Armenian Journal of Physics, 2022, vol. 15, issue 2-3, pp. 106-111

On Research of Possibility of Application of Acoustophysical Methods for Diagnosis of Malignant Formations in Living Organisms

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DOI: 10.54503/18291171-2022.15.2-3-106

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Abstract: A methodology for diagnosing malignant tumors, in particular C–180–like sarcoma, in biological objects (white mice) is offered, utilizing a new contactless diagnostic method developed on the basis of modulation acoustic spectroscopy by scanning studied biological objects with modulated acoustic waves of different frequencies. Comparative analysis of the amplitude–frequency characteristics of response signals from the scanned healthy and diseased biological objects makes it possible to determine the presence and level of prevalence of malignant tumors.

Keywords: modulated signal, modulated acoustic waves, malignant tumors, C–180 type sarcoma, tissue anisotropy.

1. Introduction

Medical diagnostics is a set of various complex researches and solutions allowing to come to the conclusion about the presence or probability of the presence of one or another disease in an organism. At present, research and discovery of new and improvement of existing methods of medical diagnostics are one of the most important fields of medical investigations and modern sciences and technology in general.

Particularly, diagnostics of oncological diseases at their early stages of evolution is one of the most important and urgent problems of contemporary medicine as it will lead to the revolutionary achievements in oncology with forehanded and successful determination and treatment of these diseases. However, the problem of late diagnosis of oncological diseases is still actual and decisive for the effective treatment, as the possibilities of forehanded detection and diagnosis of oncological diseases are directly connected with the existence of expensive high–precision unique equipment and corresponding effective methods for determining the presence of malignancies.

Currently, in oncology, various methods of diagnostics are used that in general are associated with certain effects on the body by ultrasonic waves (USW), radioisotopes, X–rays, etc. [1–6]. The most traditional diagnostic resources of oncological diseases [1–6] in general are based on various modifications of X–ray imaging techniques, which are not always safe and can lead to different side effects in organisms. As they are associated with the use of expensive and non–safe radiation therapy devices, they are also limited in their repeated use for dynamic monitoring for the purpose of early detection of diseases. In addition, not all areas of the body can be investigated and diagnosed by such means because of the impossibility of penetration of the corresponding radiations through certain types of biological tissues. Moreover, these diagnostic apparatuses mainly are rather cumbersome and have large deployment times, so their use in emergency situations sometimes is difficult and ineffective too.

The methods of ultrasonic and acoustic studies [1–9] make it possible to determine the presence of formations and the nature of the pathological processes with high accuracy and, in some cases, are superior in sensitivity to the X–ray methods, which is due to the biomechanical properties of body tissues that have different permeability for USWs. Thus, in connection with the foregoing, the development and application of more safe, mobile, and rapidly deployable systems, particularly, based on principally safer USW and acoustic waves for diagnosing oncological diseases at their early stages, become very important and urgent.

In this paper, the results of experimental studies of malignant tumors using a new acoustophysical diagnostic method, based on analyses of responses of studied living organisms to the exposure of amplitude–modulated acoustic waves (AMAW) generated by amplitude–modulated ultrasonic high–frequency signals (AMHFS) are presented.

The use of AMAWs for the diagnosis of oncologic diseases is based on the properties of their rectilinear propagation in organisms with different characteristics of penetration into the body and reflection from the boundaries of different densities both of the outer contours of biological tissues and of their internal structures, depending on biomechanical characteristics of fabrics: density, structures, elasticity, viscosity, and etc. At the same time, the change in the scattering cross–sections of AMAWs at the boundaries of cellular structures and absorption by tissues determines the likelihood of characteristic changes in the biomechanical properties of the medium.

The amplitude–frequency characteristics (AFC) of recorded response signals from the affected biological object provide certain information about the internal structure and state of the studied tissues. The distribution of AMAWs in the body is determined by the density, structure, elasticity, and viscosity of its tissues. Any tissue of the body prevents the spread of AMAW and the higher its density, the greater the reflection and the lower the absorption of AMAW.

