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New Medical Technology – Functional Microwave Thermography: Experimental Study

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Abstract

A diagnosis technique based on the functional microwave thermography (FMT) is examined in vivo. Theoretical analysis of this method is presented and the methodology of the analysis of primary experimental data on the basis of application of mathematical approach of nonlinear dynamics is discussed. Possibilities of the FMT method in translational research of different therapeutic agents against malignant tumors are revealed and several examples of the corresponding thermograms are presented and discussed.

Keywords: microwave thermography, malignant tumors, nonlinear dynamics

1. Introduction

The development of a malignant tumor is significantly non-steady state process, which is highly sensitive to continuously changed by both the interaction of the tumor and organism and an influence of external factors. The existing methods of instrument and laboratory of control will not make it possible to obtain sufficiently operationally information about the nature of the reaction of malignant tumor to the action of therapeutic agent. The practical application of methods of the control of the development of the malignant tumors of those having "characteristic times" the same as the characteristic times of interaction of new formation and therapeutic factor (medicine, the beam methods of therapy, thermal actions, etc) during their introduction in body of patient i.e. second, minute and tens of minutes are necessary.

Such methods of control are developed on the basis of the ideology of molecular biology, when rapid changes in the expression of peptide markers are recorded with the aid of the molecular biochips, the optical and magnetic- resonance methods. In this case actually are tracked the changes proceeding at the genetic and epigenetic level in the tumor cells. However, tumor is the complex dynamic formation, the forecast of development of which it is possible to make on the basis of the analysis of the changes in tumor as to integral structure only. One of the integral indicators of functional state neoplasms are temperature changes in tumor (changes at the molecular, cellular and tissue level the ratio the of thermogeneration and thermodesorption processes), which are detected by a local microwave broadband electromagnetic radiation on the basis of the principles of the contact radiometry (Fig. **1**) [1-3]. Fluctuations of the recorded electromagnetic radiation of the living normal and pathological tissues in the microwave range occur as a result of the thermodynamic changes and can serve as a diagnostic marker for the development of the tumor process and for the effectiveness of its therapeutic correction. Design and engineering-technical decisions were developed on the basis of the Institute of experimental diagnostics and therapy of tumors of N. N. Blokhin NMRCO. It allowed us to develop a method of functional microwave thermography (FMT), which is currently at the stage of preclinical testing and patent registration [4, 5]. Note, the temperature monitoring should be useful for various therapeutic modalities of mild cancer treatments, which can be realized by using biocompatible and biodegradable nanoparticles based on silicon [6, 7].

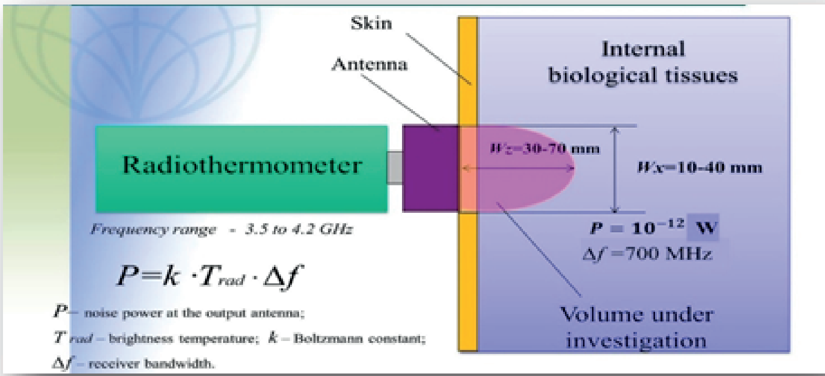

Figure 1: Schematic diagram of radiometric recording of the parameters of biological tissues.

2. Materials and methods

Laboratory mice (S57Bl/6, BDF1) in the experiments were used. The following types of tumors was transplantated: the carcinoma of lungs Lewis is (LLC), melanoma B-16 (B-16), cancer of light -67 (CL-67).The transplantation of solid tumors was carried out by standard procedure. The optimum regimes of the registration of the intensity of the thermal radiation of the internal tissues of laboratory animals in the microwave wavelength range were determined.

