THERMOGRAPHIC VISUALIZATION OF THE ORGANISM IN ONCOLOGICAL DISEASE

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Authors: E. Gedevanishvili, A. Kapanadze, A. Sepper, A. Piana,
Published by The Professional Academy of Clinical Thermology
EMAIL: info@medicalthermology.org
Editors: Meagan Vecino, Ann Barker
Translated from Russian

The progression of modern medicine is dependent on the complete development of diagnostic and medical equipment and the emergence of new medical technologies. Development of new technologies for medicine requires complete understanding of the capabilities and efficiency of the use of modern equipment in treatment of patients. Medical engineering plays a crucial role, as does staying current with emerging knowledge and technologies.

The modern scientific paradigm is based on the belief that the properties of the whole can be explained on the basis of the properties of its components. All attempts at understanding living systems have begun with the study of individual organs and systems. This is known as the *reduction approach.* Tremendous progress has been reached in biochemistry and molecular biology with this type of study. However, experimental results based on this reduction approach can only describe certain aspects of the structure and function of living systems. Thus, complete biological activity cannot be fully understood by reductionist positions. This theory leads to a wholistic approach.

Alexander Sepper, MD, PhD

This book is written in loving memory of Academician Revaz Vepkhvadze.

Preface

THE PRESENTED MATERIAL is the result of the authors' combined years of experience in the field of clinical thermal imaging and gives information about this method of clinical study within the availability of e-books format.

Like many methods of clinical diagnosis, thermography underwent radical scrutiny from the accumulation of facts, arguments, debates, discussions, indiscriminate denial by some and full admiration by others, before its final recognition as an independent method of diagnosis.

The current state of clinical medicine does not include a single and ideal method of diagnostics capable of producing a comprehensive picture of the patient's condition and the pathological process. Even the notable MRI and CT-Scan have their limitations and provide information only within their capabilities. The same applies to thermography.

Thermography is primarily a method of functional diagnostics, providing accurate data of the strength of tissue metabolism and of the circulatory status of the organism by studying the thermal structure of the skin and measuring local temperature fluctuations. Detailed thermal patterns of various conditions of organs and systems of the human body have been charted. Thermography holds a unique place in the complex diagnosis of breast pathologies, where it has established itself as a specific screening test for neoplastic conditions. This is especially true in light of new evidence casting doubt on the unlimited possibilities of mammography as a screening test.

With regard to diagnostic pathology of the skin and soft tissues, vascular disorders of the extremities, inflammatory and neoplastic lesions of the thyroid gland, inflammation of the sinuses, and the functional diagnosis of pain, thermography provides an invaluable service

by providing unique information not only as an initial diagnostic test, but also in the process of evaluating the effectiveness of the treatment.

While this sounds somewhat paradoxical, discovered first in the U.S. and Canada, thermography is now much more widely applied in Europe, South America, and Russia than in the North America. This is obviously due to the fact that over the past three decades, there has been a sharp leap forward in the quality and efficiency of beam diagnostics (MRI and CT-Scan), resulting in their eclipsing of all other methods. However, time and practice yield to place and order. Recent trends have lent to a resurgence of interest in medical thermography as a noninvasive method of functional diagnostics.

One of the authors of this book, Anthony Piana, the head of the Professional Academy of Clinical Thermology, is to be credited with promoting thermography among healthcare professionals and patients through the delivery of objective information about its possibilities and its application in various areas of medical practice. He has, amongst other things, fostered extensive theoretical and practical links with specialists worldwide, and offers continuous improvement of thermal imaging equipment and assessment criteria of thermal information using modern computational technologies, while involving professionals with varying skills in a multidisciplinary setting.

Thermography has matured over time and proven its efficacy in solving difficult diagnostic tasks within the framework of the possibilities that allow for recording and interpreting the spontaneous infrared radiation from the surface of the skin. The method is simple, non-invasive, harmless, informative and economical.

In connection with all of the above, we recall the words of one of the pioneers of medical thermography, Dr. Gershon-Cohen, who wrote: "Horizons of thermography are too broad to be predicted."

Chapter 1

Prediction of the tumor's radio sensitivity as evidenced by thermogenesis during its growth and radiation exposure

THERMOGENESIS IN A living organism is a critical area of clinical radiobiology. The prediction and assessment of radio sensitivity, as well as the effectiveness of radiation therapy of tumors, hinge on thermogenesis and are important to the diagnosis and treatment of biological irregularities such as cancer.

A comprehensive understanding of heat and thermal conductivity mechanisms and the interrelation of thermogenic patterns during the growth of the tumor and response to radiation exposure, serve to justify the importance of thermography in the diagnosis and prognosis of tumor radiosensitivity.

One of the most important tasks of current clinical radiobiology is the study of the vascularization of the tumor and its changes under the influence of radiation, as well as the role of vascularization as it applies to the radiosensitivity of tumors and the effectiveness of radiation therapy. There is an urgent need to develop methods for assessing the degree of vascularization of malignant neoplasms. One such approach includes the study of heat production of new tumors which highlights the urgent necessity of thermography in the clinical practice of radiation therapy.

Experimental data of several authors (Stolwijk V. 1975. Haudas Y. Guien J.D. 1973; Fowler J.F. 1984) shows that the controlled variable system in thermoregulation of a living organism is equal to the intensity of the magnitude of heat flux through the body surface and is proportional to the average body temperature. According to this hypothesis, the average temperature of a healthy body can be determined by the

intensity of heat flux through the skin. The application of this hypothesis to pathological conditions of the organism and its response to radiation exposure require further experimental development. A simplified thermal model of tumors (Girardey A., 1975; Osman M. et al., 1978; Cauterie M., 1984) allows one to approach the problem with the understanding of heat and thermal conductivity of the tumor. It is important to note that these models include many simplified proposals and do not provide significant consideration of tumor vascularization and heat transfer through large vessels and capillaries. Therefore, it is necessary to develop a model based on the thermographic and microangiographic tumor research[1].

1. THERMOGRAPHIC AND microangiographic studies on transplantable sarcoma 45 (S-45) in subcutaneous and intramuscular implantation of tumor cells showed the appearance of "hot" and "cold" foci in the zone of tumor development. In subcutaneous implantation of sarcoma, 45 "hot" foci were observed in the first week only, then the focal temperature was decreased and a tumor zone acquired the properties of a "cold" focus. In intramuscular tumor implantation, the symptom of a "hot" focus was noted over a period of three weeks. Angiography showed the state of the vascular network of a tumor, revealing rearrangement of microcirculation in external and central tumor zones that correlated to the site of tumor inoculation. Tumors of the subcutaneous fat were characterized by rapid avascularization with the formation of a "cold" focus symptom. A high degree of tumor vascularization corresponded to "hot" zones, while hypovascular tumors corresponded to "cold" zones. "Hot" zones could develop at the expense of arteriovenous anastomoses discharging hot arterial blood into the venous tumor bed, bypassing the capillaries. Direct correlation was established between the state of blood circulation and a thermographic picture.

THE ANALYSIS OF EXPERIMENTAL and clinical studies (G.G.Raigorodskii with 1979 Kamardina L.I. with. 1986; Mazurina V.Y.1984; Frens J., 1974; Cenak N., 1973; Lamarque J., 1972; Nagasawa A. et al., 1981 et al.) dedicated to the biomedical basics of thermology indicates that during tumor thermogenesis, changes occur that affect the thermal conductivity of the tissue, the actual tumor, as well as

the surrounding healthy tissue. The main reason for the rise in temperature is inherent in the varying histogenesis during tumor growth and radiation treatment.

In this case, it is critical to identify the role of the vascular component in the manifestation of thermal tumor symptoms with relation to radiation therapy. The current goal is to identify consistent quantitative patterns and temperature changes in normal vascular tissue in order to predict the original tumor radio sensitivity and to evaluate the effectiveness of radiotherapy.

The goals are as follows:

1. To identify patterns of temperature and quantitative vascular changes in both normal and tumor tissue during its growth and radiation exposure.

2. To create a mathematical model to predict the original radio sensitivity of transplanted tumor Sarcoma-45 growth and the thermal state of the tumor pattern during its development. This heating system of the “tumor-organism" will indicate radiotherapy effectiveness.

3. To explore the use of using thermography dynamic indicators to assess the effectiveness of radiation treatment of tumors.

With the help of functional research methods, new data was obtained and some previously unknown regularities were explained, including the temperature change characteristics of a tumor and of normal tissues during growth and radiation exposure. For the first time, quantitative and vascular parameters of both normal and tumor tissue are set during the radiation exposure, allowing the experiment to reveal a thermographically "hot" tumor, explaining the rising temperature of the tumor and of the normal tissue surrounding it.

This described mathematical model of the thermal state based on S-45 tumor’s thermoangiographic data with growth, evaluation, and response to radiation allows prediction of radio sensitivity and outcome of radiation therapy and can be seen in the first phase of the mathematical model of the tumor’s thermal state.

Normal tumor tissue under radiation alternates between hypothermia and hyperthermia in a symmetrically healthy limb and in the rectum.

A summary of the studies allows for the formulation of new concepts regarding thermogenesis of both normal and tumor tissues under radiation, and predicts tumor sensitivity, which creates a comprehensive approach to addressing important issues such as optimizing tumor radiation therapy.

With this in mind, let's consider the following points:

1. The tumor and the surrounding tissue's blood supply during the tumor's growth and the impact of radiation in determining the temperature of the tumor.

2. There exists thermographically "hot" tumors identical in morphological structure to thermographically "cold" tumors.

3. The thermal model of the tumor reflects the relationship of cardiovascular parameters and temperature during both growth and radiation, which allows for predicting the tumor's radio sensitivity and the effectiveness of radiation therapy.

The thermal vascular transplantable tumor model S-45 confirms the effect of the temperature adjustment with regard to tumor development in the locus and surrounding tissue. This model demonstrates the relationship between temperature and blood circulation right up to the capillary bed.

Thermography has proven prognostic value in radiation therapy based on angiography, tumor data and microangiography of surrounding normal tissues. The proposed method of thermography can be used as a dynamic control method in radiotherapy and as an objective test reflecting the tumor's response to radiation exposure and further predicts treatment efficacy. Clinical observations, for example in patients with breast cancer undergoing radiation therapy, confirmed thermographic data's ability to anticipate growth of the tumor and potential relapse through radiosensitivity.

The possibility of using additional quantified criteria to evaluate the effectiveness of radiation therapy, such as temperature gradients of normal and tumor tissue, and hypothermal thermogram area estimates are shown.

This research is based on 514 nonlinear male rats, weighing 120-140 grams, of which 484 were inoculated with Sarcoma-45 into the right limb using standard subcutaneous and intramuscular methods. Subsequent research was conducted on the 1st, 2nd, 3rd, 4th, 7th, 12th, 14th, and 21st days after inoculation of a tumor.

Radiation was carried out once locally to the bottom right limbs using RUM-17 unit, voltage 220 kV, amperage 15 ma, dose rate 95r/min, filter: 0.5 mm Si+ 1.0 mm A 1 doses of 15 and 30 Gr.

Thermographic, radiographic, angiographic and microangiographic studies of the rats were conducted before radiation and on the 1st, 4th, 7th, 14th, and 21st days after radiation. In all cases, the radiation of rats with tumor S-45 was performed when tumors had reached 4 square centimeters in size. The experimental model of Sarcoma-45 (the most studied in terms of its vascularization, microvascularization) is considered a scientifically evidence-based model for studying a tumor's temperature status, specifically in terms of thermoregulation of the whole organism.

The main research diagnostic methods used were thermography, angiography and microangiography. Although thermography was the most developed research method, thermoangiographic direct parallels have not been conducted to date, which would reveal the relationship between the temperature state of the tumor's center and the complex blood circulation mechanism.

#	Series Number	Animal Quantity
	Study of temperature and vascular indicators of normal tissue.	
1	Study of temperature indicators and blood supply Supply network during tumor's growing process	30
2	Thermographic and vascular patterns of normal and irradiated tissue under single radiation of 15 and 30 Gr.	264
3	Temperature and vascular tumor indicators Observation under single radiation of 15 and 30 Gr.	180
4	Temperature and volume indicators under fractionated irradiation of S-45 (15x2) Gr	40
	Total	514

THERMOGRAPHY WAS PERFORMED on the Barnes model M-1 with the registration of the object of research on the 52 Polaroid type, as well as magnetic tape. It was subsequently decoded by methods developed by the Ministry of Health of the Georgian Republic (1977).

The thermographic studies consisted of two phases. The first was the Qualitative Analysis, which involved the visual analysis of thermal images. The second phase was the

Quantitative Assessment of temperature levels in the assessment of the difference in temperatures between the symmetrical portions of the body. This included the posterior muscles in the affected limb, the medium temperature of symmetrically healthy limbs, the average temperature for various periods of tumor growth and thermography study after radiation exposure.

A quantitative assessment of the hypothermic zone of the pathological nidus was conducted using thermograms with the aid of decoder UAR-I in partnership with professor and co-author I.S. Amosov (1987).

A micro angiographic study of normal and tumor tissue was performed according to the guidelines developed by NIIMR at the USSR Academy of Medical Sciences (1984).

