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COMPLEX SYSTEMS BIOPHYSICS

A Method to Record the Surface Temperature Distribution of the Skin as a Safe and Ergonomic Approach to Diagnosis and Monitoring in Breast Cancer

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Abstract—This article discusses the relevant results on early and safe detection of breast cancer with a thermal volume tomography (TVT) device produced in Russia. The device records and analyzes the spatial temperature distribution on the skin in the tumor region. The resulting dataset can be analyzed using artificial intelligence methods, which make it possible to efficiently choose the treatment strategy by selecting optimal treatments at the preclinical stage of breast cancer.

Keywords: breast cancer, thermal volume tomography device
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INTRODUCTION

Professor L.D. Lindenbraten, who was the founder of Russian mammography, and his colleagues [1] identified the prerequisites to a successful solution of the problem of breast cancer in 1997. Early diagnosis of breast cancer helps to save lives in the female population. It is necessary to develop organ-saving treatment procedures and to reduce the costs of diagnosis and therapy. It is necessary to introduce national and regional programs of mass examinations and to create federal and regional registries of persons who have been screened and found to have breast cancer [1]. However, these measures have still not been implemented in current medicine because early and safe diagnosis is not provided by the available X-ray methods (computed tomography, positron emission tomography combined with computed tomography, and X-ray mammography), ultrasound testing, and magnetic resonance imaging [2, 3].

These diagnostic tests usually detect the disease after its preclinical stage has already passed, and that stage accounts for approximately one-fourth of the total tumor development cycle from a single cell to a fatal outcome [4]. Breast cancer causes no pain and remains undetectable by the patient at the preclinical stage. Positron emission tomography detects preclinical breast cancer, but has two drawbacks. First, the test is unsafe because a radioactive agent is injected in the mammary gland, which has higher radiosensitivity. Second, diagnosis is rather expensive, and the necessary equipment is not commonly available.

Recent publications and patents describe new means for "early" detection of breast cancer on the basis of using arrays of thermal sensors incorporated in the elastic element (fabric or latex) of a bra [5–7]. To detect breast cancer, such a bra should be worn for several hours or even several days as a screening test. Extremely high inertia is an inevitable property of the thermal sensors used in the bra. Its temperature sensitivity is consequently decreased, and heat exchange in the mammary gland is distorted by the extra layer placed between the body and the environment, increasing sweating and introducing an error in the results. The factor that makes such devices absolutely unsuitable is that they disregard the recently established fact that the breast has an unsteady temperature landscape, which changes at a relatively high frequency [8]. Its fluctuations level the test results because the duration of thermal exposure is too great compared with the frequency of changes in the temperature landscape of the breast skin (white noise of temperature traces is produced).

The factors in successful breast cancer treatment are that the test for breast cancer is safe and rapidly detects the disease at its preclinical stage. A diagnostic

Abbreviations: TVT, thermal volume tomography.
† Deceased.

instrument should provide time for successful therapy and should allow timely monitoring during treatment; it is therefore necessary to provide a means to choose the optimal treatment strategy at the stage of screening or rehabilitation. The thermal volume tomography (TVT) device (Modern Computer Medical Equipment, Russia) meets all of these requirements.

THE PRINCIPLES OF OPERATION OF THE TVT DEVICE AND MODELS USED IN THE STUDY

The following principle underlies the theoretical basis and clinical application of TVT. The skin temperature is scanned over the breast with one thermal sensor, which is positioned in the portable autonomous head of the TVT device. The temperature is measured accurate to approximately 10^{-3}°C. Scanning is performed through regular openings in an elastic bra worn on the breasts. It takes 5–8 min to scan both of the breasts, depending on the breast size. The measurement data are transmitted from the head through a cable to a computer. After computer-assisted data processing, a color mammogram is displayed on the monitor screen in the form of a two-dimensional landscape of temperature field gradients on the breast skin. The image pattern is either normal or suggests a mass lesion. The landscape reflects how the internal heat flow is distorted if a tumor hinders its propagation. The tumor can be modeled as a small body placed in a half-space at a distance from its surface.

A solution to the problem of detecting a small body in a half-space of a solid medium with a constant heat flux propagating from inside to the surface and scattering from the surface into the atmosphere with a constant temperature via convection was first published in [9]. Its further development and clinical testing for warm-blooded organisms were described in [10–17].

