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Non-Invasive Approach to Early Diagnosis of the Formation of Oncological Neoplasms

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Abstract

The currently developed instrumental approaches for detecting pathological changes in the body have a number of disadvantages. The most important of them is that the equipment is sensitive to the detection of diseases only from a certain threshold level of destructive changes in the body. The present article discusses the possibility of using the new instrumental complex "Bioscope" for early and non-invasive diagnosis of the beginning of the formation of ontological neoplasm's in the body.

Keywords

Cancer, Early Non-Invasive Diagnostic, Bioscope

1. Introduction

Modern medical methods of treatment allow in some cases to prevent the development of pathological processes in the human body. It is known that the effectiveness of such therapeutic effects is largely determined by the possibility of diagnosing the disease at the initial stages of its development. In particular, statistics show that when cancer is detected at an early stage, the probability of cure is 90% - 95% [1]. In later stages, this figure drops to 50%, and in the third and fourth stages, the probability of cure is only 10% - 12%.

The foregoing makes it relevant to search for new and more sensitive instrumental approaches to the formation of oncological formations. In this regard, the "Bioscope" hardware complex developed in Armenia is of particular interest [2] [3].

Structurally (**Figure 1**) "Bioscope" consists of a light source (L), a photodetector (F) and a sensor, a glass plate (1) covered with a thin opaque material (2). The

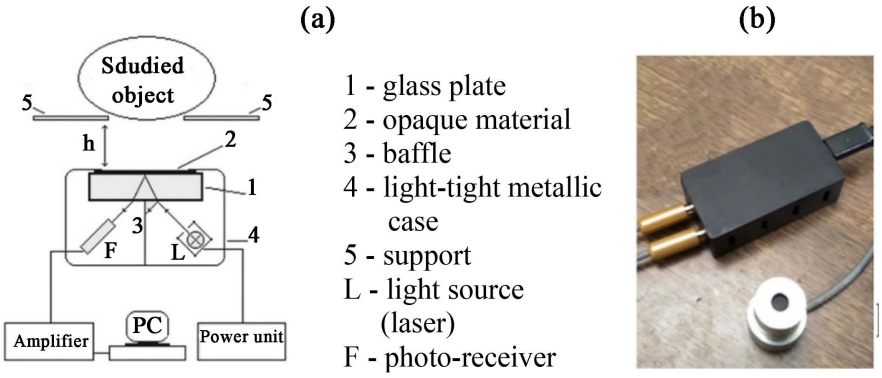

Figure 1. Principal design of "Bioscope". (a) component composition of "Bioscope"; (b) general view of the "Bioscope" and the communication module with a computer.

radiation source, glass plate and photodetector are completely isolated from external light by a covering material and a metal case (3).

Working principle of "Bioscope" is based on measuring intensity of light scattered inside the light-tight chamber. It is important that no light enters and go out the device.

At the approaching of inanimate objects having an ambient temperature, the readings of the device do not change. However, already from a distance of 5 - 7 m, the equipment reacts to the presence of a person.

Different biological objects affect the readings of the "Bioscope" to varying degrees; at the same time, the signals of the equipment also change when the physiological state of the system under study changes. This indicates the possibility of using the "Bioscope" to assess the state of the biological system in various biomedical studies.

At present, data have been obtained that demonstrate the effectiveness of the use of the "Bioscope" instrumental complex in studying the features of the influence of various pharmacological preparations [4], physical activity and stress effects [5] [6] on the physiological state of the body.

The conducted studies have shown that, unlike conventional equipment, the "Bioscope" signals reflect the state of the integral (integrative) state of the biological system under study [7] [8]. Obviously, any, even the most insignificant pathological changes in the body should lead to a change in its integral state. Therefore, one can think that the registration of these changes using the "Bioscope" hardware complex can be of diagnostic significance.

To substantiate the assumption made, the presented work presents data obtained in studies with the experimental formation of skin cancer in white mice. At the same time, an example of "Bioscope" signals in the area of the right and left mammary glands of a woman who was subsequently diagnosed with breast cancer is given.