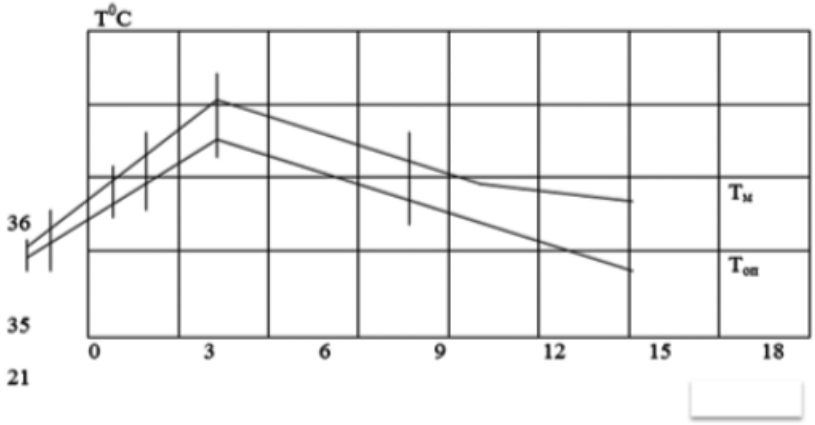
In addition to the above-described studies of the tumor growth process, an understanding of the tumor's morphology has been helpful in improving thermographic evaluation. The developed methods of qualitative thermography and micro angiogram analysis allow for objectively evaluating the changes in temperature and vascular parameters to determine their correlation to the tumor's size growth and reduction under radiation therapy; a method that promotes the establishment of thermography as a radiosensitivity prediction method and helps to evaluate the effectiveness of tumor radiotherapy.

The description of mathematical models and analysis of the data obtained used regression analysis and standard programs of the data processing machine EU-1020. The obtained data were subjected to statistical processing by student's test. In order to determine the main cause of skin temperature increase on top of the tumor and the plausibility of using thermography to evaluate tumor S-45 growth prediction, experiments were carried out on 234 rats inoculated with tumors both hypodermically and intramuscularly. Studied temperature and angiographic parameters of normal and tumor tissues in tumor growth are reviewed in Chapter 3.

According to our study, the temperature dependence correlates with vascular factors linked to the stint's localization with regard to the inoculation graft. Thus, experimental tumor S-45 thermographically appears as "cold" (with subcutaneous inoculation. Figure. 1) and "hot" (with intramuscular transplantation. Figure 2). This can be explained in that the temperature characteristics of the tumor depend on various degrees of hyper-vascularization of the tissue surrounding the tumor and of tissue vascularization of the tumor itself, resulting in a rise in skin temperature. Thus, the first experiment produced not only a thermographic "hot "tumor, but also an explanation for its occurrence.

In the subcutaneous tumor localization scenario, local temperature increases were observed during the tumor's initial period of node formation (1-7 day. Figure 1). This effect, as demonstrated in the microangiographic study, is due to blastomogenic restructuring of regional circulation around the emerging tumor nidus.

Figure 1 Thermal gradients of normal and tumor tissue during growth subcutaneously inoculated Sarcoma - 45 TM - Temperature of the symmetrical limb muscles. TOP - the temperature of the tumor.



The essence of this adjustment is primarily due to the opening of arteriovenous anastomoses and the abundant inflow of hot arterial blood through the afferent vessels (I.S. Amosov 1982). In the transition zone, a growing tumor's arteriovenous outflow of arterial blood to bypass the capillary bed is indicated. This supposed calorifier outflow, we believe, is due mainly to the hot aggressive inflow of arterial blood from the internal bodies, as well as restructuring of the metabolic processes in the vaccination zone of the tumor tissue. A gradual decrease in temperature occurs in subsequent phases of tumor lesion progression. It is shown microangiographically, that this effect is related to avascularization of the tumor nidus and also necrotic processes in development of the tumor itself and its surrounding tissues.

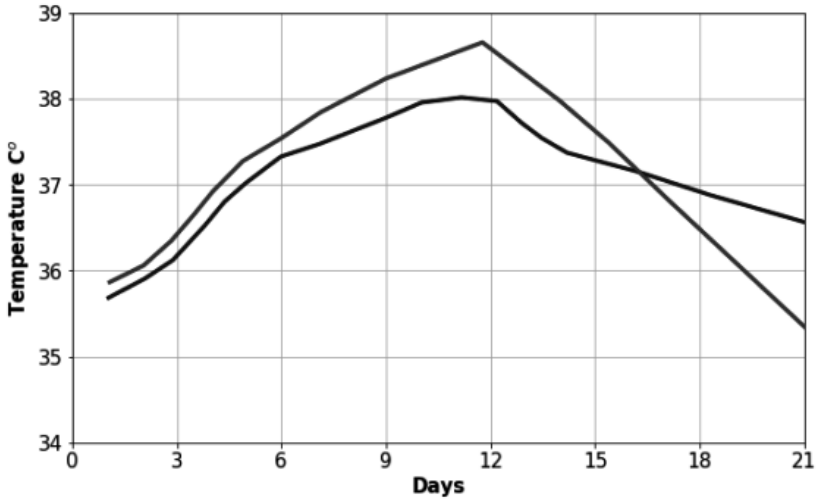


FIGURE 2: TEMPERATURE gradients of normal and tumor tissue during growth intramuscularly vaccinated tumor Sarcoma - 45 TM - muscle temperature of symmetric limbs. Top - the temperature of the tumor.

WHEN INTRAMUSCULAR grafting occurs (Figure 2) vascular and temperature correlation occurs on a different plane. The main distinguishing feature is that the images reflect the "hot" hearth of thermography for a longer period (up to 2 weeks) and are expressed to a greater extent than after subcutaneous tumor formation. The study of microangiograms leads to the conclusion that this high thermographic effect is in direct correlation with organ-specific blood circulation of the muscle, capable of abruptly changing contractile muscle activity. Tumor cells injected into the muscle tissue, as well as the subcutaneous tissue, and subsequent development of tumor tissue act to regulate the function of arteriovenous anastomoses to open anastomosis and to cause dramatically increased blood circulation and metabolism in muscle tissue. The avascularization process of the tumor, in contrast to subcutaneous localization, slows the second week after the inoculum introduction. At the same time, in conjunction with a reduction in blood circulation intensity, development of necrosis and sclerotic changes in the tumor yield a decrease in tumor temperature forming a "cold" nidus in the thermal image. This data is confirmed by both morphoradiographical and morphothermographical parallels.

In thermographic "hot" tumors, the temperature is 1.5 to 2.0 C higher in comparison with normal tissues (2 hours after tumor inoculation), manifesting in a high degree of vascularization (Figure 3). In thermographic "cold" tumors, tumor temperature as compared with normal tissue is 1.0 to 2.0 C lower (in 7 days after injection of the inoculum) and is accompanied by a decrease of quantitative and qualitative vascularization (Figure 4). The growth of experimental tumors is accompanied by a decrease of temperature gradients in the tumor's nidus on an exponential curve, which reflects the gradual process of tumor avascularization and necrotic nidus formation. Our data is supported by a number of authors (Nilsson R .1980; Taber D.J fn fl. 1966; Draper J.W., Jones C.M., 1969; Gautherie et al., 1976).

Conclusion

We found that the temperature decrease in both the symmetrical limbs and in the rectal area is the result of the reflex organism's reaction. It should be noted that the temperature status of the tumor is in direct proportion to the functioning of the blood circulatory network and tumor adjoined tissue, which is confirmed by quantitative analysis of thermal images, angiograms and microangiograms. Analysis of the results obtained allow us to interpret the nature of the existing clinical thermographic "cold" and "hot" tumors of the same histological structure. In primary and secondary developmental periods, an intramuscular tumor's thermogenesis is observed as a "hot" nidus image on the thermogram, and in the later stages as a "cold" one. Subcutaneous tumors (thermographically "cold") are characterized by low temperature relative to the symmetrical area during all development stages. The marked difference in biological thermographically "hot" and "cold" tumors increase the diagnostic value of the thermography method in the earlier periods of malignancy development and clarifies the treatment of false negative thermographic results in the later stages of the disease.

Consider experimental data comparing thermographic and vascular data in the study of normal and tumor tissue under the influence of a single local X-ray dose of 15 and 30 Gy and fractionated irradiation dose of (15x2) gr. In order to study thermogenesis of normal and tumor tissues, 310 male rats were utilized (series SH, GY and Y), weighing 120-140 grams, the right limbs of which were subjected to X-ray irradiation at the same dose. Thermographic and angiographic studies occurred 1, 4, 7, 14 and 21 hours after exposure.

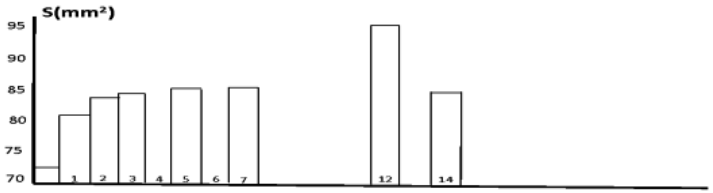


Figure 3: A histogram of the total area of vascular grafted intramuscularly tumor Sarcoma -45

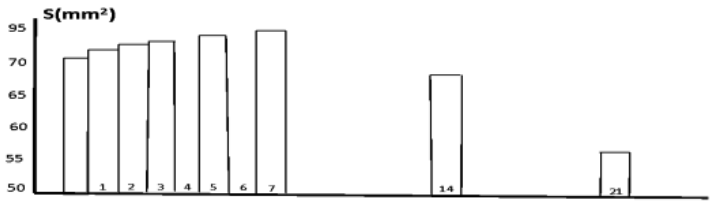


Figure 4: A histogram of the total area of the subcutaneous vessels grafted Sarcoma - 45.

IN SUMMARIZING THE data obtained, it should be noted that the change in temperature parameters and the tumor's tissue are directly dependent on the reaction of the body caused by ionizing radiation exposure. The temperature changes occur cyclically, alternating between periods of hypothermia and hyperthermia. At a dose of 30 g, both temperature and microangiographic changes were similar to those at a dose of 15 g. The only difference observed was with regard to the intensity. Quantitative analysis of thermograms, angiograms and microangiograms led to the general conclusion that the changes in temperature gradients were directly correlated to the network of blood supply to the irradiated normal tissue. Its change was elevated with the increased radiation dose in the irradiated limb and symmetrical non-irradiated limbs. The irradiation of the right extremity with tumor C-45 C, Y size = 4 cm3, temperature change (TM1 T1op, T1rec) was executed with alternating periods of hyperthermia in both the irradiated, the symmetrical limb and in the experimental animal's rectum.

The first wave of hypothermia (lowering of the temperature to 2.0-3.5 C) occurred naturally in the first hours or days after a single dose (15 Gr and 30 Gr) of ionizing radiation exposure as its peak decreased in the first 20-30 minutes that followed the temperatures' gradual increase to the initial values within 24-48 hours (Figure 5).

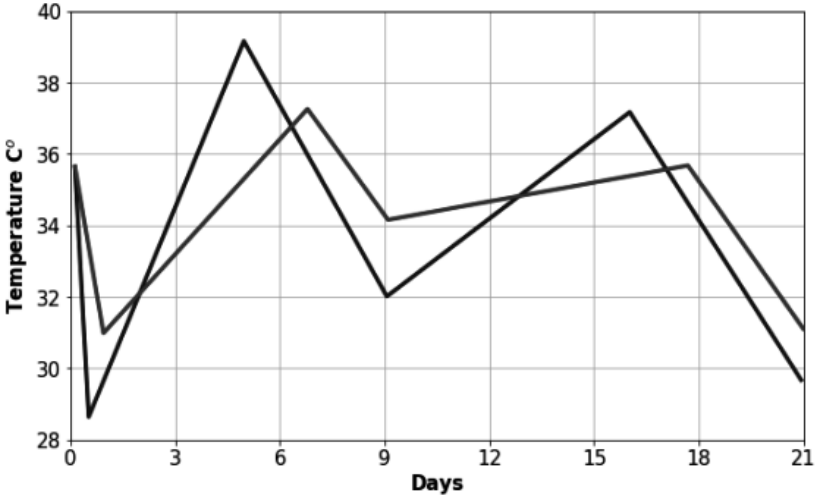


FIGURE 5 MODIFIED temperature gradient of Sarcoma -45 tumor at irradiation dose of 16 Gr. Tm – temperature of the symmetrical zone, Top - the temperature of the irradiated tumor.

Following relative normalization of the general condition that occurred 3-5 days after irradiation, hyperthermia presented (temperature increase of 2-2.50 C) as compared to the starting value (T1op -2.50 C, T1m - 1.90 C, T1rec - 2.30C). A hyperthermic response reflects changes in metabolic processes and other conditions of blood circulation factors caused by exposure to ionizing radiation.

Beginning on the 5th day, a drop in temperature occurred at 2-30C (T1op – 20C, T1m -10C, T1rec- 1.80C) that reflects a specific reaction to radiation. The recovery period in the examined animals was not observed because of the combined effect of radiation and associated increase in a tumor's size and its decay. However, on the 14th-16th day a short re-wave of hyperthermia was observed as T1op -1.50C, T1m-0.80C, T1rec-1.40 C. After came a sharp drop in temperature. This pattern of a certain degree of temperature change can be observed after the impact of 30 g and 15 g, where the identical main terminal reaction remained. There were only a few differences in the extent of their severity in that peaks of hyperthermia and hypothermia were more ex-

pressed during 30 g exposure than with a dose of 15 g. The difference between the temperature peaks reached 1-20C. It can be noted that temperature value oscillations on the left side were 1-1.30C less than in the irradiated right limb.