All organisms are anisotropic objects with altered and changing structures. Depending on the degree of isotropy of tissues (or cells), various specific pathologies appear. The anisotropy prevails in healthy tissues, and reactions to the processes and characteristics of dissymmetrization clearly occur in them [5,6].

Dissymmetry is the property of biological systems to use and synthesize matter in one of two possible spatial configurations, manifested at the macroscopic and molecular levels. In living organisms, the most important elements of the structure, the cell–forming phospholipids, and proteins are completely dissymmetric and synthesized in only one form, while the less important ones and synthesized in an unequal number of left and right forms.

In the existence of pathology to some extent, the anisotropy and dissymmetry are disturbed in fabrics accordingly. Cancer cells, unlike normal cells, have amazing isotropic properties, so AMAWs interact with them differently than they do with healthy cells, and their responses to AMAWs differ from those of healthy tissues. If the frequency of the physical impact of modulating the EMWs ultrasonic frequency waves on biological objects and their tissues corresponds to their own frequency, then there is a phenomenon of resonance, which is understood as an increase in the response of a biological system, i.e., an increase in processes of life activity of biological systems. The results of these influences are responses of biological systems, which can be recorded and analyzed using the corresponding registration and examination units.

Thus, the task of diagnosing is to determine the dependence of the parameters of the reaction of organisms to the impact of AMAWs on the state of their biological tissues, which makes it possible to differentiate healthy and cancerous tissues by comparing the degree of their anisotropy. The analyses of AFCs of response signals of structures of body tissues allow getting certain information on the interior and the condition of the structure of fabrics. By registering and analyzing the changes in AMAW signals after their passage through the tissues or reflections from the corresponding surfaces, it is possible to judge the structural and functional state of the tissues and organs and conduct diagnose between cancer and benign formations, and draw a conclusion about the stage of development of the pathology of the organ under the investigation.

This problem is similar to the problem of acoustic wave propagation in multilayer isotropic media with a certain type of heterogeneous and geometric forms, which was successfully solved at the Institute of Applied Physics Problems of the National Academy of Sciences of the Republic of Armenia (IAPP NAS RA), which made it possible to develop a new method for noninvasive diagnosis of malignant formations in living organisms using some recording and analyzing techniques and Acoustophysical methods, a new direction of physics developed in the IAPP NAS RA [7,8,10–14].

2. Experimental setup

To carry out the experimental investigations a special experimental setup was developed [8], the schematic view of which is presented in Figure 1.

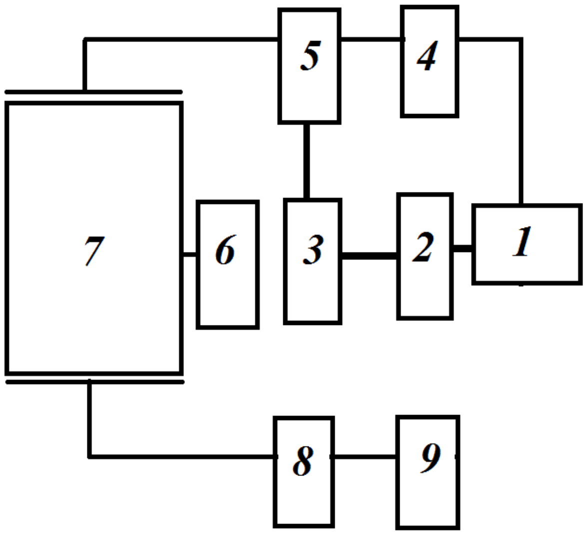

Fig. 1. Schematic view of the experimental setup. 1– Power supply, 2 – fine–tuneable low–frequency generator, 3 – linear low noise amplifier, 4 – fine–tuneable high–frequency generator, 5 – special tunable modulator, 6 – accelerating power supply, 7 – experimental chamber, 8 – response registration unit, 9 – PC

Special high precision tuneable generators of 0,01÷400 Hz (Fig. 1.2) and 0,01÷30*10^6 Hz (Fig. 1.4) frequency ranges, low noise linear amplifier (Fig. 1.3), and a unit (Fig. 1.5) modulating signals from generator (4) with tunable depth modulations of 0–80%, were developed. With the aim to register the responses of investigated biological objects and their anatomic parts a special high precision low noise registration unit with feedback was created too (Fig. 1.8).