2. Methods

Experiments to study the processes of skin cancer formation were carried out on

12 white male mice weighing 20 - 25 g. Four mice were isolated as a control (intact) group. The remaining 8 made up the experimental group.

In the first series of studies to determine the normative indicators of the state of intact mice using the multichannel instrumental complex "Bioscope", night recording of the equipment signals was carried out for 10 days.

In the second series of studies for 8 mice of the experimental group, the initial "Bioscope" signals were recorded and the next day the animals were infected with skin cancer (Crocker's sarcoma strain). After that, night registration of their condition was carried out for 30 days.

Subsequently, it turned out that out of 8 mice of the experimental group of animals, six mice died on 35 - 40 days after infection with skin cancer. Accordingly, the experimental group was divided into subgroups of dead and surviving animals.

Figure 2 shows a typical response of "Bioscope" signals when a biological system approaches it.

To analyze the "Bioscope" signals in the LabView software environment, a complex software package was developed. In the analysis program, the spectral distribution of the "Bioscope" signals was calculated. In addition, the time intervals between successive peaks of the "Bioscope" oscillatory signals (BB intervals) were calculated, and spectral distributions were also plotted for the curve of successive BB intervals. At the same time, 16 statistical indicators were calculated for the set of BB-intervals. Of these 16 indicators, 11 were conditionally identified as primary, using which 5 additional (secondary) indicators were calculated (Table 1).

When analyzing the data obtained, a 250-minute night recording of the "Bioscope" signals was distinguished, and its band-pass filtering was carried out from 0.1 to 500 counts/min. Average, absolute and relative values of statistical indicators characterizing the physiological state of various groups of animals were calculated. In the context of 10-day registration for the intact and experimental groups of animals, the variability of all statistical indicators was assessed.

Relative changes in statistical parameters for different days of registration for mice were assessed individually. Subsequently, their values were averaged over all animals of the corresponding experimental group of animals. The significance of the difference between the calculated indicators in different experimental groups was assessed using Student's t-test at a significance level of $p < 0.05$.

All work with animals was carried out in accordance with the rules of the "European Convention for the Protection of Animals Used in Experiments"

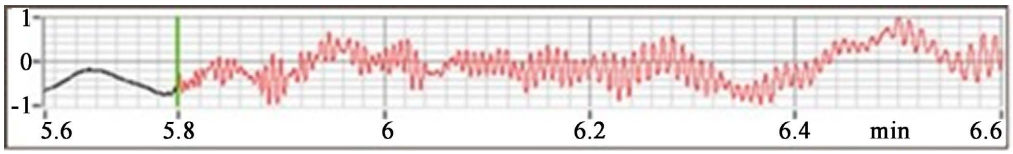

Figure 2. Typical signals of "Bioscope" to the approaching the biological system. Vertical lines: the moment of approaching the biological system to the "Bioscope".

Table 1. Statistical indicators of "Bioscope" signals.

NN	Abbreviations	Acronyms
PRIMARY INDICATORS		
1	<BB> (min)	Mean value of BB-intervals
2	Std_BB (min)	Dispersion of BB-intervals
3	CV (%)	Coefficient of variation of BB-intervals
4	RMSDD_BB (min)	Square root of the sum of squared differences of successive pairs of intervals of a series of BB-intervals
5	Max-Min (min)	Difference between the maximum and minimum values of BB-intervals
6	Max/Min	Ratio of the maximum and minimum values of BB-intervals
7	AMo (%)	Amplitude of histogram mode of BB-intervals
8	Mo (min)	Histogram mode of BB-intervals
9	F_BB = 1/<BB>	The average frequency of signal oscillations
10	FFT	Spectral power density of "Bioscope" signals
11	FFT_BB	Spectral power density of BB-intervals
SECONDARY INDICATORS		
12	A = AMo/(Max-Min)	
13	B = 1/(Mo * (Max-Min))	
14	C = AMo/(2 * Mo * (Max-Min))	
15	D-Total number of BB-intervals assigned to AMo	
16	E = AMo/Mo	

(Directive 2010/63/EU).