It is natural to assume that among the many factors affecting the body's temperature response, the most important are vascular changes which prompted us to conduct special microangiographic studies of blood vessels in the implantation area and in the tumor itself. Immediately after radiation of the tumor and normal tissues, almost all animals registered vascular depletion in the exposure zone and in a symmetrical section of the contralateral region. These data convincingly explain the nature of hypothermic peaks at 20 minutes.

On the basis of the thermographic parallels, we can conclude that wave hyperemia is associated with the spastic state of the blood vessels and a sharp limitation in the tumor's blood circulation and its surrounding tissues. Beginning on the 3rd day, a picture of the relative restoration of vascular tone and, therefore, blood circulation in the tumor and in the contralateral area was microangiographically visible. It should be noted that the first peak of hyperthermia was observed on day 4-5 as a result of expansion of large and small vessels in the tumor and in the surrounding tumor tissues. On day 6-9, vasculature diminished due to repeated waves of hypothermia that developed from the combination of the deep, small functional changes of blood vessels in the tumor itself as well as in the surrounding normal tissues.

Microradiographic changes during hyperthermia's re-wave (Day 10-16) developed as a response to blood circulation in separate zones, expanding vessels and restoring blood circulation. This wave of blood circulation restoration persisted and in the terminal phase, the blood vessels exhausted rapidly yielding a drastic demise in blood circulation.

Figure 6 strongly supports the preceding research in demonstrating quantitative changes in the tumor's vascular area after radiation exposure.

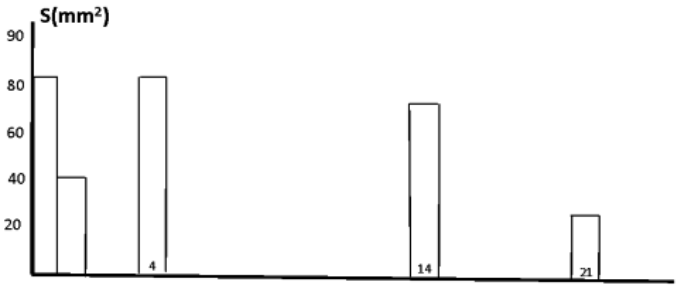


FIGURE 6: A HISTOGRAM showing the change in the radiated tumor sarcoma S-45 with the dose of 15 gr.

THE ANALYSIS OF THE data leads to the conclusion that temperature affects vascular data not only during a tumor's growth, but also after its exposure to radiation.

Simultaneously with the study of temperature and vascular changes were tumor size changes in the two irradiation conditions. According to our research, when the tumor was irradiated at a dose of 30 Gr., the tumor regression was more significant than with irradiation at a dose of 15 Gr. thus, better exhibiting the evidence of the reduction in tumor size. Tumor volume was recorded using an X-ray method of research. Through quantified assessment of radiographs using the color decoder UAR-1, it was possible to evaluate the effectiveness of the radiotherapy with sufficient accuracy.

A noninvasive thermographic method can, to a certain degree, recognize malignant diseases allowing for studies approaching radiosensitivity and hence the ability to choose the most efficient dose to treat the tumor. It is especially relevant in the justification of the different fractionation modes and in considering the reaction of the tumor tissues to the radioactive impact. It is accepted, due to number of clinical studies

(Croys, 1978; Amaluc, 1977; Gautherie, 1984, 1986), that there is a relationship between a rise in temperature and the prognosis of carcinomas, i.e. the temperature determines the degree of malignancy, therefore indicating the higher temperature leads to a worse prognosis. Furthermore, the tumor's size reduplication time correlates to the dimension of its hyperthermia.

The aim was to identify the connections between temperature characteristics and the tumor growth rate of the S-45 after it was fractionated by X-ray irradiation, as well as to collect information that helps to predict radio sensitivity and evaluation in ongoing radiation therapy of tumors.

One of the goals of the issued study was a thermographic X-ray examination (10 male rats, weighing 120-140 gr., with a tumor inoculated into the right thigh). Irradiation was carried out when tumors had reached 4 cubic centimeters while under local fractionated irradiation (15x2) gr. Irradiation was carried out in two schemes.

In Scheme 1, S-45 tumor irradiation was performed with a single dose of 15gr, once daily (i.e. the value of the minimum temperature in comparison to the original one).

In Scheme 2-C, irradiation of the S-45 tumor was carried out with a single dose of 15gr, every 4 days (the value of the maximum temperature in comparison to its initial value).

The determination of intervals between fed fractions (i.e. rhythm of irradiation) was based on the temperature characteristics after a single local irradiation of a tumor with the dose of 15 gr was administered. Thermographic and X-ray examinations were carried out on a daily basis during the first 7 days; and then at two and three weeks after X-ray irradiation. As shown by the data analysis, the tumor regression was more significant using the functioning of option scheme 2.

It can be explained by repeated dose fraction of 15 gr falls on the time frame when irradiation occurs after tumor re-oxygenation (Now the maximum temperature recorded corresponds to the maximum de-

gree of vascularization). It is also known through the work of S.P. Yarmonenko (1980) with co-author R.K. Karakulova (1984) et al., that there is a correlation to the parameters of inoculated oxygen tumors. This fact, in turn, gives grounds to conclude that temperature parameters can indirectly indicate (predict) the oxygen status of the tumor, therefore, its radio sensitivity.

Thus, the method can serve thermography as a resource to forecast radiosensitivity. Radiosensitivity prediction is one parameter determining the course of radiotherapy. An attempt to create mathematical models allows for the prediction of radiation therapy efficacy. For these purposes, 180 mongrel male rats were used, weighing 120-140 grams, with inoculated tumors (90 rats hypodermically and 90 rats intramuscularly) in the right hind leg. The following formula describes the speed of the tumor growth:

Y = A exp – C where V=tumor volume, t=time, A and C - coefficients, and at t = 0, V = A-C, B- tumor growth reference.

B= t2-t1/fn=(Y1/2) fn(Y1/1)

Formula (1) can predict a tumor's growth, especially in the early and intermediate periods. Thermal methodology in clinical practice is not only useful for its dynamic observation capabilities but also determines the state of the organism as affected by different stressful conditions. Therefore, experimental and clinical studies are of particular interest with regard to thermogenesis under the impact of radiation. Based on our experimental data, differing conditions are due to the relationship between vascular factor (S mm2) and temperature (T0 C) of the tumor's period of growth and radiation exposure at doses of 15 and 30 Gy to the normal tissue.

This is the first phase of developing the mathematical model of the thermal state of the tumor versus normal tissue. This connection is described by linear equations confirming the fact that temperature yields a measurable and visible vessel-size increase in the angiographic image.

Selected parameters were obtained from 264 rats grafted subcutaneously and intramuscularly with the tumor S-45 using thermographic techniques and angiographic and microangiographic research, both quantitively processed by a computer and a color decoder UAR-1. A standard computer program EU-1020 was used to obtain expressions reflecting the thermal balance of the tumor in conjunction with analysis of the experimental data.

An analysis of the equations leads to the following conclusions:

1. Temperature sensitivity is more vascularly relevant to intact animals than to rats with a tumor (- 2 times). It shows that with the development of a tumor, the vascular network is incapacitated and its thermoregulatory role diminishes.

2. With an increasing irradiation dose (from 15 to 30 Gr) sensitivity to the vascular factor is reduced (- 1.7 times). It confirms conclusions (1) and points to a different thermal processes characteristic (a "hot" state) in the tumor tissue. For intact animals, the temperature coefficient regarding sensitivity to a vascular factor is insignificant: from 0.406 to 0.394.

3. With an increasing radiation dose in the tumor, the temperature increase reaches 30 (at 10 for an intact animal) at points where d, b = normalized gravimetric coefficients so that d+b+ =1.

The coefficient value determines the contribution of tumor tissue to general enthalpy of the body depending on the tumor size and degree of vascularization. In the process of thermoregulation, the body seeks to regulate Trec caused by the tumor development by changing its heat production, heat transfer and thermal conductivity (i.e., e, blood flow vascularization of the tissue).

Analysis of the data obtained results in the principle difference between the nature of the body's thermal processes and the various neoplasm's depth. In addition, thermal status of the tumor is mainly indicative of the condition of metabolic and vascular factors, allowing for evaluation of the necessity and nature of the therapeutic effect, con-

sidering two thermal body states (the first corresponding in control of healthy tissue, the second in lack of control action).

Analysis of the experimental data revealed significant correlations:

1. At any tumor localization, the relationship of temperature correlated with vascular factors exists. S (r = 0,79 - 0,95). This indicates the body's thermostatic preservation functions, specifically, vasomotor thermal reaction.

2. There have been differences in the direction of the tumor thermos influence and the depth of its occurrence. For subcutaneous tumors, T = Top – Tm <0. Thermographically, the neoplasm is "cold". For intramuscular tumors, T> 0 (thermographically, a "hot" tumor). In addition, over time the growth of T neoplasm (R = -0.91 and r = 0.84 respectively). In the case when the tumor is localized in the subcutaneous adipose, tissue thermographically looks "cold" because the subcutaneous fat tissue is supplied with less blood than is found in muscle tissue; whereas a grafted tumor always appears as "hot".

3. In these experiments, Trec correlation values and S were not detected and eventually the cancer cell grew in the subcutaneous tumor location (r = 0,08 and 0.008, respectively). The same applies to the correlation between T and S (r = 0.07); the subcutaneous link location of cancerous tissue from the body is weakened, and with regard to thermology, the tumor "alienates". This assumption is consistent with paragraph 2.

4. In all experiments, Top correlates with the Trec and Tm (r = 0.89 ... 0.97) and (r= 0.92...0.07) and the relationship to vascular factors S (r = 0.86 ... 0.95) and (r = 0.74 ... 0.77) is observed.

5. A vascular factor has a strong influence over the formation of a thermal state with intramuscular localization of tumors: Trec to r = 0.87, Tm r = 0.87, accordingly to Top r = 0.88. It is consistent with the predominant findings of paragraph 2, in this case of the heating processes.

Data analysis conducted allows two conditional periods of the organism's thermal state control in the process of S-45 tumor growth: the first period (3-17 days) corresponds to the effects controlling the side of the healthy tissue; the second, the lack of controlling impact. Interestingly, both are inherent in the S-45 tumor, regardless of its anatomical location. The findings suggest a different understanding of the nature of the body's thermal processes when tumors are present as the heat status of the tumors mainly reflects the state of metabolic and vascular factors based on the received information and may determine the most effective use of radiotherapy.

Conclusions

1. THE ABOVE THERMOGRAPHY method can be used for the assessment of vascularity during the process of tumor growth as well as to assess reaction to irradiation. This can be used to predict the radiosensitivity of the tumor and to monitor the effectiveness of radiation therapy.

2. Local temperature of the tumor nidus is subject to change, objectively reflecting the morpho functional state of swelling on various stages of its growth and response to radiant impact.

3. The first experiment established the existence of thermographic "hot" transplantable tumors showing that at the same morphological structure of the tumor its' thermographic image can be either ("hot" or "cold"), caused by different degrees of vascularization.

4. The temperature change in normal and tumor tissue after radiation exposure in both symmetrical limbs and the rectum can be characterized by alternating states of hyper- and hypothermia and presented as a manifestation of the reaction in the system "tumor-organism".

5. Immediately after S-45 tumor local irradiation, in the intramuscular grafted right limb, with the doses of 15 and 30 gr, the decrease in temperature is observed at 2-3.50 C at 20 minutes due to a nonspecific reaction of the organism to stressful influence.

6. In order to predict the radiosensitivity of tumors, the model for determining a tumor's radiosensitivity has been improved based on volume and speed of its growth, and tumor thermal model S-45 developed based on thermographic data.

7. The proposed mathematical model of the thermal state of the tumor organism suggests a fundamental nature of the thermal processes occurring in the body at different depths of the tumor's location which

establishes the connection between the heat tumor status and the nature of its vascularization.

8. The development of histographic analysis of microangiograms and angiograms gives an indication of the dynamics of development and vascularization of the tumor and surrounding tissue during its growth and response to radiate forcing.

9. The study resulted in additional quantitative criteria for predicting the effectiveness of radiation treatment for breast cancer and soft tissue, namely, the temperature in the state data of blastomogenic locus (Top), symmetrical sections (Tm), the difference in temperatures between (T = Top- Tm): the value of hyperthermia zone area, as well as data regarding the temperature in the rectum.

Chapter 2

The reaction of the organism to local exposure to ionizing radiation

AT THE END OF THE TWENTIETH century, the work of Folkman alerted the scientific community to the treatment value of tumor angiogenesis. Clinical radiobiology has encountered the unresolved issue of tumor oxygenation in radiation therapy.

Oxygen has a dual function in the process of radiation exposure: If it is present during radiation, it increases the radiosensitivity; if it is present after exposure, it helps in the repair process.

Here are a few well-known and generally accepted rules:

- In the course of radiation treatment, normal tissue surrounding the tumor is affected by radiation.

- Radiosensitivity (radiation sensitivity) is determined by oxygen.

- The main source of oxygen in the body is via vascular blood delivery.

