HYDRATATION CHANGES OF THE RED BLOOD CELL MEMBRANES OF GASTRIC CANCER PATIENT EVOKED BY RADIATION THERAPY

L. Batyuk[1], N. Kizilova[2], V. Berest[3], O. Muraveinik[4]

[1]Kharkiv National Medical University, Kharkiv, Ukraine
[2]Warsaw University of Technology, Warsaw, Poland
[3]V. N. Karazin Kharkiv National University, Kharkiv, Ukraine
[4]Kharkiv City Clinical Hospital No 7, Kharkiv, Ukraine

[1]*liliya-batyuk@ukr.net*, [2]*n.kizilova@gmail.com*, [3]vpberest@hotmail.com, [4]oksanaanatoliivna602@ukr.net

Tumors diseases and dielectric characteristics of structural-functional state of erythrocyte membranes

Cancer is one of the most essential medical and social problems in the world due to its significant prevalence and serious consequences: the loss of efficiency, disability and the high percentage of death. One of the leading therapeutic methods for malignant tumors is radiation therapy [1]. The heterogeneity of the red blood cell (RBC) membrane composition, its ability to quickly change the nature of the interaction between the components determine the presence of a wide range of structural and functional reactions of the cell to its adaptation to environmental conditions. Complex dielectric permittivity $\varepsilon^* = \varepsilon' - i\varepsilon''$, where ε' is the relative permittivity, ε'' is the loss factor, of the red blood cells differ significantly in healthy blood and in the cancer patients [2], that can be used in medical diagnostics and estimation of the individual treatment success. Analysis of the dielectric characteristics of the RBC in cancer patients provides additional information on the tumor development and treatment processes that is of great interest in connection with elaboration of more efficient methods for the early diagnosis of cancer [3]. The purpose of the investigation a model that can account in a unified way for the dielectric response of RBC in suspensions in the formalism of Kluitenberg's theory, and later to derive the expression of the complex dielectric function that generalizes the one of Debye, to compare the results obtained with experimental data.

Thermodynamic approach

The physical phenomena at the micro/nano scale in MW fields is described by the enhanced irreversible thermodynamics (EIT) that introduces the Helmholtz free energy $\Im$ as a function of its parameters X,Y, their fluxes $J_{X,Y}$, and their time and space derivatives in the

Materials and methods

In the present study the suspensions of red blood cells (RBC) and RBC shadows of gastric cancer patients (20 people) have been used. The control group consisted of 25 healthy donors. According to the international classification system TNM (tumor, nodus и metastasis), the patients were distributed as follows: T2N1O (second stage of the disease without signs of distant metastases) - 45% and T3N1MO (third stage, without signs of distant metastases) - 55%. The median age was 47 years. A group of patients received radiotherapy as an independent treatment course in the mode of classical fractionation, with a total focal dose of 45 Gy. Blood sampling was driven by a vein puncture after irradiation. The dielectric properties of the RBC have been studied by microwave dielectrometry at the frequency f=9.2 GHz in the wide temperature range T=0-46°C. The dielectric relaxation time of water molecules, the change in the free energy of activation of the dipole relaxation of water molecules were study and the hydration of cells before and after radiation therapy was evaluated. Since the obtained data showed a non-parametric nature of the distribution, the Wilcoxon criterion was used to estimate the significant difference in the results of treatment, and Fisher's exact method was used for the data analysis with $p < 0.05$.

form $\Im = \Im(X, Y, J_{X,Y}, \nabla J_{X,Y}, \dot{J}_{X,Y})$, where dot corresponds to the time derivative. Therefore, the classical physical laws like Fourier heat, Fick's diffusion, Darcy mass transfer, and other laws possess the generalized form [3]

$$\tau \dot{J}_X + J_X = -k\nabla X + \lambda \nabla^2 X + f(X), \qquad (1)$$

where τ is the relaxation time ($\tau = 0$ in slow varying fields), λ is the scale related parameter ($\lambda = 0$ at macro scale), k is the transfer parameter. In the complex MB+NP suspensions in MW fields a series of novel coupled transfer phenomena appeared due to (1). In this study the coupled heat J_T and mass J_ρ transfer phenomena are studied. The entropy production is computed and the generalized Dufour, Soret, thermo-, electro- and diffusiophoresis relations are obtained. According to the theory of absolute reaction rates, the change in free energy during the transition of one mole of a substance to an activated state may be due to the dielectric relaxation time. Thus, to determine the restructuring of polar liquids by the change in the activation entropy, it is necessary to have information about the temperature dependences of the dielectric permittivity spectra in the relaxation region, from which the value of τ can be determined.