There was also a short series of participatory experiments involving women. At the same time, a 3-minute registration of the "Bioscope" signals in the region of the right and left mammary glands was carried out. For the registered signals, their spectral distributions were constructed.

3. Results

To assess the possibility of early prediction of the death of white mice after infection with skin cancer, the nature of the change in their statistical parameters in the first ten days after infection was evaluated. Figure 3 shows relative to the values of the control group of animals, the statistical indicators of surviving and dead mice.

On the abscissa axis: statistical indicators. Designations are presented in Table 1. On the axis of ordinate are the relative values of statistical indicators.

As can be seen from the figure, both in surviving and dead mice, the values of almost all indicators significantly differ from those for the intact group of ani-

mals. At the same time, the direction of change in the values of indicators for surviving and dead mice in relation to control indicators turns out to be diametrically opposite.

An interesting picture is also formed for the coefficients of variation of statistical indicators. As can be seen from Figure 4(a), in surviving mice in the first 10 days after infection, the coefficients of variation of all integrative parameters do not statistically differ from those for the intact group of animals. For dead mice, for a number of indicators (Figure 4(b)), the coefficient of variability increases by a factor of 2. In particular, this is the case for such main statistical indicators as the frequency of oscillations (9), the power of the "Bioscope: signal spectrum (10), and the power of the spectrum of their BB intervals (11).

A pronounced difference for the intact, dead, and surviving groups of mice is also observed in the spectral distributions of the "Bioscope" signals (Figure 5).

According to Figure 5(b), in dead mice, when averaged over the first 10 days of registration after infection, characteristic peaks in the frequency range of 0.03

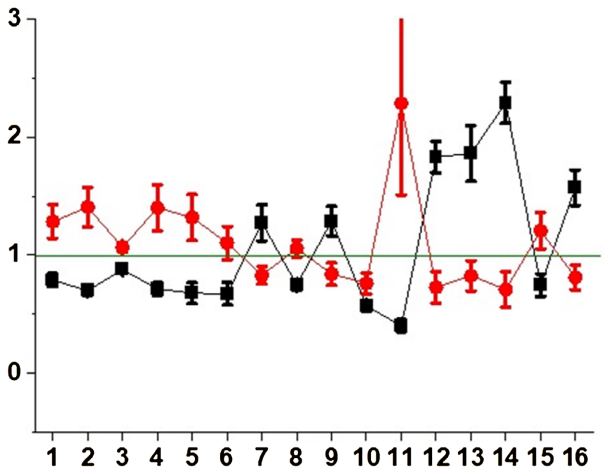

Figure 3. Relative to control values of statistical indicators of the body of surviving (black) and dead (red) mice.

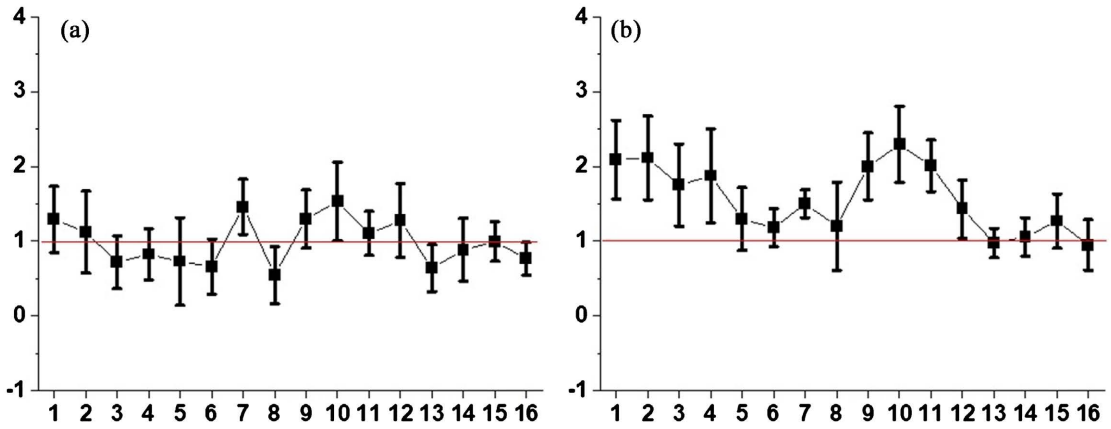

Figure 4. Relative to control coefficients of variability of statistical indicators of the body of surviving (a) and dead (b) mice. The abscissa shows statistical indicators. Designations are presented in Table 1. On the axis of ordinate are the relative values of statistical indicators.