From this perspective, the question of the physiology of the tumor's blood supply and of the surrounding normal tissue during radiation is relevant. This incited a review conducted by our research group into the study of physiological responses to ionizing radiation of the human vascular system.

In the 1970's, The Institute for Medical Radiology, Radiology of the Georgian SSR, The Obninsk Institute of Medical Radiology, and The Academy of Medical Sciences of the USSR conducted a joint research project dedicated to the study of microbronchography, microangiography and x-ray cinematography. A small circle of blood circulation was used to monitor the condition of the bronchial tubes and capillaries of healthy rabbits under local γ-irradiation. A radiation field of

3x3 cm was used. Doses of 3 and 10 Gray (Gr) single and fractionated doses were administered to a total dose of 50 Gr.

The study found that changes in the post radiation lung following local γ-irradiation had a dystonic nature. Depending on the method (single or fractionated) of irradiation used, the changes occurred cyclically or remained stable. Dystonic disorders are similar and do not appear in hypotension and hypertension in the different components of the lung's bronchial and vascular systems and are not limited to the irradiation field. There is a general reaction to the vascular bed and other organs including the bronchial tubes. Increasing treatment by a single dose increases the degree of damage which can be seen at six months of follow-up.

Subsequently, a joint research project was conducted in the 1980's by The Cancer Scientific Center of the Georgian SSR, The Obninsk Institute of Medical Radiology, and The Academy of Medical Sciences of the USSR. The methodology enlisted x-ray microphotography to monitor the state of the vascular architecture of sarcoma tumor-45 (S-45) in rats during growth and exposure to radiation doses of 15g, 30g as well as two doses of 15 Gr in conjunction with the thermography method mentioned above. The study found that three zones could be observed micro radiographically in the tumor S, each exhibiting different capillary density. In the central zone, there were depleted vessels; the peripheral zone exhibited a high density of capillaries; and on the border of the tumor tissue, a high density of capillaries were seen.

The total S-45 tumor vascularization varied based on the loci of the inoculation. When grafted into the muscle, the overall tumor density of capillaries was much higher than in the tumor grafted subcutaneously. A vasoconstriction of capillaries occurred and lasted up to 20 minutes from vascular reaction of the S-45 tumor grafted into the rat's hind leg muscle by ionizing radiation at doses of 15, 30 and 15 Gr. The same vasoconstriction was observed on the opposite unexposed side. Over time, the vasoconstriction was replaced by vasodilation, indicating that

reaction time increases with the dose increase. Following the application of the second fraction (15g), the capillary blood supply peaked, resulting in a significant tumor reduction.

Thermographic and micro radiographic parallels were investigated during radiation. It had been found that the noted temperature drop after irradiation corresponded to the microangiographic vasoconstriction related to the microangiographic blood filling of capillaries. There was also a change in synchronous rectal temperature.

Conclusions

1) S-45 tumor's vascular architecture has a distinct depletion of central area vessels while the peripheral area developed a strong capillary bed.

2) S-45 tumor's vascular reaction is dependent on the inoculation locus, with muscular grafting yielding a more expressed capillary network than when grafted subcutaneously.

3) After exposure to ionizing radiation, capillary vasoconstriction is observed not only in the irradiation field, but also in the opposite unexposed side.

4) A second dose of radiation (15 g) at the tumor's capillaries blood supply peaks causes a significant reduction in tumor size when compared to the control.

5) Observed micro radiographic changes in capillaries correlate with the resulting surface temperature (a decrease of capillary density corresponds to a decrease in temperature, while an increase in the area of capillaries corresponds to an increase in temperature). This is registered thermographically.

GEORGIAN NATIONAL CENTER Study of Multifractional Radiotherapy

In the 1990's, The Oncology Georgian National Center carried out an independent research project. The use of thermography monitored the patient's process of multifractional (MF) radiotherapy.

The first stage focused on lung cancer, as the thermographic examination of the chest yields poor thermal visual results. Therefore, changes in the temperature of the thorax's surface in patients with lung cancer can be attributed to the reaction of normal tissues. Irradiation was carried out using gamma rays by MF from two opposite fields, including ROD 1.6 Gr twice a day at intervals of 3.5-4 hours and SOD 56-60 Gr. When studied thermographically prior to irradiation and before the second irradiation, it was determined that the temperature rises before the second irradiation in the irradiation field on 0.8-1.2C . Temperature also rose in the opposite, unexposed side at a rate less than 0.5-0.7 °C. The following day, temperature changes did not occur. The experiment revealed a better response to local exposure at a significantly lower single dose.

The second step was carried out to further study bodily changes as a result of local radiation. A new technology called digital thermal imaging was applied. Patients with breast cancer who received radiotherapy as postoperative (sectoral resection), as well as those on the radical program were monitored. Irradiation was carried out by the MF, ROD 1.2 Gr with two tangential fields at intervals of 3.5-4 hours SOD 40-50 Gr. A thermal study was conducted before exposure, right after the first exposure, before the second exposure, immediately after the second exposure, and the next day before the first irradiation.

Temperature changes correlated with previous experimental and clinical trials. After the first exposure, a decline in temperature was observed not only in the irradiation field, but also the entire front surface of the thorax. Before the second irradiation, the temperature rose to its original value. However, after the second exposure, a decrease in temperature occurred, though less expressed than after the first irradiation.

The next day (18-20 hours after the last exposure) prior to the first irradiation, the thermal image normalized.

In order to assess the overall distribution of the blood in the body, a computerized differential impedancemetry was used. This method is based on the impedance metrical-stage single-step evaluation of indicators of peripheral circulation as compared with indicators of the central circulation. 240 hemodynamic parameters (rest and graduated weight bearing) were evaluated.

The result of this study was a complete picture of the blood distribution throughout the body to the regions of the head, torso, pelvis, thigh, and lower leg. It also determined the optimal blood supply to specific regions.

Research was conducted in patients with malignant tumors during radiotherapy. Preliminary results of the study showed that immediately after an irradiation session, a decrease in blood supply to almost all regions was observed, as were changes of hemodynamic parameters. Investigations are pending as to the nature of an organism's local reactions to radiation exposure.

Discussion

With over 30 years of experience amongst our research group, the results allow us to conclude that there is a general organism response to local impact of ionizing radiation that can be detected in micro radiographic experiments, as well as in thermoscopic and impedansometric experiments considering various therapeutic dose levels.

Analysis of the organism's reaction has taken on particular significance after extensive multi-fractioning in clinical radiotherapy. Radiation therapy is generally an empirical treatment. Difficulties arise during the transition from experimental to clinical application due to the fact that information on the many defined parameters of the response to radiation exposure, in both tumor and normal tissues, is extremely scarce and insufficient as a base for clinical execution.

Several scientific discoveries in experimental radiobiology have described the *oxygen effect,* the recovery of lethally damaged tumor vascular systems and related hypoxia. This has created a solid basis for the scientific development of clinical and radiobiological research.

Experimentation has shown that the radiosensitivity of tumors and normal tissue depends on several factors; the most important of which are the ability to repair sublethal and potentially lethal damage, the degree of oxygenation, the repopulation rate, re-oxygenation and the cell phase of the life cycle at the time of radiation effects.

Clinical observations suggest that the tumor's response to radiation effects depends on histogenesis, the degree of cell differentiation elements, forms of growth, location, status of surrounding normal tissue, and condition of the organism.

The radiosensitivity of tumors and normal tissues are subject to many factors of which are scarce or completely absent. Others are affected by significant changes in the process of fractionated irradiation and are also incalculable, including the heterogeneity of human tumors and their conditional division into radio sensitive and radio resistant.

Many of the factors that determine tumor radiosensitivity and normal tissues depend on the blood supply; and in turn, the state of the bloodstream. Dependence of radiation reactions and complications as to the susceptibility of blood vessels and, in particular, its endothelium, have been noted by many authors. Changes in the tumor response to irradiation based on history of anemia and blood oxygenation change have similarly been noted by other authors who also researched functional vascular changes in response to irradiation.

The above considerations and the results of our research suggest that we have identified in clinical terms, that the temperature reaction of an organism's local radiation exposure indicates the status of the blood supply within the irradiation zone and outside of it. This indicates that 3.5-4 hours after irradiation, the repair of sublethal and potentially lethal damages of normal cells of the surrounding tissues takes

place. However, there is a vascular reaction of the whole organism (a temperature increase on the opposite, non-irradiated side) that causes an increase in oxygenation of surrounding tissue, and therefore, increases radio sensitivity, particularly regarding the vascular endothelium within the irradiation field. This causes the surrounding tissue to react in some Magnetic Frequency (MF) scenarios, the long-term results of which are not different from the usual fractionation. Thus, the radiobiological rationale of MF is supplemented by justification of the physiological nature and takes into account the body's response to local action by non-specific stimulus.

It can be assumed that radiotherapeutics now consider the state of the organism's circulation in the local radiation exposure; which can make a significant contribution to designing new fractionation schemes and have an impact on individual treatment plans.

A review of the theoretical example of a possible experiential application in the construction of new fractionation schemes includes exposure of equal fractions several times a day (from 2 to 5) without changing the exposure area (irradiation area, usually calculated with the capture of the normal surrounding of the tumor tissue of 2.5-3 cm.). Based on our data, it can be suggested that before the second fraction, an increase in temperature and blood circulation of normal surrounding tumor tissue occurs, resulting in radiosensitivity growth. The second exposure within the same field will increase the lesion of oxygenated surrounding tissues, while causing a decline in long-term results. Therefore, the second radiation should be carried out with a sharply reduced (to the true size of the tumor) field, allowing for reduction of radiation exposure to normal tissue surrounding the tumor.

This research concludes that the body reacts as a whole to a local radiation exposure at both low and high doses. We can consider this response a reaction to non-specific stimuli. It is possible that this results in a so-called *Adaptive activation reaction*, which implies an increase in the organism's non-specific resistance. Consequently, it is possible to

choose the minimum reactional dose to irradiate maximum volume (irradiation field with the capture of normal tissues of 2.5-3 cm from the edge tumor). In this case, a temperature increase both in and out of the exposure field will result in increased blood flow, oxygenation, and radio sensitivity; and will manifest the stimulating effect of low dose radiation so that immune cell infiltrating tumors will be spared, while intracellular contacts increase to prevent the risk of metastasis. After the first exposure, treatment should be performed with the highest dose narrowed to the tumor size. The result would be greater damage of oxygenated cells that had no time to repair sublethal and damaged tumor cells. The process also spares immune cells that infiltrate the tumor as stimulated by a small radiation dose to surrounding normal tissues.

This research suggests that radiobiology based only on cell kinetic models cannot fully meet the demands of the radiological clinic. The cell may not be an element of the "body" system because it does not bear all the main characteristics of the system "organism". The results, along with further study, will increase the ability to improve the effectiveness of radiation at a relatively low therapeutic dose level.

Chapter 3

A method of thermographically evaluating radiation treatment effectiveness in breast cancer patients

MODERN DEVELOPMENT of radiation therapy requires the development of methods that ensure efficient monitoring of treatment and efficacy. Thermography allows for the early diagnosis of malignant neoplasms and a serves as tool for measuring the effectiveness of radiation therapy.

The temperature emitted by the human body renders a "portrait" of radiation registration, offering new information distinguished from other methods of investigation. Thermography allows for objective evaluation of the effectiveness of radiation therapy of malignant tumors. This aspect of the thermography method is under-appreciated. Most radiologists are not yet educated as to the importance of thermography in the evaluation of radiation therapy efficacy in breast cancer patients. This guide is based on the experience of the radiotherapy department of *The Therapy Cancer Research Center of the GSPC* and aims to address this vacancy.

Living tissue is characterized by continuous biochemical processes which release heat. Heat transfer is carried out in two ways: through blood flow and thermal conductivity of deeper tissues. Thermoregulation inherent in warm-blooded organisms keeps the internal temperature constant at an optimal level. There are both *internal* and *external* factors affecting skin temperature. The internal factors include the thermal conductivity of the surrounding tissue, metabolic activity, and blood flow. The external factors include convection, heat radiation, and evaporation. The temperature of the skin is an important physiological index reflecting bioenergy and thermal physics of the body.

Normal skin temperature, at any point, is the result of the actions of many factors and may significantly vary and depend on:

1) The amount of heat transferred to the surface of the underlying tissue layers.

2) The amount of heat lost from the surface.

3) The amount of heat received by skin from environmental surroundings.

To ensure that a thermogram only reflects its own body temperature, it is necessary to bring the skin to a state of thermal equilibrium with the environment. This can be achieved by environmental exposure of the body areas of interest. In clinical studies, a patient unclothed from the waist up stands with her hands up behind her head, at a constant room temperature equal to 20-21C for a ten-minute period. The skin should be clean and dry, as extraneous substances may alter the radiation coefficient of the skin, or the *emissivity*, leading to false readings.

It is also necessary to ensure that prior to the survey, the patient refrained from vasodilators, vasoconstrictors, or procedures that can change the actual temperature of the area of interest.

EVALUATION OF THERMAL INFORMATION

In order to determine the validity of thermography as a method to evaluate the effectiveness of radiation therapy in patients with breast cancer, a study of 34 patients between 30-70 years old who underwent radiotherapy was thermographically conducted. The thermographic analysis was carried out before starting the treatment and then at 3, 6, 9 and 12 months after finishing the treatment.