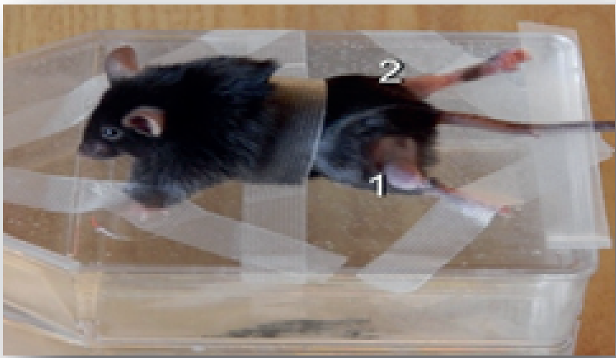

Figure 2: Fixing of a laboratory animal.

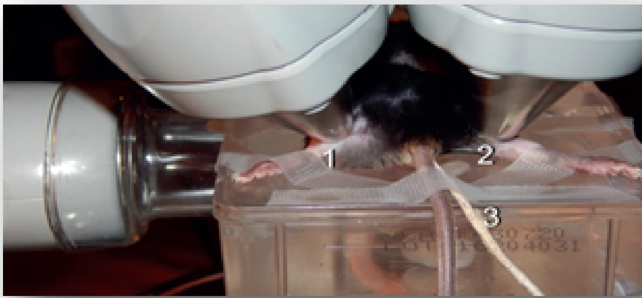

Figure 3: Experimental installation for the two-channel registration of the thermograms.

Prior the experiments the skin of mouse was preliminarily prepared (sheared fur), and then with the aid of the special cream it was depilated the contact surface of the antenna of radio-sensor and skin. Laboratory animal itself motionlessly was fixed with the aid of the hypo-allergenic medical adhesive tape to the base layer (Fig.2). Duration of the experiment varied from several minutes to 3 h. The average duration of the registration of the microwave emission of laboratory animal comprised 1 hour. The antenna- applicators with a diameter 7 mm. were used in all experiments and the two-channel diagram of the synchronous registration of microwave signal (**Fig. 3**).

A calibration testing of the obtained systems of the registration of microwave emission was carried out by heating in the water bath and the kinetics of its cooling synchronously was written by two sensors of microwave emission. The practically identical dynamics of this parameter for both sensors was obtained. This allowed us all subsequent experiments on laboratory animals to carry out without the fear to obtain

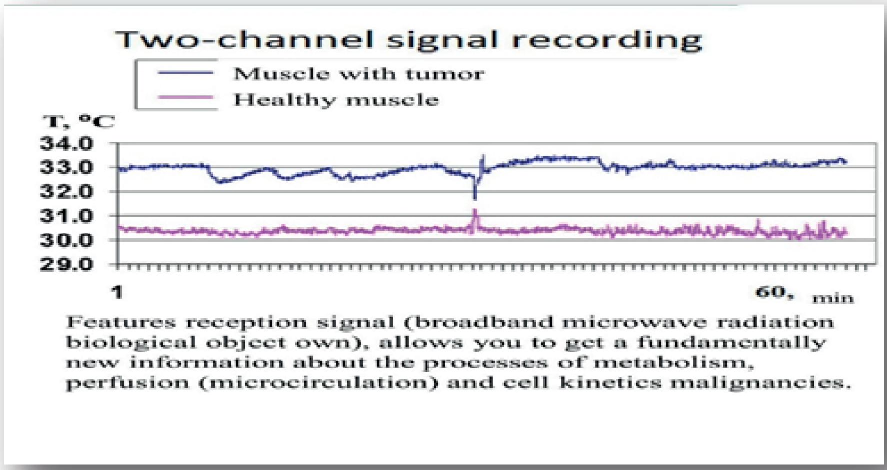

Figure 4: Two-channel signal recording termogram of normal tissue and tumor.

the artifacts, caused by asynchronism of the work of two channels of obtaining information.