Professor M. Gautherie (Pasteur Institute, France) conducted a clinical study of breast cancer in a large population (85 000) of patients. The parameters of breast cancer development were examined by inserting a thin needle (a thermal couple) in the tumor. The temperature was measured with the thermal couple and the coordinates of the inserted needle were controlled using X-rays [18]. The method has several drawbacks; it is unsafe [19, 20] and is not approved for use in patients younger than 40 years [21]. However, the large scale of Gautherie's study and the reliability of its results make it possible to utilize the results in the TVT method, which is safer, quicker, and more ergonomic than conventional methods. The Ministry of Health of the Russian Federation has approved the TVT method to examine the breasts in patients of any age. In particular, the method can be used at the preclinical stage of breast cancer, yielding neither false positive, nor false negative results [22].

The TVT method has several advantages over remote thermal imaging, as listed below.

(1) The equipment is far less expensive.

(2) The device does not require an external power supply, is portable, and allows a reference-based adjustment by absolute temperature during examination.

(3) The error of measuring a temperature gradient is 10^{-3}°C.

(4) Thermal imaging is unsuitable for visualizing the tumor; the characteristic tumor size cannot be measured when the tumor is more than a half-size away from the breast surface.

(5) With thermal imaging, the temperature estimate depends on the angle between the skin and the directrix line of the target body area.

(6) With thermal imaging, the temperature estimate additionally depends on the skin condition, the presence of hair, sweating, and the heat emissivity, which varies from 0.24 to 0.9.

The results of the TVT examination and subsequent digital data processing with a computer are comparable with a tomogram, but have a lower spatial resolution. The results are still suitable for use at the preclinical stage of breast cancer, making it possible to choose adequate therapy for a patient of any age and to have substantial time reserves.

EXAMINATION RESULTS AND THEIR INTERPRETATION

As has been demonstrated, the doubling time Δt_u remains unchanged in the course of breast cancer and varies among individual patients from several weeks to 400 days [23, 24]. A malignant tumor grows exponentially, starting from one cancer cell, which is approximately 10 μm in diameter. The growth is therefore described by the following equation:

$$V_t = V_0 2^{t/\Delta t_u}, \quad (1)$$

where V_t is the final tumor volume, V_0 is the initial tumor volume, t is the time, and $t/\Delta t_u$ is the number of cell divisions. An increase in tumor volume depends on the time t and the doubling time Δt_u. Because the latter is specific to an individual, tumor growth curves are shown for two doubling time values (Fig. 1, curves *A* and *B*).

Based on Eq. (1), the tumor volume as a function of t can be determined as

$$V_t = \frac{\pi D_s^3}{6} = \frac{\pi D_0^3}{6}\exp(kt), \quad (2)$$

where D_0 is the initial diameter and $k = (\Delta t_u)^{-1}$. Let D_s' be the lethal diameter and $\Sigma\Delta t$ be the time to the lethal diameter. It follows from Eq. (2) that

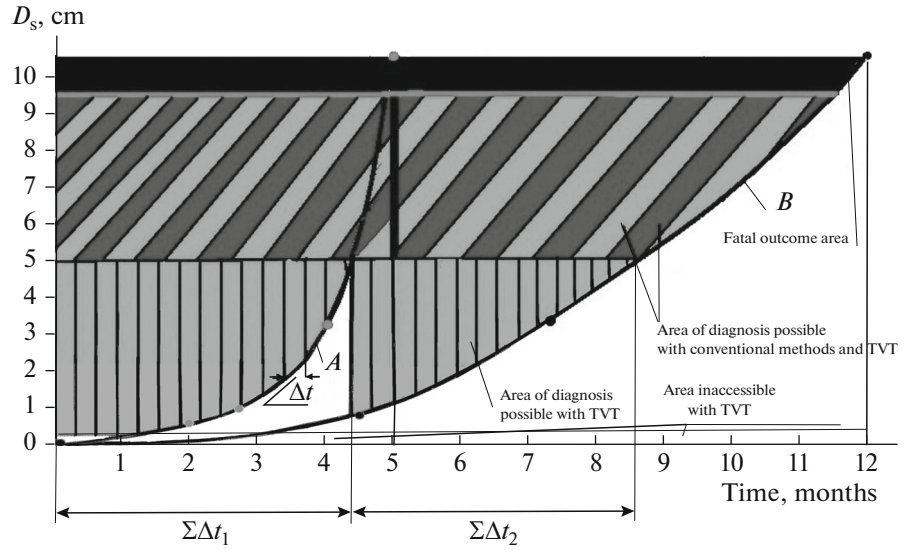

Fig. 1. Malignant tumor growth over time as a function of the doubling time. The doubling time for curve $A \leq$ that for curve B. D_s is the tumor diameter.

$$k = 3\ln\left(\frac{D_s'}{D_0}\right)\Big/\left(\sum \Delta t\right). \quad (3)$$

With the known cancer cell diameter (10 μm) and $D_s' = 10$ cm, we have for the two k values (Fig. 1) that $k_A = 0.27$ days^{-1} and $k_B = 0.11$ days^{-1}. The two estimates characterize rapid aggressive tumor growth, which is observed in 20% of breast cancer cases, while the development of a 1-cm tumor takes 5–7 years in the case of a moderate tumor growth rate [2].