Patients presented with carcinomas belonging to class T2 and T3 (International TNM classification). Most of the patients had refused other types of therapy, or had inoperable tumors due to cardiovascular diseases.

During the treatment, all patients underwent only radiotherapy (Co60) and treatment results were regularly monitored. Irradiation was carried out in almost identical conditions, in compliance with the exposure factor of radiation meter (injected by Orton and Ellis). Post-radiation consideration consisted of clinical, radiological, and thermal studies systematically conducted at 3, 6, 9, and 12 months after finishing the treatment course.

Heat changes after irradiation were presented graphically for each patient. Attention was paid to the temperature difference between the hyperthermic area of the skin surrounding the tumor, and that of the opposite symmetrical breast. Analysis of the temperature changes that took place after radiotherapy revealed three groups. Patients with linear and progressive regression were place in to Group A. Group B consisted of patients who at first regressed, then after some delay, progressed with increasing temperature of the studied area. Those who had little changes were placed in Group C.

Tumor Groups

A- Tumor Regression
B- Tumor Regression then Progression
C- Little Change

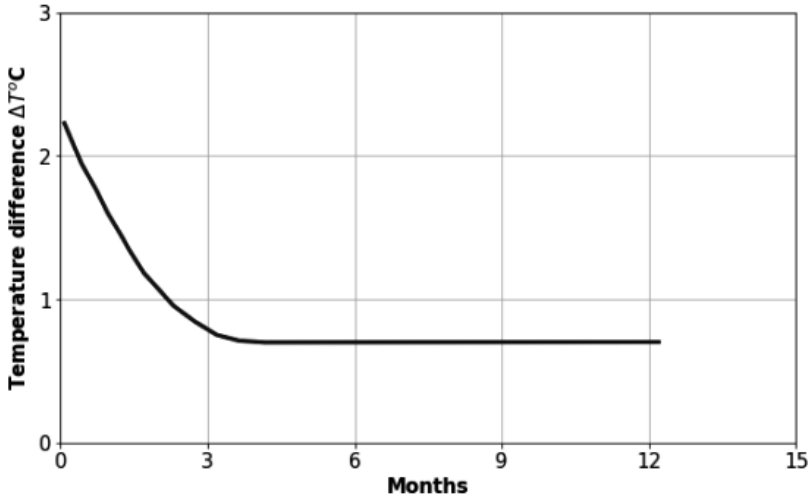


Fig. 1. Group A. Tumor's heat regression

The regression of the tumor's heat (Figure 1), can be seen in 19 patients with internal and surrounding tumor hyperthermia with concurrent skin hyperthermia observed before radiotherapy (Group A). Progressive regression occurred after irradiation and in most cases completely disappeared.

These observations suggest that ionizing radiation reduces cancer heat and thus, suspends its growth. However, the similar effect does not occur immediately during the course of irradiation, but rather, gradually over several weeks or even months.

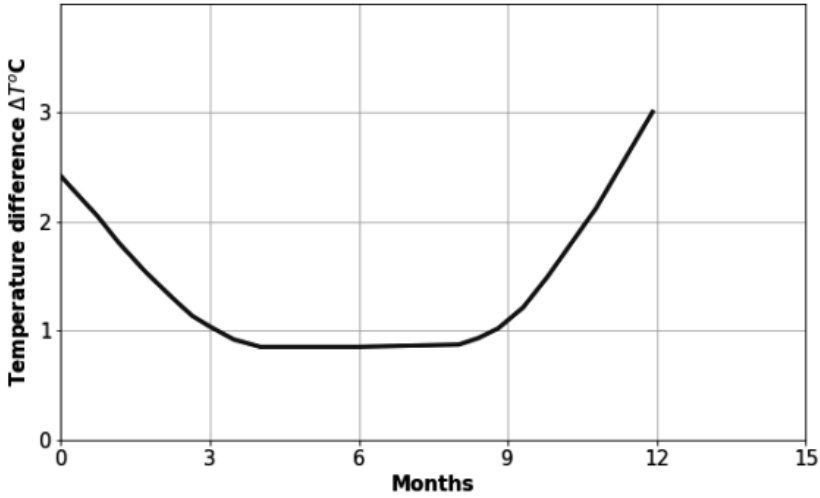


Fig.2: Group B. The regression of the tumor heat release to the skin hypothermia followed by recurrence.

Group B represents 10 patients with regression of tumor heat under irradiation, followed by a period of stabilization, and finally, hyperthermic recurrence (Figure 2). Nearing the ninth month, these patients' anomalies resurfaced; sometimes more aggressive in nature than before irradiation.

Group B radiation therapy action was of a temporary nature in that the ability of the cancer to generate heat was not overcome. In this group, the tumor regression proceeded more slowly with a faster relapse. The thermal analysis had detected tumor reoccurrence earlier than a clinical or X-ray examination of the breast.

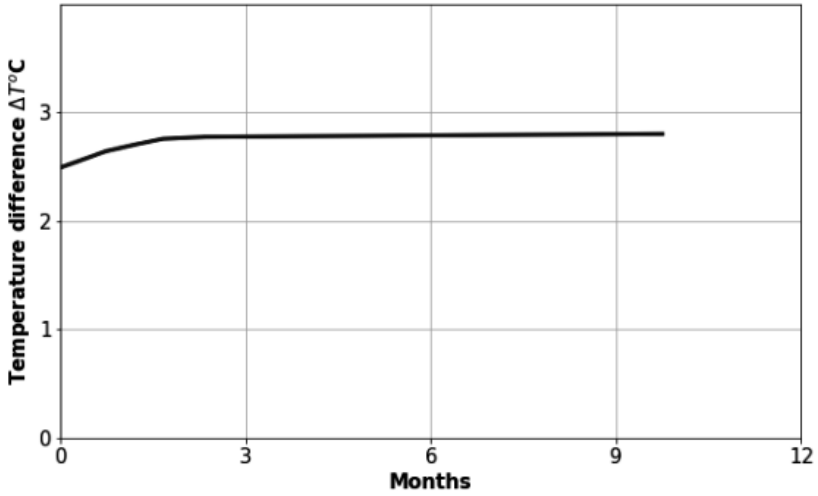


Figure 3. Group C. The insignificant regression of the tumor's heat emission along with skin hyperthermia

GROUP C INCLUDED THE patients with insignificant regression tumor heat. (Figure 3) Seven patients were included in this group. They had slight hyperthermia of the tumor and skin, virtually remaining unchanged from the original level.

Despite the local ionizing radiation, surviving and reproducing cancer cells, remained unchanged. Their metabolism and growth, as projected by heat emission, presented the same as prior to irradiation. These tumors are characterized *as radio resistant carcinomas*.

A slight decrease in temperature values is noted, along with a hyperthermal area decrease. This outcome is not unexpected, as all of the patients were irradiated under identical conditions.

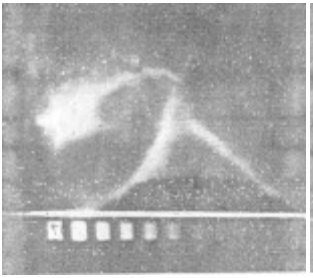


Figure 4.

Thermogram prior to radiotherapy.

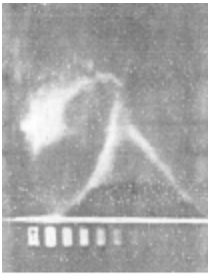


Figure 5.

Thermogram 3 months after radiotherapy.

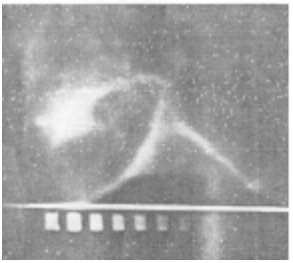


Figure 6.

Thermogram 6 months after radiotherapy.

- ΔT1 = 2.30 C
- ΔT1 + 1.8° C
- .ΔT1 = 1.50 C

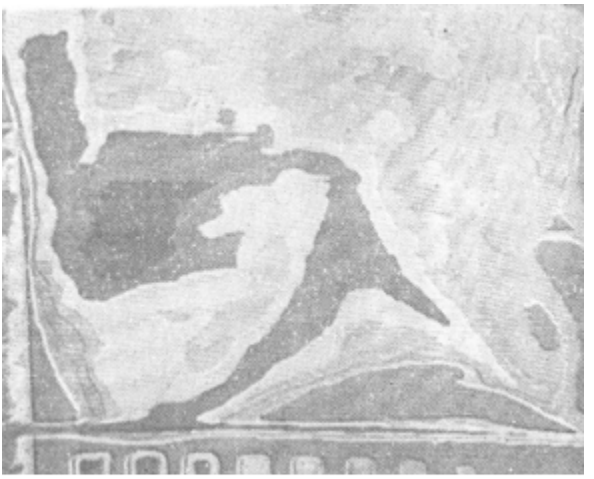
QUANTITATIVE EVALUATION

To quantitatively evaluate changes in the pathological nidus area for a given patient, a decryption color method was applied using the color UAR-1 decoder.

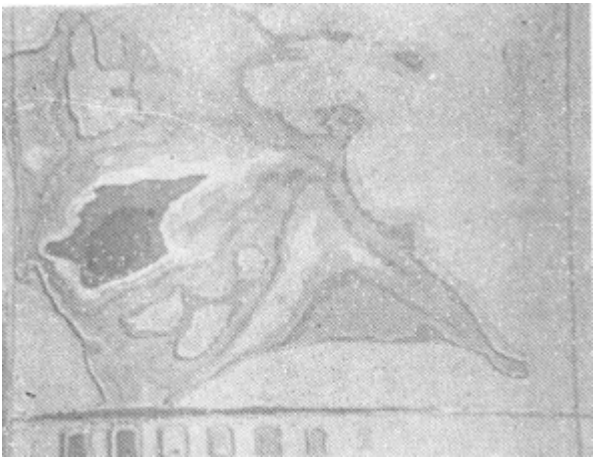
The images are presented in a discrete mode of the color decoder. The contours of the pathological nidus are well visible, while the range of temperature characteristic are limited to 1 - 2.5° C. Based on the quantitative approach assessment, patient's N histogram of the pathological nidus was constructed, reflecting the dynamic of the pathological nidus area change after radiotherapy. The histogram marked a decrease in the pathological nidus area after radiotherapy, indicating its effectiveness.

A comparison of clinical and thermographic data shows a discrepancy between the descriptions of the tumor size reduction. A clinical study does not allow for objectively evaluating the dynamics of change in the pathologic nidus area of the breast under radiation therapy, nor for timely identification of recurrence.

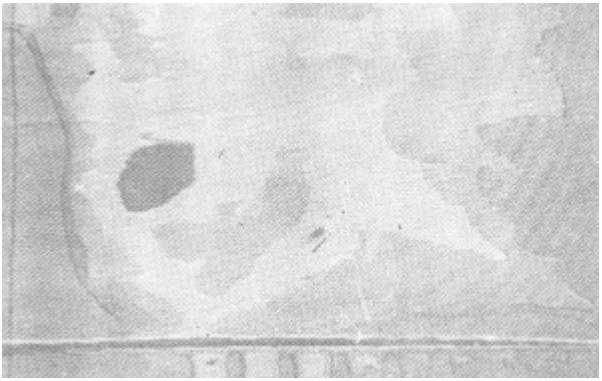
The radiologic study method, when compared with the thermographic method, displays the pathological nidus area late, bringing skepticism into the effectiveness of radiotherapy correction.



Before Radiotherapy



3 Months After Radiotherapy



6 Months After Radiotherapy

Figure 7. Thermogram of N patient in a discrete mode of the color decoder UAR-1.

CONCLUSION

Thermographic study evaluates the effectiveness of radiation therapy for breast cancer patients with objective reliability and has advantages over X-ray in its ability to assess the effectiveness of radiation

therapy. Three options of thermographic patterns for patients with breast cancer undergoing radiation therapy have been described. The observed temperature change pattern of breast cancer patients undergoing radiotherapy can determine the course of treatment to enhance efficacy.

When taking into consideration the harmlessness, significant data yield, and simple research techniques, the thermography method can be recommended for evaluating the effectiveness of radiation therapy, and also as a control method in breast tumor chemotherapy and surgical treatment methods.

Chapter 4

Monitoring of early and late effects of multifractionated radiotherapy in breast cancer

ACCORDING TO WORLD Health Organization data, there are ten million cancer cases per year with six million fatalities (60% Mortality Rate). As UNESCO stated (2005), there are one million new breast cancer cases, resulting in the leading cause of death in young women. In fact, breast cancer remains the most prevalent of all cancers worldwide, presenting for the necessity of improved detection methodologies.

The main treatment modalities for breast cancer are surgery, radiation therapy, and chemotherapy. Radical mastectomy causes many medical, physiological and psychological effects in women. Many women suffer from *postmastectomy syndrome,* a form of depression and psychological collapse leading to *social death*. Mastectomy can radically impact a woman's life. Advances in treatment technologies have increased the likelihood of a patient's survival with a positive prognosis; however, with a later diagnosis, women are left in a social world of pain and depression. This warrants a search for improved early diagnosis methods, resulting in earlier treatment and reducing the need for radical treatment options.

Towards the end of the 20th century, the conservative removal of breast tumors has been prioritized. In such cases where the breast remains, whole radiotherapy is conducive to local control. With this treatment protocol, one can highly improve outcomes and quality of life.