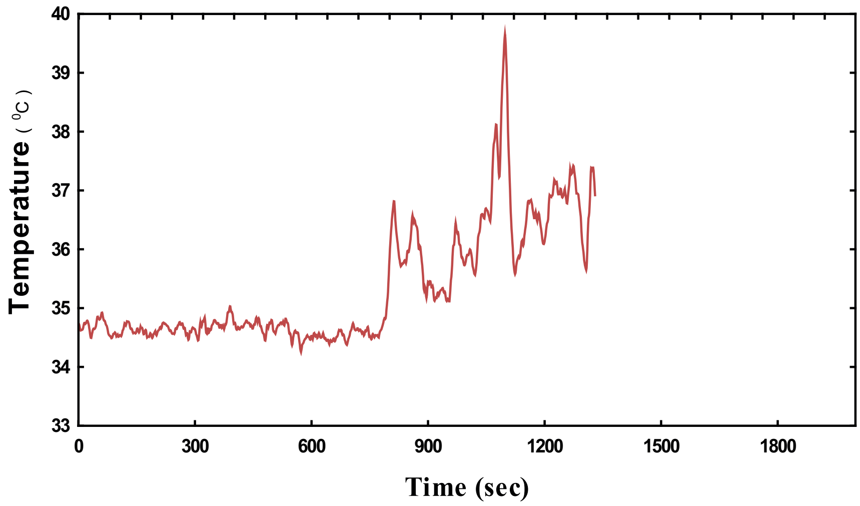

Figure 5: Temperature transient for high-intensity mode of photodynamic therapy.

3. Results

Typical graph of the synchronous registration of the thermogrames in one and the same laboratory animal is shown in Fig.4. Upper the graph- thermogram of solid the tumor, which grows invasive is intramuscular; the thermogram of healthy muscle of thigh. Thermograms have both qualitative and quantitative differences. The primary unit of tumor has a temperature on 2-3 deg. It is higher than healthy tissue, and this

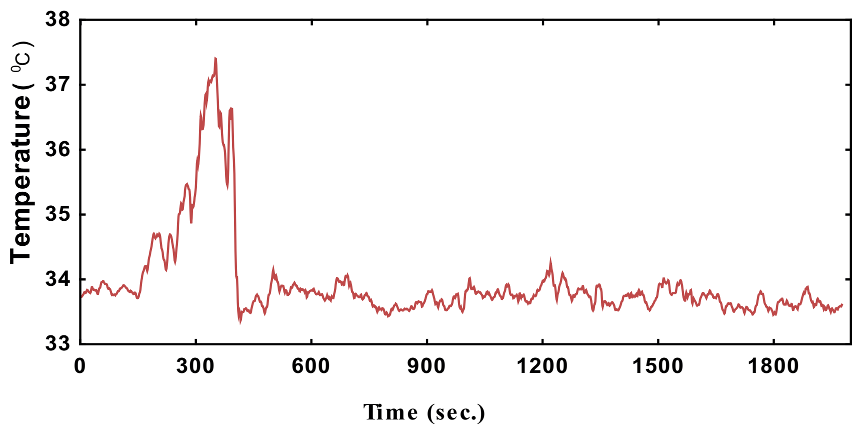

Figure 6: Temperature transient under applied low-intensity mode of photodynamic therapy.

difference remained in entire interval of the conducted measurement. In the tumor tissue the modal quasi-harmonic component of obscure genesis is detected. However, in the normal muscular tissue the chaotic process with certain modulation, most likely, vascular nature, is dominant.

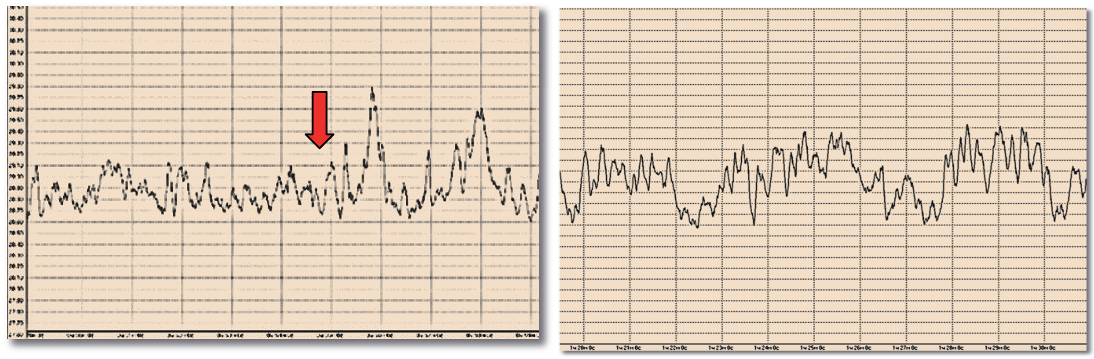

Figure 7: Thermograms of a malignant tumor LLC in the action of chemotherapeutic drug.