The main concept shown in Fig. 1 is that the TVT method can be used to advantage in diagnosing breast cancer at the preclinical stage, which corresponds to the D_s range from 0.3 to 0.5 cm in Fig. 1, because the method is safe, allows repetitive screening at any reasonable frequency [25], and avoids the masking effect of the nonstationary character of the temperature gradient field [8]. A feature of the method is that the heat exchange characteristics are detectable at the preclinical stage, when metastasis is absent and the tumor retains its coordinates. As the tumor grows, the test shows degradation of the heat flux maximum in terms of the intensity of the positive temperature gradient, as is shown in Fig. 2. Because the tumor increases in size without changes in the coordinate Z, the positive temperature gradient decreases with the thermal conductivity of tumor tissue decreasing from the normal value 0.532 to 0.451 W/(m degree), by 15% [25].

Figure 2 shows the stages of tumor development from its minimal size on detection at the preclinical stage.

$$Z = \sqrt{2T^2/T^2 - T_0^2}, \quad (4)$$

where Z is the depth at which the center of a hot tumor occurs, T_0 is the temperature gradient in the pole of the respective isotherm, and T is the actual temperature in the respective pole as obtained from pole coordinates on the breast skin [10].

The changes in gradient projection on the breast skin can be explained by a lower heat flux from the bottom wall of the tumor and a simultaneous shielding of the normal heat flux by the tumor growing in cross-sectional area. When the upper margin of the tumor

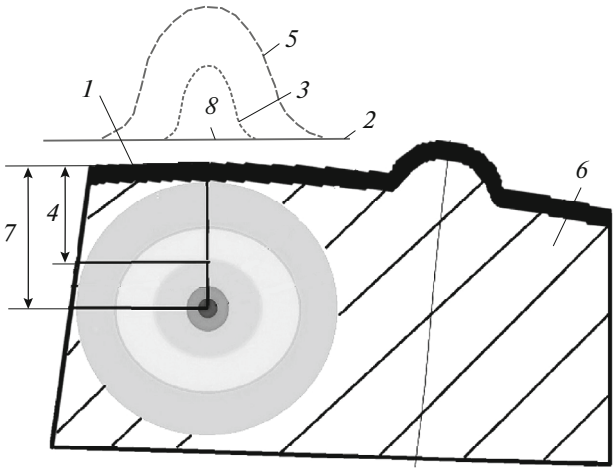

Fig. 2. Measurement of the gradient maximum at the pole with tumor growth: (*1*) mammary gland; (*2*) normal shape of the gradient; (*3*) a gradient at the upper margin of the growing tumor; (*4*) an intermediate tumor size; (*5*) the gradient maximum at tumor detection; (*6*) normal mammary gland tissue; (*7*) the depth at which the minimal tumor occurs; (*8*) a negative gradient detected after the tumor has reached the skin.

