaxation processes, the value of ε water in the UHF range is well known and is equal to ε = 80.

In a rectangular resonator, the value of εв in the water column should be determined at its height above the narrow wall of the waveguide. The local volume of the dielectric placed in a rectangular resonator can be calculated from

$$V_\varepsilon = 0.5(f_0 - f_1)\,V / (\varepsilon - 1)\,f_0. \quad (4)$$

In the expression (2), the volume of the dielectric V_ε is replaced by the effective value of the volume of water in the resonator.

The authors have found that the permittivity decreases sharply as the height of the water column lowers. This happens due to the formation of a multilayer dielectric column with different capacities. Therefore, it is necessary to determine separately, in a resonant way, a given volume with the subsequent substitution of its value into the equation (2) for a given gap in the screen of the effective volume of a biological object placed in a screened cylinder. This cylinder is installed in a rectangular resonator so that the axis of the cylinder coincides with the longitudinal axis of the resonator, and its middle is located in the maximum RF field by the appropriate mechanism (see Fig. 3, item 5).

5. SPECIFIC FACTORS OF APPLICABILITY OF RADIATION INTHE UHF RANGE

Maximum relaxation of the intercellular fluid in the biological body occurs in the UHF range of radiation.

Penetration depth of radiation in this frequency range into the biological material is about 10 cm, and, in turn, 2 times greater than that in the SHF and other emission bands.

Possibility of placing a relatively large biological object in the resonator device. For a biological object, it is necessary to maximize the resonator filling along the height of the waveguide and to have a minimum gap in the shielding screen when the required value of the electrical signal from the resonator is obtained.

CONCLUSIONS

The experimental data obtained when a relatively large size dielectric volume is introduced into a rectangular resonator confirm the correctness of the choice made: to conduct further studies of the effect of transverse electric and magnetic fields with the control of the biological object placed under radiation in the UHF range. These developments will provide a transition to study a possibility of limiting the malignant tumors spread in the tissues and organs of biological objects through enhancement of the immune defense.

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ПОДАВЛЕНИЕ ЗЛОКАЧЕСТВЕННЫХ ОБРАЗОВАНИЙ В БИОЛОГИЧЕСКИХ СТРУКТУРАХ МЕТОДОМ ИММУННОЙ ТЕРАПИИ

А.Н. Довбня, В.П. Ефимов, Г.Д. Крамской

Предлагаемый подход к решению проблемы сокращения зоны злокачественных образований основан на комбинированном воздействии постоянных магнитного и электрического полей на сосудистый эндотелий кровяного потока в биологических структурах для усиления иммунного ответа в организме. Контроль состояния области их воздействия осуществляется резонансной диагностикой в дециметровом диапазоне длин волн.

ПРИГНІЧЕННЯ ЗЛОЯКІСНИХ УТВОРЕНЬ У БІОЛОГІЧНИХ СТРУКТУРАХ МЕТОДОМ ІМУННОЇ ТЕРАПІЇ

А.М. Довбня, В.П. Єфімов, Г.Д. Крамській

Запропонований підхід до вирішення проблеми скорочення зони злоякісних утворень заснований на комбінованому впливі постійних магнітного та електричного полів на судинні ендотелії кров'яного потоку в біологічних структурах для посилення імунної відповіді в організмі. Контроль стану області їх впливу здійснюється резонансною діагностикою в дециметровому діапазоні довжин хвиль.