A review of the data suggests that Indications for such type of radiotherapy are breast cancer cases presenting in Stages I-IIA, with a tu-

mor size of less than 3cm, with the breast being of average size. Post-operative radiotherapy causes the reduction of tumor recurrences in breast cancer.

Radiotherapy holds its own share of problems and complications, with both acute and late effects. There are many radio resistant forms of tumors, as was demonstrated in Chapter 3. Finding new treatment options continues to be of the utmost importance, including, but not limited to, a change in treatment delivery. Thermographic monitoring of patients has a strong future in the improvement and development of such areas.

The very first radiotherapy treatment assessed under thermographic imaging, determined that delivering smaller fractional doses yielded less acute complications. There are several accepted modalities of fractionation utilized today, but at the time of writing this text, the standard regime was 2 Gray per daily fraction, five fractions per week. It is empirically confirmed that administering less than 2 Gray per day won't yield satisfactory results, while more than 2 Gray causes bleeding and other complications, mainly due to necrosis developed in the tissue or other acute radiotherapy effects; as has been demonstrated in thermographic imaging.

Radiotherapy as a treatment modality has limitations and is dependent on the tumor's intrinsic physiology. A tumor can be *radio resistant,* where radiation cannot sufficiently destroy tumor metabolism. Equally important, the high radio sensitivity of normal tissues express adverse reactions from the organs at risk. The use of multifractionated radiotherapy is the most successful when confronting these limitations. As previously stated, the ideal execution of treatment is a total daily dose of 2-5 Gray fractionalized over a range of 4-6 hours.

The radiobiological basics of this method include the reparation of lethal injuries caused by radiotherapy about 4 hours after the radiation hits the cells. The hypoxic tumor cells are incapable of immediate repair and resort to a more radiosensitive cell cycle phase when the sec-

ond radiation is administered. The speed and quality of re-oxygenation plays an important role and is dependent on several factors. These include: the type of tumor cells and the kinetics of their growth, the daily fractional dose given and the time interval between fractions, as well as the vascularization of the treatment area. Multifractionated radiotherapy can be most efficient for only very sensitive tumors, yet can also be shown to be fruitful for most tumors despite their histogenesis. Control data confirms that the positive results of multifractionated radiotherapy far exceed that of conventional fractionation. Follow-ups show that late affects are almost the same for both.

The main concern of radiotherapy is maintaining the desired therapeutic interval. Keeping balance between early reactions and late complications of normal structures caused by ionization radiation, while achieving sufficient tumor control, still remains an important requirement. This includes differentiating the treatment doses regarding time and space.

The quest for maintaining the normal function of healthy cells surrounding the tumor is paramount. We must learn how to optimize the influence of radiation to the human body, and anticipate the prognostic factors of radiotherapy. We must also establish new methods of fractionation. The aim of our work was to compare and evaluate early and late effects of conventional and multifractionated radiotherapy, including their clinical and radiobiological substantiation after conservative resection of Stage I and IIA breast cancer.

Study of Stage 1 and 2 Breast Cancer Cases with Fractionated Radiotherapy

Our study included 212 Stage I and II Breast cancer patients with histologically confirmed infiltrative carcinoma. The study ran from 1998 to 2002 and acute and late effects of combined therapy were studied.

All patients completed an expended sectoral resection of the breast, followed by postoperative radiotherapy.

The patients in the trial were divided into two groups. The first group (Group 1) of patients received conventionally fractionated radiotherapy (2 Gray daily dose/ 5 fractions per week). The second group (Group 2) received a daily dose split into 2 fractions. For both groups of patients, tumor coverage was achieved with two tangential static fields, but for multifractionated radiotherapy, two daily fractions were given—1.6 Gray per fraction.

The following methods of investigations were chosen for ideal non-conventional observation of the patients' clinical conditions:

- Digital Thermography (Thermodiagnostics)
- Doppler Ultrasound for the observation of local blood circulation
- Immunological control with the colored reaction of urine sediment (Buskaino- Kimbarovski method)
- Clinical Evaluation using the Karnovski Index

Patients were monitored during the entire treatment process and after 3, 6, 9, and 12 consecutive months from the combined course of therapy. Thermodiagnostics was used as a noninvasive method based on the registration of infrared rays, allowing the measurement of body temperature.

Diag 1 Before Fraction 1
Diag 2 5-8 minutes after Fraction 1
Diag 3 1-1.5 hours before Fraction 2
Diag 4 3.5-4 hours after Fraction 1
Diag 5 5- 8 minutes after Fraction 2
Diag 6 Day 2 before Fraction 1
Diag 7 20-21 hours after Fraction 2 on Day 1
The diagnostics were performed on the very first and last day of treatment

THERMOGRAPHIC EVALUATION

The method of this investigation defined the temperatures of the anatomical regions of the breast and surrounding areas according to the following chart. The average value of the data was calculated on approximately 16 thermodiagnostic investigations on each patient.

Lymph Nodes	5 in each Quadrant Bilaterally
Nipples	Bilateral
Supraclavicular Region	Bilateral
Infraclavicular Region	Bilateral
Axillary Lymph Nodes	Bilateral

AFTER SURGERY, AND prior to irradiation therapy, the hyperthermic region of the surgery showed a 2-3 C increase. It was repeated in almost every patient, and changes were observed according to the size of the operational incision and the duration of the postoperative timeframe.

After the first treatment fraction, there was a temperature increase, not only in the treatment field, but throughout the entire chest wall. The temperature continued to increase for one hour on both sides, however, most noticeably in the irradiated area. At around two hours after the first irradiation, the temperature increased on the healthy side.

The patients who received multifractionated radiotherapy showed a temperature decrease on the healthy side, with an average of 0.5 C, before the second irradiation on the first day; while the irradiated area had a temperature increase of 2-2.1 degrees C.

Before the first fraction on Day 2, about 20-21 hours from the second fraction on the previous day, a decrease was observed in both the irradiated region and in the healthy region, though they did not revert to their starting temperature. This data warrants the claim of restoration of cell physiology.

The graph (figure N1) shows the changes in temperature were almost the same for the contralateral breast; only the range was reduced noticeably. The same temperature change dynamics were demonstrated with the thermodiagnostic investigations performed on the last day of the treatment. The difference in the temperature between the irradiated and healthy breast was higher. On the first day of the treatment it was 0.5 C average, while on the last treatment day of treatment it was about 1.65 C average.

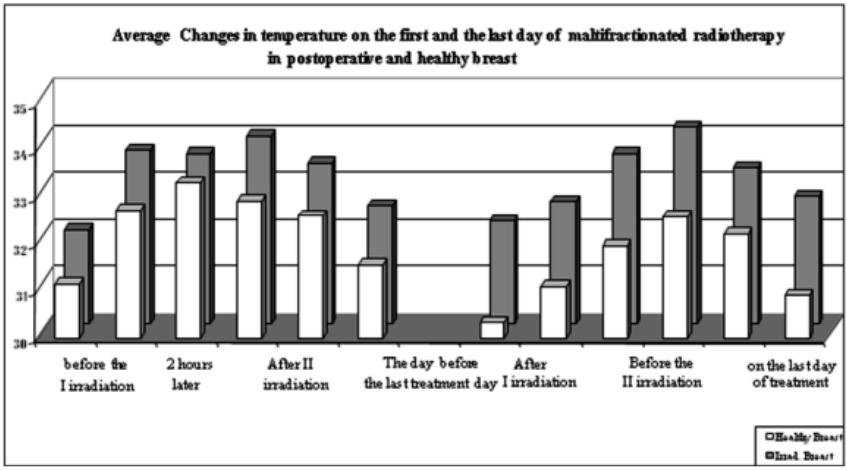


Figure N1

The months following radiotherapy are shown in figure N2, with regard to breast temperatures. While there was a noticeable increase in the temperature of the operated breast during radiotherapy, there was a decrease during the 9-month period of observation. After a 12-month period, the temperature of both the operated and healthy breast were very closely approximated. The dynamics of the changes in both breasts were parallel.

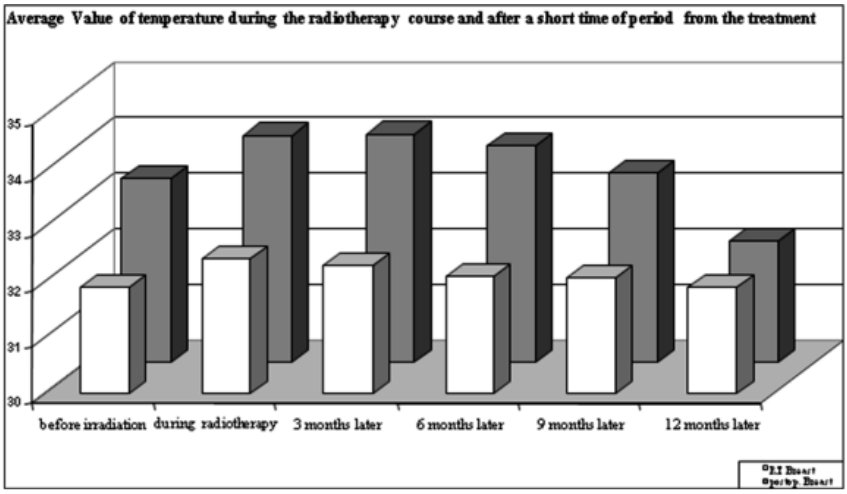


Figure N2

SOME CASES OF RECURRENCE were recorded during the trial. A discussion of the diagram of changes in the temperature for Patient K serves as an example. (Fig N3).

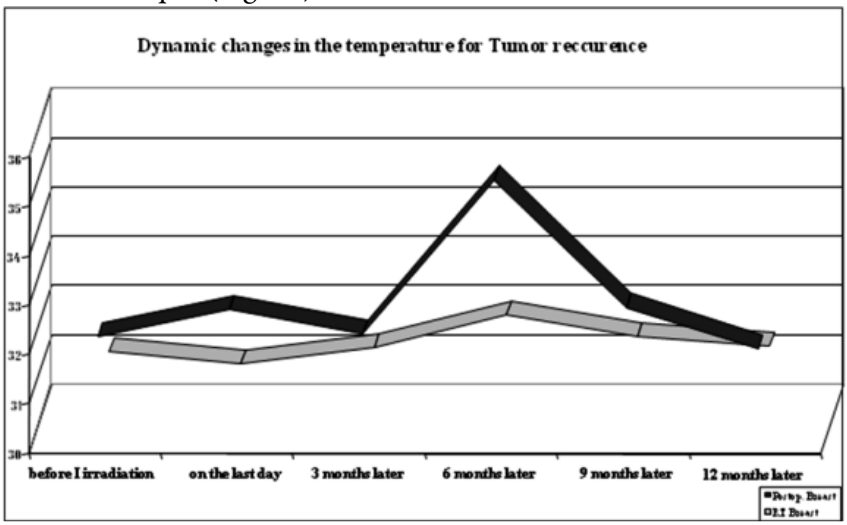


Figure 3

TUMOR RECURRENCE WAS diagnosed on the sixth month after completion of the radiotherapy course. The dynamic changes of the patient's temperature showed an increase by 2.9 degrees in the temperature if comparing to the first value, and by 3.4 degrees compared with the symmetrical value (contralateral breast). It is noteworthy that the temperature of the healthy breast was a bit higher than the value previously investigated.

Ultrasonography was used to investigate local blood circulation. The results of the blood stream speed investigation are very important as they indicate the vascularization of the breast. It needs to be considered that during the first stage of treatment (surgery), tumor cells, as well as healthy cells, are removed, completely altering the circulation of blood in the breast. The blood stream speed was measured in 3 areas of concern: the scar, the tumor bed, and the surrounding healthy tissue. The data were divided into several quadrants. The data were then compared with that of the contralateral breast.

One can expect analogical changes when irradiating the breast as the speed of blood is changing in the same manner in the contralateral breast.

A comparison of the sonographic data to the changes in temperature on the skin surface shows little correlation between these data. But when doing qualitative evaluation of the dynamic changes in the data, the dopplerographic data are somehow slowed down. In fact, thermographic data usually outrun them.

The result of dopplerographic investigation of the recurrence in the same patient looks this way (Fig N4).

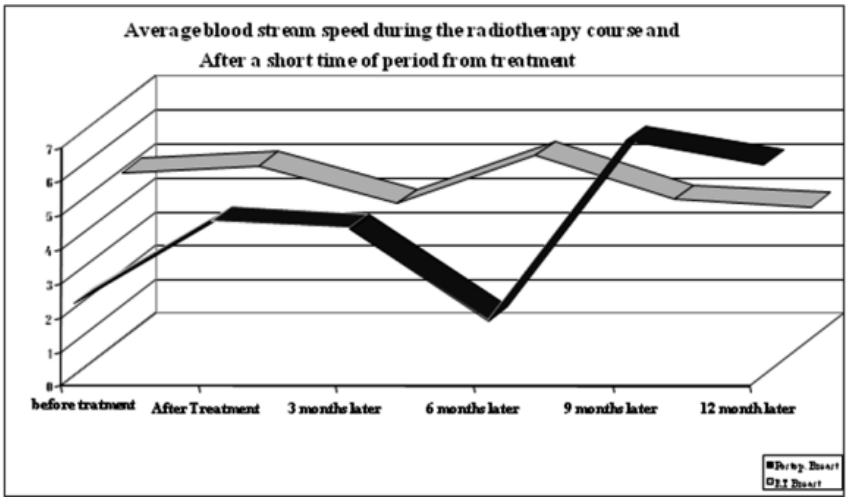


Figure N4

Immune tests were performed using urine sediment color reaction (Reaction of Buskaino-Kimbarovski). Individual changes of this data weren't significantly different, and approximated changes to be average. Before treatment, the index was 57% (Normal <20%). During the treatment, it was increasing, indicating that the patients need some symptomatic medication. At the end of treatment, the index began to decrease slowly, and only returned to its original value after 12 months, showing a strengthening in patient immunity (Fig. 5).