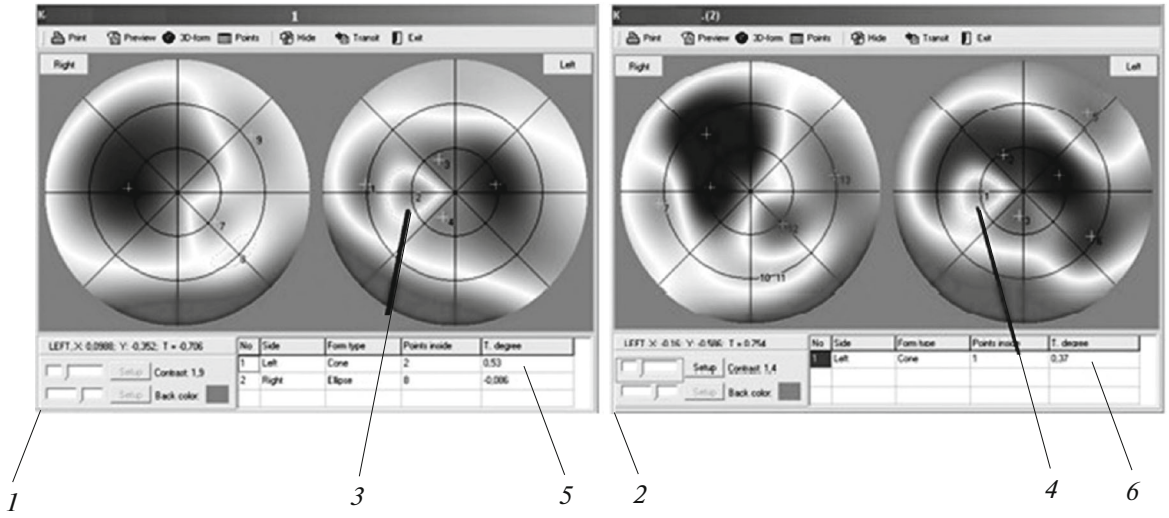

Fig. 3. Two TVT mammograms recorded consecutively with a 1-month interval. The images show tumor degradation at the preclinical stage.

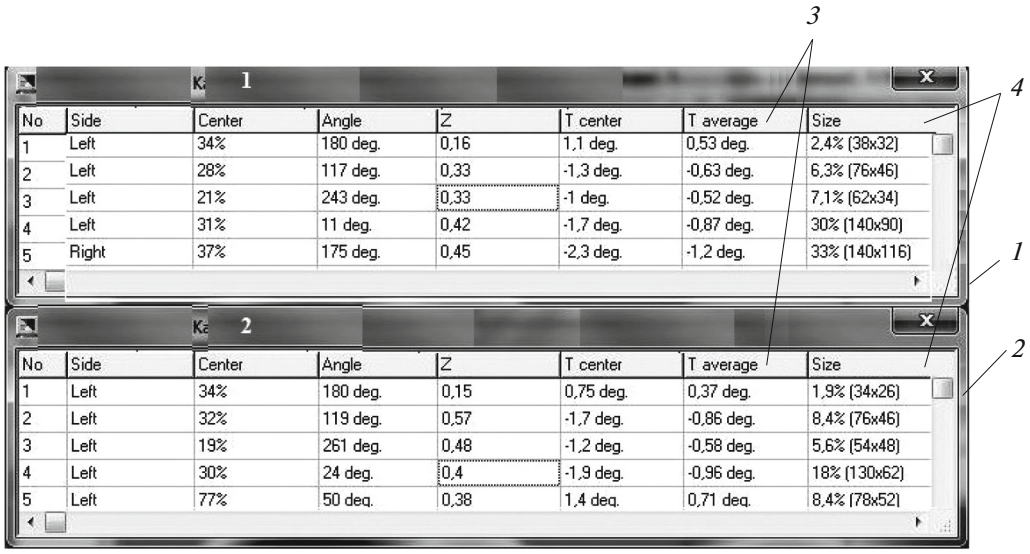

Fig. 4. The tables that are accessible via the upper menu of the TVT mammogram (Fig. 3) show data on (*1*) temperature gradients and (*2*) their projection areas on the breast skin.

comes into contact with the breast skin, the normal heat flux disappears in the contact site, with a zero temperature gradient occurring in the pole. As the tumor grows further, its upper margin is flattened as a result of skin elasticity, normal tissue is displaced to the periphery, and a negative gradient thus forms in the same isotherm pole because the bottom wall of the tumor is displaced, as shown in Fig. 2. The change is illustrated well by two TVT mammograms obtained for patient L. (56 years of age) consecutively with a 1-month interval (Fig. 3). The bottom menu of a mammogram shows the average temperature of the pathological lesion, its shape, and the breast where the lesion occurs. The top menu shows a table (Fig. 4) with the results of processing the temperature datasets transmitted from the head of the TVT device. The table provides numerical data on all pathological sites and, in particular, the area of the gradient projection onto the breast skin.

As is seen from Figs. 3 and 4, the data on the gradients and projection regions (Fig. 2, *4* and *3*; 0.537 and 0.37°C and 6.5 and 1.9%, respectively) are well correlated and agree with the theory of breast cancer development [26].

The TVT procedure of breast cancer diagnosis is less time consuming and far less expensive than, for

example, the standard procedure accepted in the United States [27].

CONCLUSIONS

The TVT method has several advantages over the conventional methods used in medicine.

The TVT method provides unambiguous analysis of tumor growth at the preclinical stage of tumor development.

The doubling time can be estimated using TVT during a prolonged preclinical period; i.e., the possible duration of the disease cycle can be determined by the safe screening test.