counts/min and 0.3 counts/min are formed in the spectrum of BB intervals, which is absent, both in intact and infected, but surviving animals.

In this regard, an individual analysis of the spectral distributions of BB-intervals for dead mice was carried out (Figure 6).

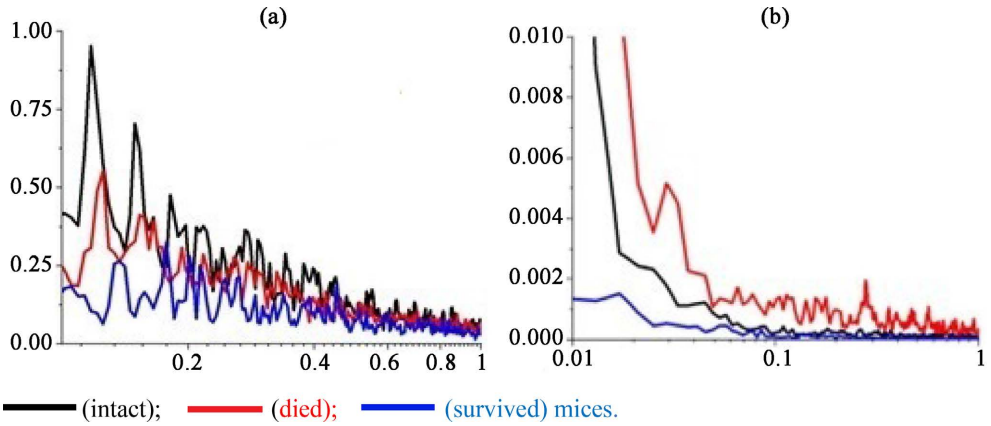

Figure 5. Average spectral distributions of "Bioscope" signals (a) and spectral distributions of their BB-intervals (b) of white mice. On (a) and (b), along the abscissa of the oscillation frequency on a logarithmic scale in counts per minute. On the axis of the ordinate, power of the spectrum in relative units.