The measurements were conducted in a specially designed experimental chamber (Fig. 1.7), which was provided with appropriate corresponding facilities for connection with electronic units, including the registration (8) and analyzing (9) units.

Laboratory white mice infected with C–180 type sarcoma, one of the most aggressive malignancies of biological objects, were used as biological test objects (TO). To carry out experimental investigations, healthy and infected TOs were placed in a specially fabricated shielded chamber (Fig. 1.7), on which amplitude–modulated acoustic waves were generated with the help of applied to its side walls AMHFSs from the modulator (Fig. 1.6) – high–frequency signals in a frequency range of 0,01÷30*10^6 Hz, amplitude modulated (with a tunable depth of modulations of 0–80%) by signals with a frequency range of 0.01–400 Hz.

During the experiments, TOs were scanned with the generated AMAWs along with the simultaneous registration and analyses of the AFCs of their response signals by changing the amplitudes and frequencies of modulating and modulated AMHFS signals.

3. The results of experimental investigations

In general, a series of experimental measurements on several groups of healthy and sick biological objects at various stages of disease were conducted, and the AFCs of response signals obtained during each subsequent experiment from the same group of infected biological objects differed from the AFCs obtained preliminary from healthy mice and mice with earlier stages of the infected disease.

After digitizing the registered response signals from the experimental chamber with the investigated TO, their AFCs were analyzed, which carry information about the biomechanical properties of the structures of formations at the molecular and intercellular levels of the investigated organism. The scanning of TOs was carried out in the frequency range of $0{,}01 \div 30*10^6$ Hz with 100 Hz increments of the carrier signal, and in cases of existence of visible pathological changes of studied TO – in 1 Hz increments, which made it possible to obtain more informative pictures of conditions of studied TO organisms. At the end of each experiment, the AFCs of the response signals from the diseased mice were compared with the previously obtained AFCs of the healthy TO too. In Fig. 2 an example of obtained AFCs of the response signal for the tested healthy biological object is presented.

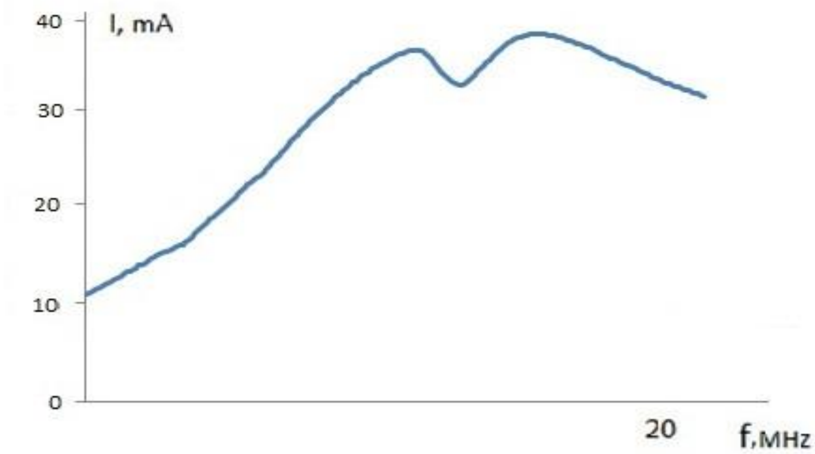

Fig. 2. The curve of the AFC of the response from a healthy white mice.