3.1. Compared two modes of conducting photodynamic therapy (PDT) of the tumors

In the first case (Fig. 5) we used a high-intensity mode of PDT: λ = 635 nm; W = 500 mW; P = 150 J/cm^2, t = 300 s. As a result of exposure to laser radiation specified parameters change in temperature (ΔT °C) in the tumor was 5 °C. the temperature fluctuations in the tumor tissue be low-frequency and high-amplitude (about 1.5 °C) after cessation of exposure to laser radiation, which most likely indicates a breach of its bioenergetics and microcirculation of blood flow due to destructive changes.

In the second case (Fig. 6) we have applied a low-intensity mode of PDT: λ = 635 nm; W = 500 mW, P = 100 J/cm^2, t = 200 s. Specified parameters change in temperature (Δt) in the primary site of the tumor was 3.5 °C. After exposure to laser radiation, the change of amplitude-frequency characteristics of the temperature fluctuations in the tumor tissue was substantially less (for example, the amplitude of temperature fluctuations of about 0.5 °C) than in the previous case, which indicates a less pronounced destructive changes in the tumor tissue.

3.2. Termogram of malignant tumor in the action of chemotherapeutic drug

Aranosa was administrated to BDF_1 mice bearing i.m. Levis lung carcinoma (LLC). Aranosa 200 mg/kg were given i.p. (the time of introduction is indicated by the arrowon thermogram). Qualitatively change the spectrum of fluctuations of thermal radiation of malignant tumors : their amplitude increases and they become quasi-periodic (Fig.7).

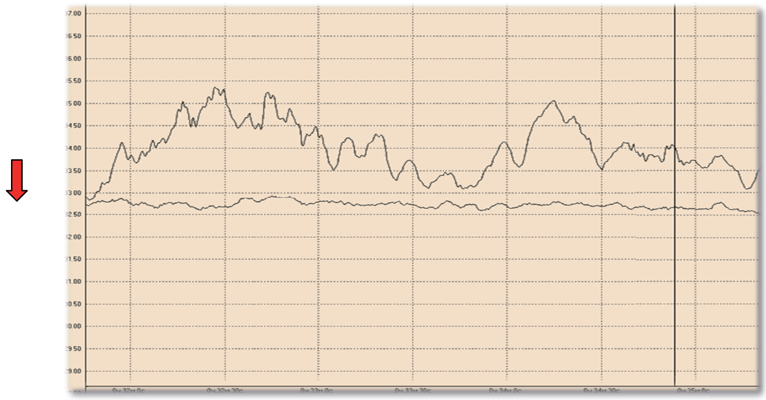

Figure 8: Termograms experiencing leukemia cell suspension (L1210) with added hypertonic glucose solution.

Figure 9: Thermogram of a LLC tumor when administered to a laboratory animal with hypertonic glucose solution.

3.3. Thermography of the malignant new formations of laboratory animals under the conditions of carbohydrate load

Experimental studies by FMT method were carried out under the conditions of carbohydrate load. Glucose, in this case, is universal metabolicmarker of the functional state of the cloth of tumor. Fig.8 shows typical thermogram of tumor LLC during the introduction to laboratory animal of i/v of the hypertonic solution of glucose. 2.5 minutes after introduction it was possible to observe the considerable strengthening of thermo-generation. It appeared the high-amplitude of temperature fluctuations as a result of use by cells of the tumor of glucose as energy substratum and the gradual return of thermal balance to the previous value.

We designed special device for the analysis of the thermograms of the suspensions of tumor cells. Fig. 9 shows typical thermogram of the surviving suspensions of the leukosis cells by the added hypertonic solution of glucose is represented (L 1210). Temperature grows (1.5 °C), and in volume of suspension appear the quasi-harmonic fluctuations, probably connected with the fluctuations in the glucose cycle of tumor cells. Temperature in this case not only substantially grows (2.5 °C), but also in volume of suspension appear the quasi-harmonic fluctuations, probably connected with the fluctuations in the glucose cycle of tumor cells. Thus, the represented above results confirm well our proposal about the expediency of the modification of the developed method FMT (functional microwave thermography) for the purpose of an increase in its sensitivity and selectivity. At present it is comprised the data base for the dynamics of a change in the termogram malignant tumors of different histological types in the conditions of carbohydrate load on the organism of laboratory animal. A deeper analysis of the obtained results for the purpose of their numerical formalization seems to be possible by nonlinear dynamics methods.