Results

The results presented in Fig.1a (before radiotherapy) as show as the diagram of temperature dependence of dielectric relaxation frequency of the water molecules in suspensions of erythrocytes demonstrates an increase of relaxation frequency f_d of the water molecules in suspensions of erythrocytes of patients with gastric cancer compared with donors. This process demonstrates the hindered rotation of the water molecules and decrease of amount of the bound water that is probably connected with the erythrocytes aggregation and an increase of concentration of the tumor necrosis factor in blood. The results of the study indicate the existence of a thick layer of hydrated water over the surface of RBC in cancer patients with gastric cancer. It has been shown by numerical estimations that each water molecule in the layer forms up to two hydration bonds, approximately. Probably bound water fills the entire space between the glycoproteins of the cell receptors. A number of structural transitions in RBC membranes in the 6, 8-15, 15-20, 36-40 and 42-46° C temperature ranges have been observed. These transitions are accompanied by a change in the activation energy of the dielectric relaxation of water molecules. Similar changes have been detected on the RBC ghosts. Therefore, the observed effect is mostly connected with cellular membrane, not with haemoglobin solution. It was established that in groups of donors and patients with gastric cancer, after radiotherapy, Fig.1b, this effect is observed on the whole studied temperature interval that is logically connected with changes of physical and chemical properties of erythrocyte membranes and with dysfunctions of the blood formation revealed at the presence of tumor in organism.

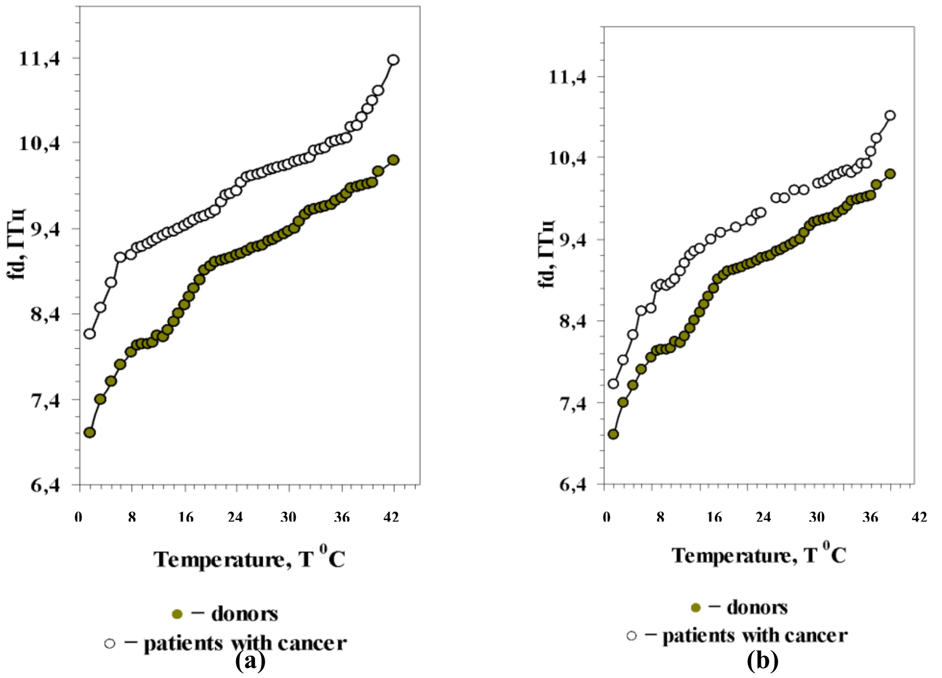

Fig.1. Temperature dependence of dielectric relaxation frequency f_d of H2O in RBC suspensions before (a) and after (b) radiotherapy (● – patients with gastric cancer; ● – donors).