Using the screening test, it is possible to select adequate therapy at the preclinical stage as a result of its extended duration and to monitor tumor degradation. Therapy at this stage is less expensive than at more advanced stages that are possible to diagnose with conventional methods.

The TVT device is portable, absolutely safe, and relatively inexpensive and does not require highly qualified staff to operate, thus providing a useful tool to a doctor.

With the TVT test, artificial intelligence methods can be used to automatically analyze the resulting digital datasets.

The diagnostic procedure is fast, making it possible to employ the TVT method in preventing breast cancer.

COMPLIANCE WITH ETHICAL STANDARDS

Conflict of interest. The authors declare that they have no conflict of interest.

Statement of compliance with standards of research involving humans as subjects. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants involved in the study.

REFERENCES

1. L. D. Lindenbraten, L. M. Burdina, and E. G. Pinkhosevich, Mammography: An Aducational Atlas (VIDAR, Moscow, 1997) [in Russian].
2. L. M. Klyukin, in Development of Science in the 21st Century: Proc. 20th Int. Correspindence Conf. (NITs Znanie, Kharkov, 2016), Vol. 3, pp. 21–32 [in Russian].
3. A. M. Maffione, M. Piva C. S. Stamata, et al., Arch. Gynecol. Obstetric **280** (4), 521 (2009).
4. R. Shah, K. Rosso, and S. D. Natanson, World J. Clinic Oncolol. **5** (3), 283 (2014).
5. L. M. Klyukin and C. Yu. Morozov, RF Patent No. 2 537 762 (January 15, 2013).
6. G. R. Cantu, https://tehnoobzor.com/hi-tech-news/1194-podrostok-izobrel-byustgalter-diagnostiruyuschiy-rak.html
7. https://www.google.ru/search?q=itbra&newwindow=1&rlz=1C1AOHY_ruRU724RU731&tbm=isch&tbo=u&source=univ&sa=X&ved=0ahUKEwj9iJGOqYLaAhWkF5oKHR6sDUoQsAQIOA&biw=1280& bih=911
8. L. M. Klukin and V. A. Namiot, Biophysics **60** (1), 138 (2015).
9. L. M. Klukin and V. A. Namiot, Pis'ma Zh. Eksp. Teor. Fiz. **6** (10), 615 (1980).
10. L. M. Klukin and V. A. Namiot, Nauka Tech. Rossii, Nos. 2–3, 10 (2001).
11. L. M. Klukin and V. A. Namiot, Mezhdunar. Med. Zh., No. 2, 170 (2001).
12. L. M. Klukin, US Patent 7 214 194 B2, May 8, 2007.
13. L. M. Klukin and V. A. Namiot, Phys. Lett. A **288**, 115 (2001).
14. L. M. Klukin, RF Patent No. 2 622 362 (June 14, 2017).
15. L. M. Klukin and V. A. Namiot, Biophysics **46** (3), 500 (2001).
16. L. M. Klukin and V. P. Igumniv, Radiol. Prakt., No. 3, 56 (2003).
17. L. M. Klukin, Nauka Tech. Rossii, Nos. 2–3, 24 (2005).
18. M. Gautherie, Biomed. Thermol. **107**, 21 (1982).
19. Abstract Book of the 95th Scientific Assembly and Annual Meeting of Radiological Society of North America (2009), vol. 30.
20. S. K. Ternovoy and A. B. Abduraimov, Radiation Mammology (GEOTAR-Media, 2007) [in Russian].
21. Near-Patient Screening Testing and Monitoring of Breast Malignant Neoplasms by a Safe Method of Contact Thermography, RF Ministry of Public Health License No. 2010/258, July 1, 2010.
22. V. P. Collins, R. K. Loeffler, and H. Tiivey, Am. J. Roentgenol. Radium Ther. Nucl. Med. **76** (5), 988 (1956).
23. N. E. Davidson, Cancer **97** (3), 825 (2003).
24. J.-V. D. Valde, G. De Bock, M. Greuter, et al., In Abstract Book of the 95th Scientific Assembly and Annual Meeting of Radiological Society of North America (2009), vol. 30, RO 22-24.
25. L. Rosenfeld, Fundamentals of Clinical Remote Thermodiagnostics (Zdotov'e, Kiev, 1988) [in Russian].
26. Ya. Tyuryumina and A. A. Neznanov, in Information Technology and Systems: Abstr. 39th Interdisciplinary Conf. (Springer, 2015), pp. 38–51 [in Russian].
27. J. C. Keen, National Comprehensive Cancer Network **4** (5), 480 (2006).

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