4. Discussion

The noninvasive physical methods of the control of the effectiveness of treatment (infrared thermography, magnetic-resonance and ultrasonic laminography, the laser spectral analysis of molecule- biomarkers in exhaled air, etc) used at present in the clinical practice, as a rule, reveal those already taking place at micro- and the macrolevel morphological changes in the primary unit of tumor, as the result of interaction of the developing tumor process and conducted therapy. So, it is not possible in proper time to conduct the adequate correction of the therapy assigned and it is essential to increase its effectiveness in that case.

Action on the tumor (straight line or undirected) leads to a) to microcirculation change in the cloth of tumor and respectively the kinetics of transport processes; b) to a change of the metabolic and bioenergetic processes in the tumor cells; c) to a change in the cellular kinetics of the processes of proliferation, necrosis and apoptosis of the cells of tumor. All three types of processes are accompanied by a change in the relationship of thermo-generation and thermo-dissipation at the molecular, cellular and woven level. All three types of processes have different their own characteristic times.

The objectivity of the interpretation of information, obtained by the developed method, can and be reinforced by correlation studies with the application of traditional invasive and noninvasive (physical, biochemical, histochemical, etc.) procedures of the evaluation of functional state and control of the effectiveness of the treatment of the primary malignant tumors.

5. Conclusions

The registration of temperature variations in the primary site of cancer associated with the kinetics of its growth and the change in its morphology is the basis of the developed our method of functional microwave thermography. Applications of nonlinear dynamics methodology (calculation of fractal topological characteristics of the signal, the entropy of the normalized time series analysis attractors phase trajectories et al.) makes it possible to determine the patterns of change in the parameter detected in real time on the effect of various therapeutic agents. One of the ways to increase the sensitivity of the methods is the addition of the agents (e.g., carbohydrate loading, nanoparticles etc), which should strengthen the thermal intensity of primary tumors. The proposed method of the analysis of the functional stat dynamics of experimental malignant tumors and the control of the effectiveness of their treatment can facilitate screening and thorough study of new antitumor preparations, and also the search for the optimum parameters of the application of physical factors in oncologic experimental studies and clinical practice. Further development of the method and its realization into clinical practice will make it possible to considerably increase the potential of substantiated selection of treatment scenario for the purpose of personalize medicine.

Acknowledgments

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References

[1] Vesnin S, Sedankin M, Ovchinnikov L. Microwave radiometer for medical application. Conference materials, ESHO 2014, Turin, Italy.

[2] Vesnin, S. G. Microwave radiometry – national the treasure of Russia. Zdorovie № 9, 2007, pp. 159-164 (in Russian).

[3] Siskov M. A. Hardware-Software complex for the study of functional processes of the brain methods of microwave radiometric. Ph. D. Thesis, Ekaterinburg, 2012. (in Rusian).

[4] Zinovyev S.V. Development of the method of the functional microwave thermometry of pervichnogoochaga of malignant new formations. Materials of the V Troisk Conference "Medical physics and innovation in medicine" (TKMF-5), Troitsk, 4-8 June 2012; 2012, V.2, p.165.

[5] Zinovyev S.V. Thermo-fluctuations in the malignant new formations laboratory animals // IV the congress of the biophysicists of Russia. Symposium is III "physics - to medicine and ecology". Materials of reports. – Nizhniy Novgorod, 2012, V.3, p.96.

[6] Kabashin A. V., Timoshenko V. Yu. What theranostic applications could ultrapure laser-synthesized Si nanoparticles have in cancer? Nanomedicine, 11 (17): 2247-2250 (2016).

[7] Osminkina L.A., Nikolaev A.L., Sviridov A.P., Andronova N.V., Tamarov K.P., Gongalsky M.B., Kudryavtsev A.A., Treshalina H.M., Timoshenko V.Yu. Porous silicon nanoparticles as efficient sensitizers for sonodynamic therapy of cancer, J. Micropor. Mesopor. Materials, V.210, 169 (2015).