An increase in the static dielectric permittivity ε_s may indicate an increase in the thickness of the hydrated permembrane layers of erythrocyte water in patients and, accordingly, decreasing the proportion of depolarized water, Fig.2. Deviations in the static dielectric permittivity of RBC suspensions after radiotherapy, Fig.3, indicate an increase in the hydration of the cell membrane, and a decrease in the amount of free water. The effect of temperature explains these variations in that the main dipole-dipole interactions that control these media are related to the presence of hydrogen bonds, these links have a weak dissociation energy, so raising the temperature helps to break these bonds, which implies a decrease in the number of electric dipoles in the solution and, consequently, a decrease in the permittivity

Conclusions

Radiotherapy leads to a decrease in the concentration of strongly bound water. Probably, as a result of therapy, the irreversible adsorption of glycoproteins that are part of cellular receptors occurs; this may partially lead to loss of integrity of the cell membranes and cell rupture. Therefore, dielectric parameters of the RBC membranes can be used for quantitative estimation of the stage of disease and control over the anticancer radiation therapy. The method can be used for testing the success of the prescribed chemotherapy/X-ray therapy by RBC examination.

1. Kizilova N. Review on modern techniques in diagnostic and planning radiology. Int. J. Biosen. Bioelectron. 2018;4(6):242-247.
2. Batyuk L. Influence of cancer disease on dielectric characteristic of structural–functional state of erythrocytes membranes. Science Rise. Medical Science. 2015;7/4(12):11–17.
3. Batyuk L, Kizilova N. Dielectric properties of red blood cells for cancer diagnostics and treatment. AS Cancer Biology. 2018;2(10):55-60.

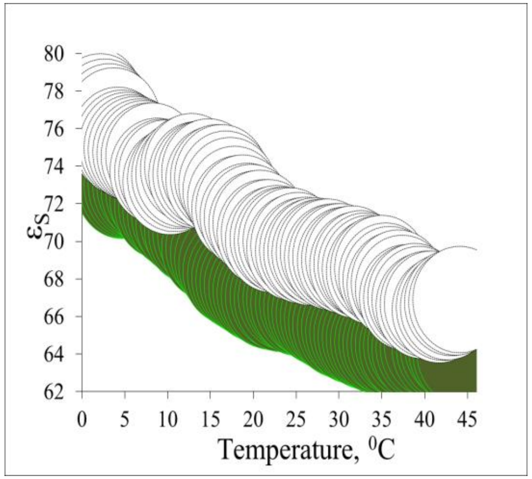

Fig.2. Temperature dependence of hydration of membrane of RBC before radiotherapy (○ – patients with gastric cancer; ● – donors).

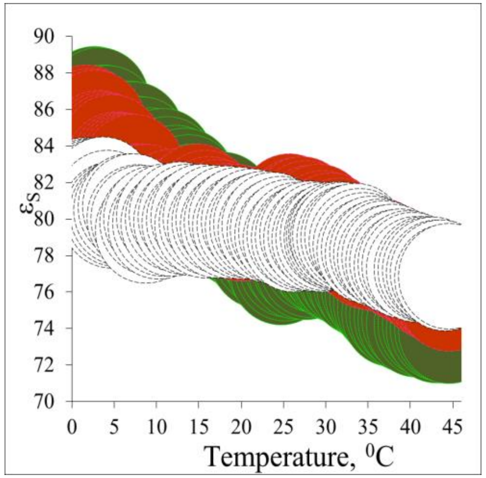

Fig.3. Temperature dependence of hydration of membrane of RBC and ghosts of RBC after radiotherapy (○ – membrane of RBC of patients with gastric cancer; ● – RBC ghosts of patients with gastric cancer; ● – RBC ghosts of donors).

.