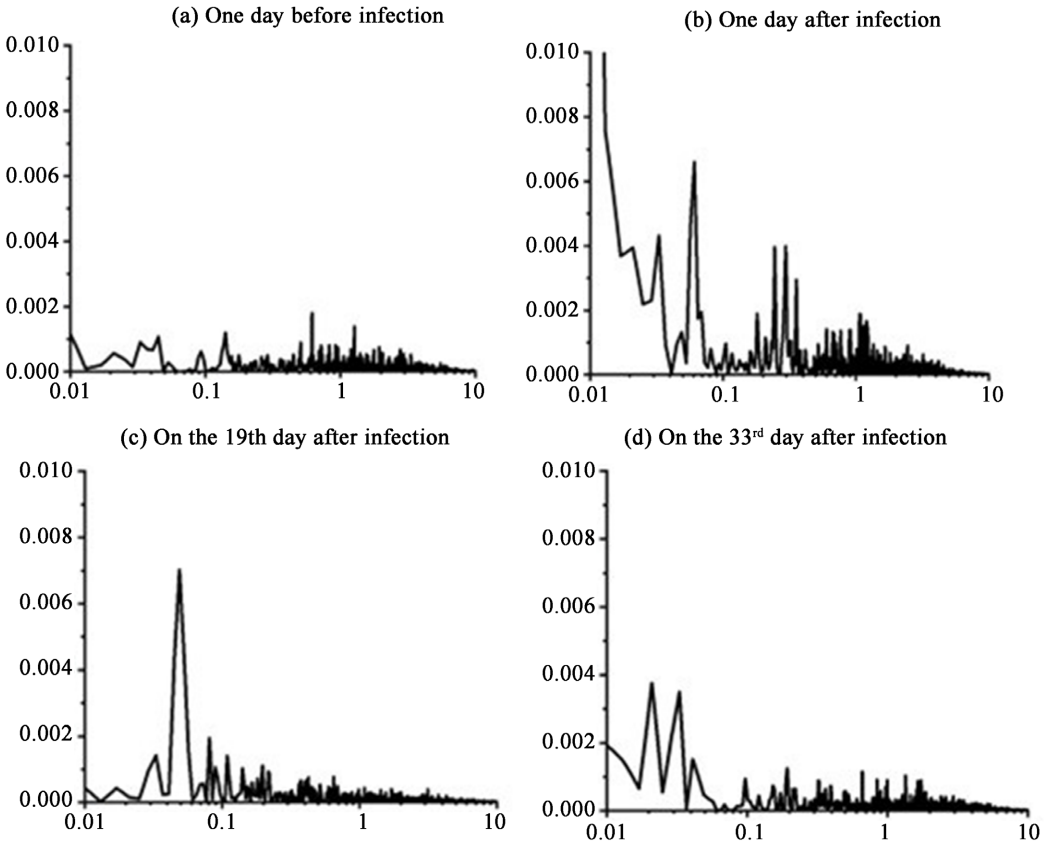

Figure 6. Spectral distributions of the BB-intervals of the white mouse "Bioscope" signals at different stages of the development of skin cancer with a lethal outcome. On the abscissa axis, the frequency of oscillations on a logarithmic scale in counts/min. On the axis of the ordinate, power of the spectrum in relative units.

At the same time, it was shown that already a day after infection with skin cancer, pronounced "cancer peaks" are formed in the spectral distribution of the BB intervals of the "Bioscope" signals, which persist until the death of mice. (Figure 6(b)). We also note that in mice that were also infected with skin cancer, but did not die, "cancer peaks" do not form.

And, finally, in the last series of studies, experiments were carried out with a 3-minute registration of bioscopic signals in the area of mammary glands of women.

One of the participants in the experiment complained of discomfort in the area of the right mammary gland. Mammography revealed nothing. However, "Bioscope" signals indicated a sharp difference in the states of the right and left mammary glands (Figure 7).

It is noteworthy that after 2 months, using conventional instrumental approaches, the onset of development of a neoplasm in the right mammary gland was confirmed.

We also note that in other women who did not have any breast complaints, bioscopic signals and their spectra were similar to those in the left breast area of the above study participant (Figure 7(b), Figure 7(d)).