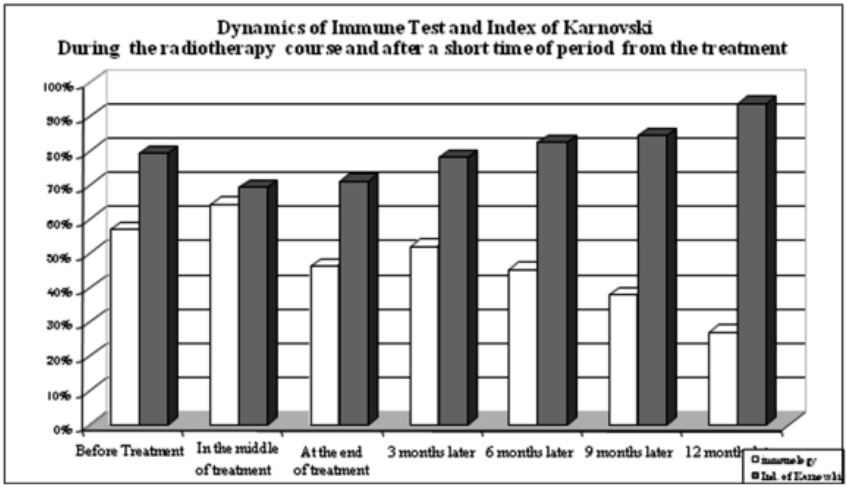


Figure 5

THE CLASSICAL METHOD of The Index of Karnovski was used to describe the overall patient condition. This method allows us to evaluate the activity of the patient with the scale in the range of 0-100%.

The results of individual changes of the data describing the patient's overall condition were not sharply different, considering the dynamics in changes of their average value.

1. Before treatment it was 78% (very low).

1. After starting the treatment, it decreased.

1. At the end of treatment, it started to return to the original value (90-100%) after 12 months.

It was determined that there is an inverse relationship between urine sediment color reaction and patient's activity. A high value in the color reaction of urine sediment meant low index of Karnosvski. Both criteria are useful in evaluating the overall patient's condition, although for immuni-

ty testing, the standard is 0-20%; while for Karnovski it is 100%. An improvement in overall patient conditions will yield a decrease in urine sediment color reaction data and, at the same time, an increase in the Index of Karnovski.

DISCUSSION

After one-year, recurrence occurred in 1.85% of patients in the multifractional group with a rate of 6.3% in patients undergoing treatment with conventional fractionation. There was no incidence of recurrence during the 3 year period following the multifractionated radiotherapy, while two cases of recurrence occurred for conventional fractionation, totaling 10.4%.

Breast cancer patients studied under age 40 have a high risk of recurrence at 7.5%, when compared to patients over 40. The regional dissemination of the tumor was the same for both groups at 5.76%.

A five-year survival rate average for both groups of patients was 95.75%.

When broken down into age groups, the survival rate for Stage 1 tumors for under 40 was 93.75%; while the rate for over 40 was 97.4%. The overall average survival rate for Stage 2 patients was 98.3% and for Stage 2A was 94.77%.

CONCLUSION

In conclusion, multifractionated radiotherapy for breast cancer stage I and IIA is highly effective in preventing local recurrences where life expectancy is less than 5 years. The quality of a patient's life can be greatly improved, as they can tolerate this method quite well. This allows the administration of radiotherapy in a comparatively short time with less acute complications, skin reactions, radiation.

A multifractionated radiotherapy course of breast cancer (stage I/IIa) treatment improves the quality of the patient's life (in 98.15%), can be very easily tolerated by the patient and is carried out in a shortened period of time.

Chapter 5

Breast and Ovarian Cancer Mass Screening

STUDY PERFORMED IN the National Cancer Center of Georgia, 1988 to 2005.

Based on clinical and experimental studies conducted by our research group

R.J. Vepkhvadze, Alexander Sepper, et all

Clinical studies conducted from 1988 to 2005 showed that the local effects of ionizing radiation used in radiation therapy cause adverse reaction of the organism.

In order to develop new medical and physical visualization technologies in the human body, a new generation of devices in the field of thermal imaging has emerged.

This new technology allows for:

1. Risk assessment of circulatory disorders on organismic and regional levels before and after irradiation.

2. Evaluation of responses to ensure the circulation of blood and the patient's perfusion mechanisms.

3. Evaluating the effectiveness of therapeutic procedures of vascular response to radiation.

4. Breast and ovarian screening

THE LACK OF DIAGNOSTIC capability of ovarian tumors is an extremely important issue. There is an increasing frequency of the disease and thus, a growing rate of reproductive disorders can be observed. Ovarian tumors rank second amongst tumors of the female reproduc-

tive organs. According to various authors, the frequency of ovarian tumors in the last 10 years has increased from 6 - 11% to 19 - 25%.

The literature on ovarian tumors is extensive and mostly focuses on malignant tumors, yet the majority of ovarian tumors (75-87%) are benign. Ovarian cysts represent, on average, 17% of all ovarian entities, including follicular cysts (85 - 90%), cysts of corpus luteum (2 - 5%), tekaluteal cysts (1 - 2%), and endometrial cysts (5 – 10%).

Frequency of preoperative errors for all ovarian tumors is 1.2%; within that figure, 25-51% are malignant tumors and 3-31.3% are benign. The main causes of diagnostic errors are prolonged observation of patients with small ovaries, prolonged unsuccessful anti-inflammatory treatment in the uterus, prolonged observation of patients with a presumptive diagnosis of uterine fibroid tumors in the pelvis.

THREE-QUARTERS OF CASES of ovarian cancer are not diagnosed until the moment when the disease has reached stage III or IV. Under standard diagnostic techniques such as ultrasound using transvaginal probe, CT, and laparoscopy (minimally invasive surgery), ovarian cancer is often missed in its early stages given the small size of the tumor.

104 healthy women were studied.

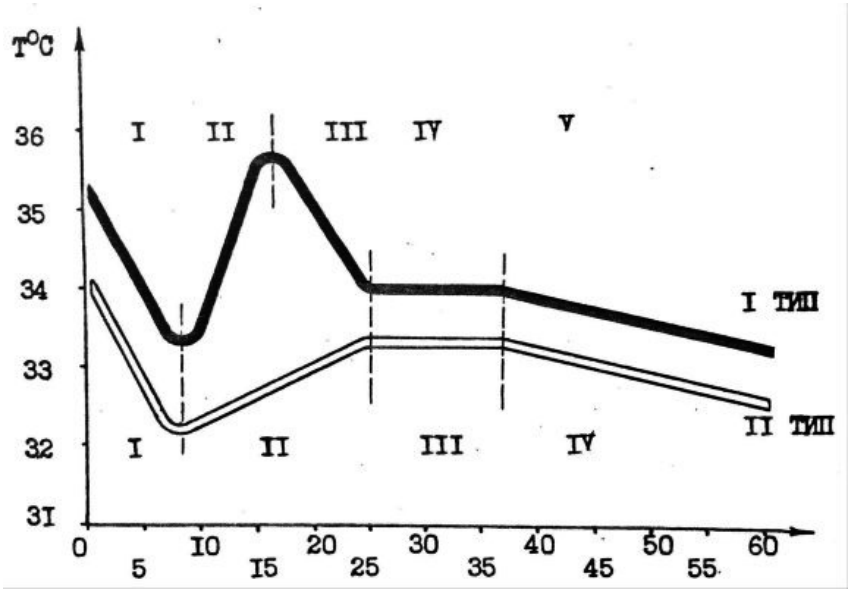
Ambient temperature was maintained at 20-22°C

The thickness of subcutaneous fat layer was:

1-2 cm. – 21 panelists
3-4 cm. – 20 panelists
5-6 cm. – 21 panelists
7-8 cm. – 22 panelists
9-10 cm. – 20 panelists

The research has identified two main types of temperature curves:

Type I Curve – 22.1% of panelists
Type II Curve – 77.9% of panelists


T°C
36
35
34
33
32
31
I
II
III
IV
V
I ТИП
II ТИП
0
5
10
15
20
25
30
35
40
45
50
55
60

TYPE I CURVE (22.1%)	TYPE II CURVE (77.9%)
STEP 1 – Lowering of skin temperature on 1.2 - 1.5°C relatively to the initial value	STEP 1 – Lowering of skin temperature on 1.7 – 2.0°C relatively to the initial value
STEP 2 - Gradual rise of skin temperature by 0.5 - 0.8°C relatively to the original value or 1.5 - 2.3°C with respect of Step 1	STEP 2 - Gradual rise of skin temperature by 0.9 – 1.0°C relatively to the original value but did not reach the initial value and maintained on 0.8-1.0°C bellow it
STEP 3 - Lowering of skin temperature at 1.0 - 1.2°C relatively to the original value or 1.5 - 2.0°C with respect to Step 2	STEP 3 – stabilization of the skin temperature on the level of 0.8 - 1.0°C below the initial value
STEP 4 – stabilization of the skin temperature on the level of 1.0 - 1.2°C below the initial value	STEP 4 - Gradual lowering of the temperature of the skin over time with the advent of the so-called "overdaptation"
STEP 5 - Gradual lowering of the temperature of the skin over time with the advent of the so-called "overdaptation"	

The thickness of subcutaneous fat layer (cm.)	TYPE I CURVE stabilization of the skin temperature (min)	TYPE I CURVE duration of stabilization (min)	TYPE II CURVE stabilization of the skin temperature (min)	TYPE II CURVE duration of stabilization (min)
1-2 cm	15	10	15	10
3-4 cm	20	10	25	10
5-6 cm	25	10	30	10
7-8 cm	30	10	35	10
9-10 cm	35	10	35	10

CONCLUSION

THE TIME OF ONSET OF temperature stabilization of the skin on the projection of internal genitalia, is in direct proportion to the development of subcutaneous fat tissue.

RECOMMENDATIONS

Adaptation Duration:

- For women with the thickness of subcutaneous fat layer up to 6 cm - 25 minutes

- For women with the thickness of subcutaneous fat layer more than 6 cm and up to 10 cm - 35 minutes

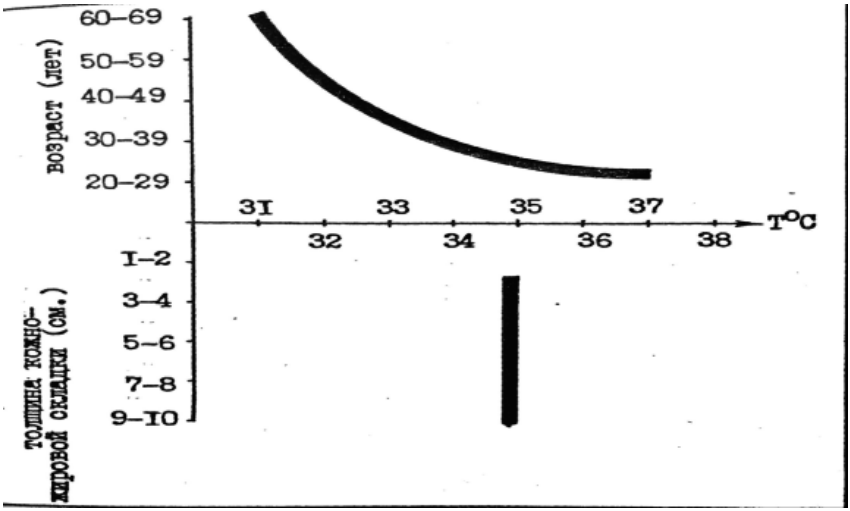
CRITERION OF DIFFERENCE BETWEEN
UMBILICAL AND GENITAL TEMPERATURES (DELTA T3)

• The umbilical region is devoid of subcutaneous fat, which ensures its relative thermal stability.

• 332 observations were conducted: 183 healthy patients and 126 patients with histologically verified ovarian tumors.

• An inverse correlation between the change in umbilical temperature and the age of the patient was observed.

• A correlation between the change in the umbilical temperature and extent of the subcutaneous fat layer was not observed



• In 183 healthy women, Delta T3 fluctuated between 1.7-3.7°C depending on the thickness of subcutaneous fat layer of the anterior abdominal wall.

• In 126 patients with histologically verified ovarian tumors (cancer), Delta T3 amounted:

- 1.5-1.6°C in ovarian cancer stage I
- 0.3-1.6°C in ovarian cancer stage II
- 0.3-1.8°C in ovarian cancer stage III
- 0.1-1.5°C in ovarian cancer stage IV

The effectiveness of the analytical criterion Delta T3 amounted to 91.2%. Application of this criterion allowed for an increase in the efficiency of thermovisual diagnostics of internal genitalia by 8.7%. It should be noted that the criterion Delta T3 enables quantitative analysis of thermal information without going beyond the same diagnostic category.