Comparative analysis of AFCs of response signals received from healthy and infected mice gave clear information about the stage of the disease. Based on the conducted experiments it was also determined that given the time factor, it is possible also to reveal the dynamics of the pathology of the disease. According to the deviations of the AFCs of the response signals from tested healthy and infected biological objects, conclusions were made about the presence and prevalence of malignant tumors. As an example in Fig 3 one of the obtained curves of differences in the AFCs of the responses of healthy and infected mice is presented.

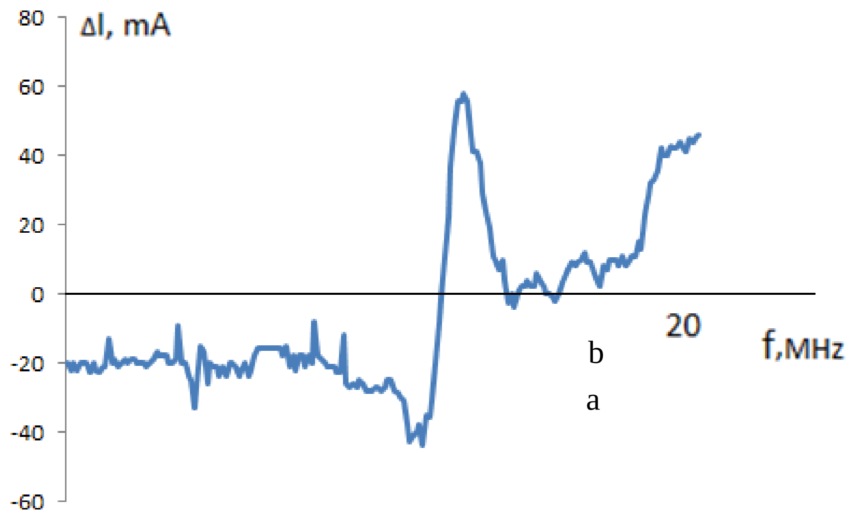

Fig. 3. An example of a curve of differences in the AFCs from responses of healthy and infected mice.

Detail comparisons, analyses, and evaluations of changes of these AFCs of response signals caused by the presence and absence of malignant formations in biological objects are accurately conducted. Depending on the stage of the disease the variations in AFCs become more valuable. At the last stage of the disease, sharp changes in AFCs were noted, marked as a characteristic energy burst on AFC curves.

4. Conclusion

The developed new acoustophysical methodology for detecting and diagnosing malignant tumors in living organisms has a number of advantages over known available methods [6,9], including, in particular, the following:

- allows to carry out not only reliable but also differential diagnostics of the tumor, destructive, dystrophic, etc. disorders in tissues by measuring the reflected or transmitted through the living organism signal and getting detailed information about its intracellular structure;
- allows to conduct multiple periodical safe non–invasive diagnoses of malignant neoplasms in living organisms;
- gives a possibility to increase the diagnosis accuracy by reducing and tuning the scanning steps, etc.

Utilization of the developed methodology gives the chance by means of exterior AMHFSs to carry out non–invasive safe diagnostics of pathological violations in tissues of living biological objects. Experimental investigation in this field will be continued further on various biological objects and by applying other malignant formations.

Declarations and Statements

Conflicts of interest

The authors declare no conflict of interest.

Author Contributions

- The author A.H. Mkrtchyan raised the idea, carried out theoretical analyses, set up the experiment, and participated in the writing of the article;
- The author V.V. Nalbandyan participated in the theoretical analyses, managed the experimental activities, and participated in the writing of the article;
- The author S.A. Mkhitaryan carried out the systematization and scientific formulations of the results of the experimental activities and participated in the writing of the article;
- The author V.E. Badoyan developed and provided technical facilities and units for experimental activities;
- The authors I.A. Babayan and A.H. Nalbandyan participated in the experimental activities and registered and systemized their results.

Declaration of Competing Interest

The authors have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this article.

Acknowledgment

The authors would like to thank the IAPP NAS RA for providing all facilities to make this work complete.

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