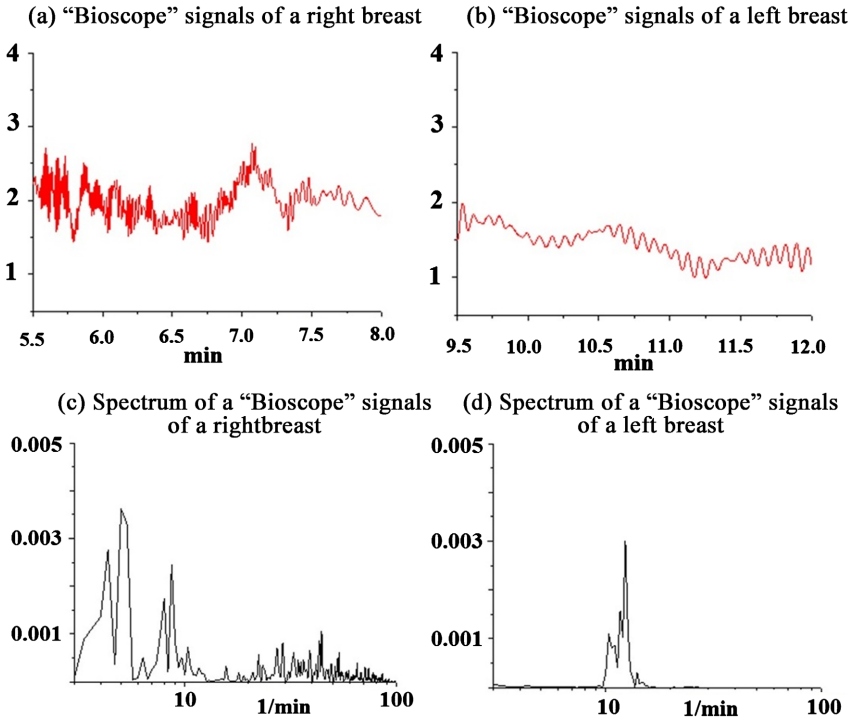

Figure 7. Early diagnosis of breast cancer. ((a), (b)) on the abscissa axis, registration time. On the axis of the ordinate, the amplitude of "Bioscope" signals in conventional units. ((c), (d)) on the abscissa axis, the frequency of oscillations on a logarithmic scale in counts/min. On the axis of the ordinate, power of the spectrum in relative units.

4. Discussion

In the presented article, the nature of the change in the signals of the instrumental

complex "Bioscope" in white mice was studied during the formation of skin cancer in them. After contracting skin cancer, mice usually died within 30 - 35 days. The task was to determine the possibility of early prediction of the death of mice according to the values of statistical indicators and the spectral distribution of the Bioscope signals recorded during the first 10 days after they were infected with skin cancer. This determined the need for a series of experiments to determine the values of indicators of statistical indicators of the state of control (intact) animals within 10 days.

The analysis showed that, both in surviving and dead mice, the values of almost all statistical indicators significantly differ from those for the intact group of animals. At the same time, the direction of change in the values of indicators for surviving and dead mice turns out to be diametrically opposite with respect to control indicators. Moreover, it turned out that in surviving mice in the first 10 days after infection, the coefficients of variation of all integrative parameters did not statistically differ from those for the intact group of animals. And despite the fact that in dead mice, the values of the coefficients of variation of many statistical indicators are 1.5 - 2 times higher than those for intact animals.

An analysis of the spectral distributions of the "Bioscope" signals for various groups of animals led to very interesting results. It turned out that in the low-frequency region of the spectrum there is a pronounced difference in the nature of the spectral distribution for intact mice, surviving and dead animals. This can be seen even more clearly in the spectral distribution of successive BB intervals of the "Bioscope" signals.

We also add that an individual analysis of the spectral distributions of the BB intervals for dead mice showed that pronounced peaks are formed in the spectral distribution of the BB intervals in the spectral distribution of the BB intervals, which persist until the death of the mice, as early as a day after skin cancer infection in dead mice. Importantly, mice that were also infected but did not die did not develop such peaks.

The results obtained demonstrate the high sensitivity of the "Bioscope" signals to the processes of skin cancer formation in white mice. Moreover, according to the values of statistical indicators and the nature of the spectral distribution of the "Bioscope" signals of cancer-infected mice, it is possible to predict whether the mouse under study will survive or die.

Of particular interest are the results of the latest series of experiments involving women. Of course, a single fact is presented, however, it indicates the possibility of early diagnosis of the onset of the formation of breast cancer in just 3 minutes of registration using the "Bioscope" hardware complex.

We also add that work is currently underway to modify the "Bioscope" complex, which will allow the registration of "Bioscope" signals to be carried out also independently at home. In the future, "Bioscope" signals recorded at home can be transmitted via a telemetric communication channel to the cancer center for processing and analysis, and, if necessary, patients can be invited there for a

more detailed examination.

5. Conclusion

The presented results clearly indicate the diagnostic significance of the indications of the "Bioscope" and create prerequisites for its use in the early assessment of pathological changes in the state of the body. By virtue of its design, the "Bioscope" is a passive device, there are no age restrictions on its use. Subsequent research in the future may lead to the development of new non-invasive approaches to control the state of the body.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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