NORMAL THERMOSEMIOLOGY OF INTERNAL GENITALIA

DIVISION OF NORMAL THERMOGRAMS BY TYPE

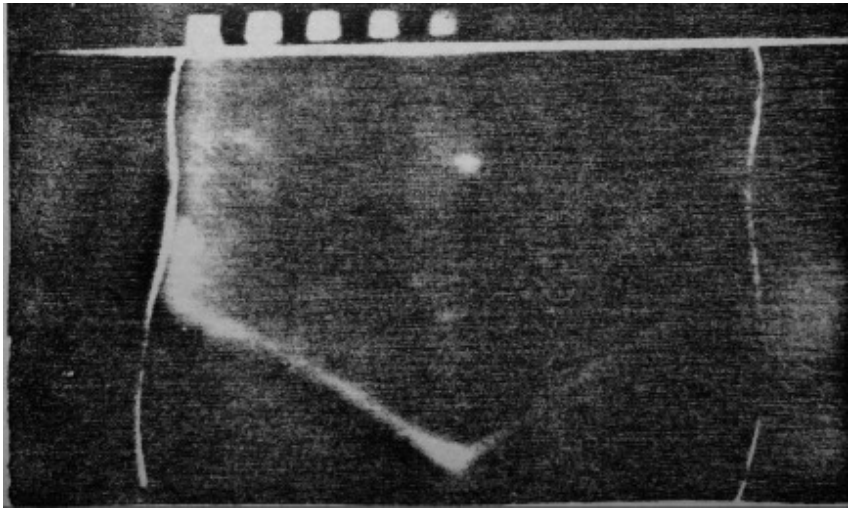
HYPOTHERMIC TYPE

• Observed in 57.1% of women.

• Anterior abdominal wall is visualized as an uneven area of reduced thermogenic activity with highlighted areas of increased irradiance of the umbilicus and inguinal areas.

• Hypogastrium, in comparison with mesogastrium, is characterized by a tendency to hyperthermia not more than 0.7°C.

• Most common between the ages of 40-60 years.



ISOTHERMIC TYPE

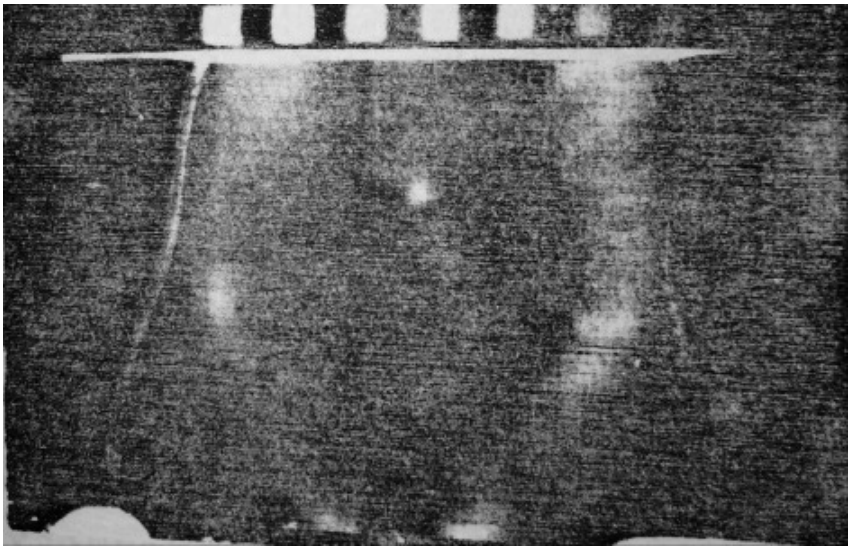
- Observed in 24.6% of women.

- Anterior abdominal wall is characterized by relative isothermia.

- Abrupt transitions into a strong expression localization cannot be traced.

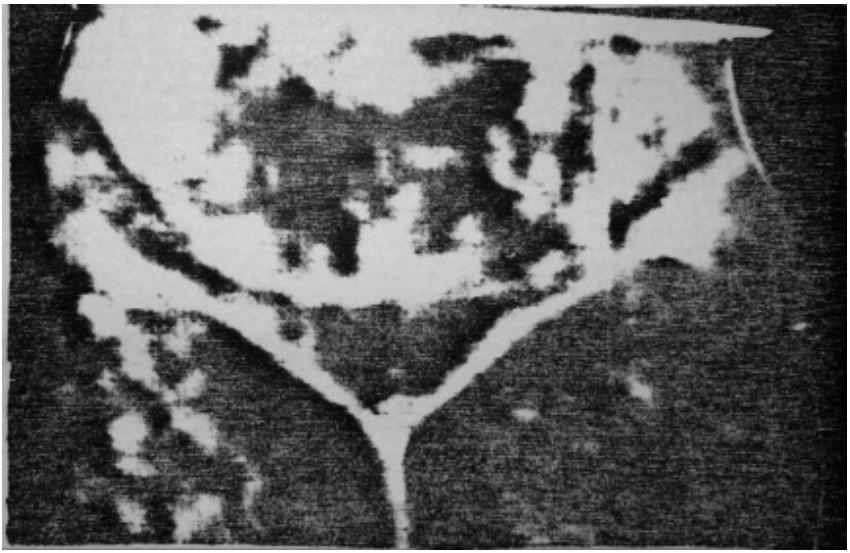
- The only clearly marked area of increased radiance is the navel.

- Mainly characteristic for the age subgroups of 20-29, 30-39, and over 70 years.



LARGE PATCHES TYPE

- Observed in 13.3% of women.
- Anterior abdominal wall is characterized by alternating zones of high and low thermogenic activity.
- These zones are differing by irregular shape.
- Temperature difference between the zones does not exceed 1.0C.
- Typical for women with abundant deposits of subcutaneous fat.



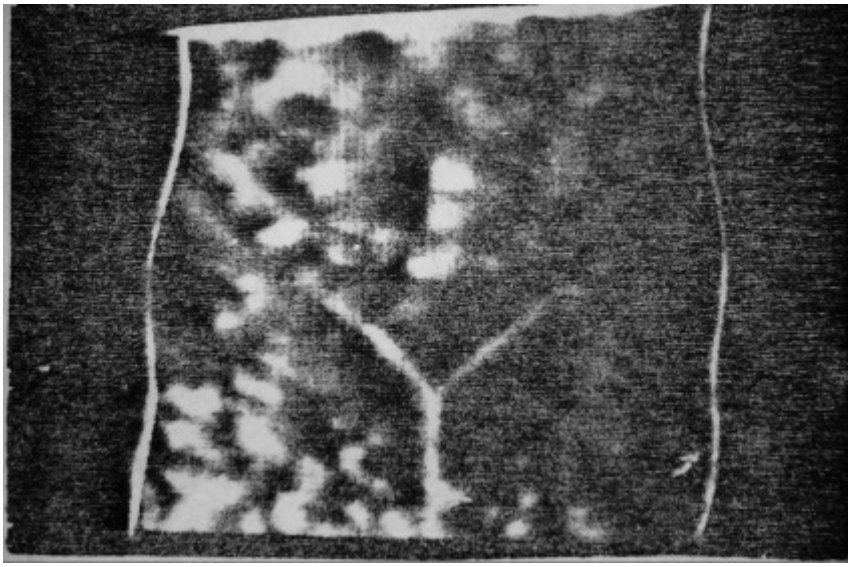
SMALL PATCHES TYPE

- Observed in 5.0% of women.

- Characterized by chaotic hyperthermic spotting over the entire surface of the anterior abdominal wall.

- The density of the spots is more pronounced in the lower abdomen.

- This type does not depend on the age and constitutional features.



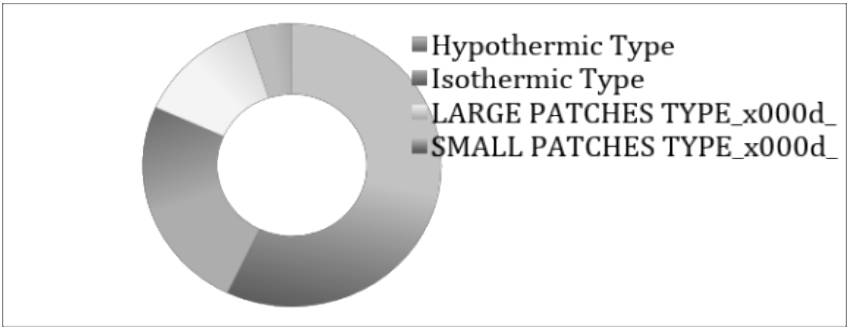
DIVISION OF NORMAL THERMOGRAMS BY TYPE

• Described types of thermographic images are not standard.

• In some cases, there may be a combination of two or more different types.

• Most accessible to interpretation are Hypothermic and Isothermic types of thermograms.

• More difficult for analysis are Large Patches and Small Patches types of thermograms.



Patient H:

• Chart No. 124—National Center of Oncology, Tbilisi, Georgia

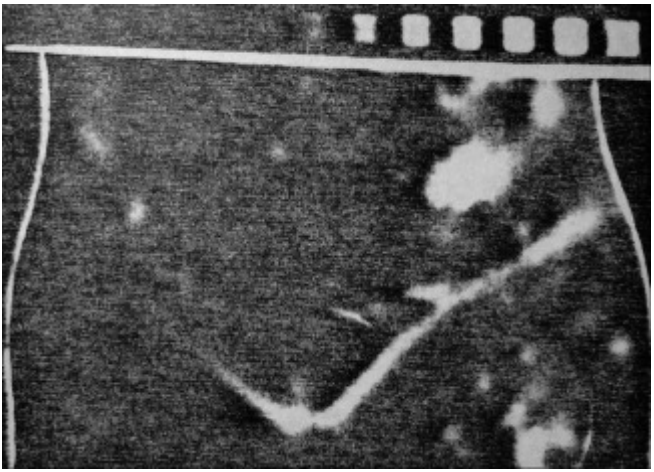
• Clinical Diagnosis: Left Ovarian Tumor

• Postoperative Histological Diagnosis: Adenocarcinoma

• Thermographic Diagnosis: Malignant Tumor of Left Ovary

ON THE PROJECTION OF the left adnexal, the atypical local increase of thermogenic activity is determined.

T1 = + 1.3°C, T3= +1.4°C

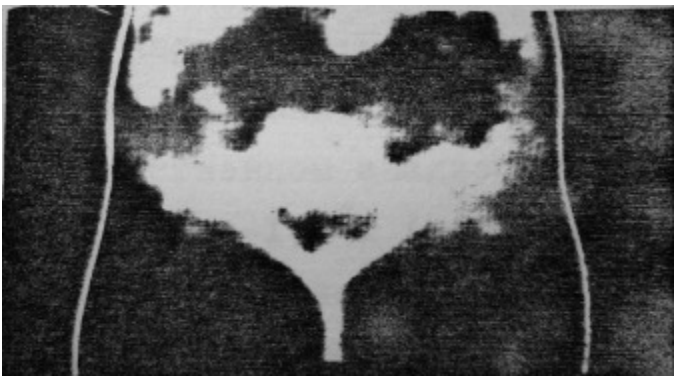


Patient M.

- Chart No. 263—National Center of Oncology, Tbilisi, Georgia
- Clinical Diagnosis: Ovarian Cancer
- Postoperative Histological Diagnosis: Malignant Cystadenocarcinoma
- Thermographic Diagnosis: Malignant Bilateral Ovarian Tumor

On the projection of the internal genitals, the atypical local increase of thermogenic activity is determined.

T1 = + 1.4°C, T3= +1.5°C

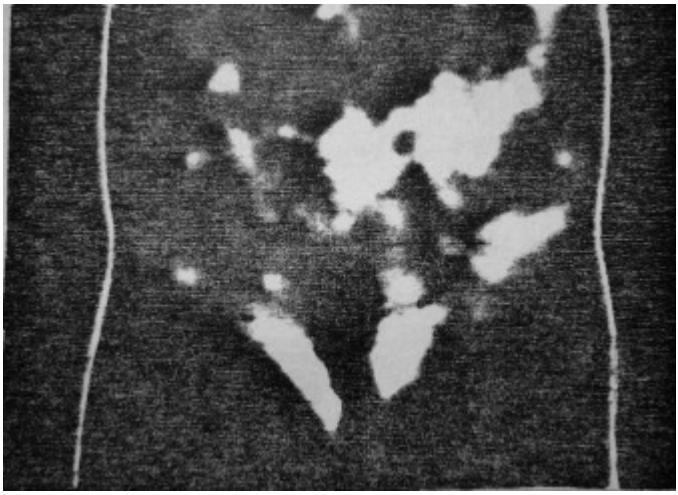


Patient A:

- Chart No. 81—National Center of Oncology, Tbilisi, Georgia
- Clinical Diagnosis: Left Ovarian Cancer
- Postoperative Histological Diagnosis: Malignant Cystadenocarcinoma
- Thermographic Diagnosis: Malignant Left Ovarian Tumor. Metastatic process in left inguinal area

On the projection of the left ovary, the atypical local increase of thermogenic activity is determined.

T1 = + 1.7°C, T3= +1.3°C

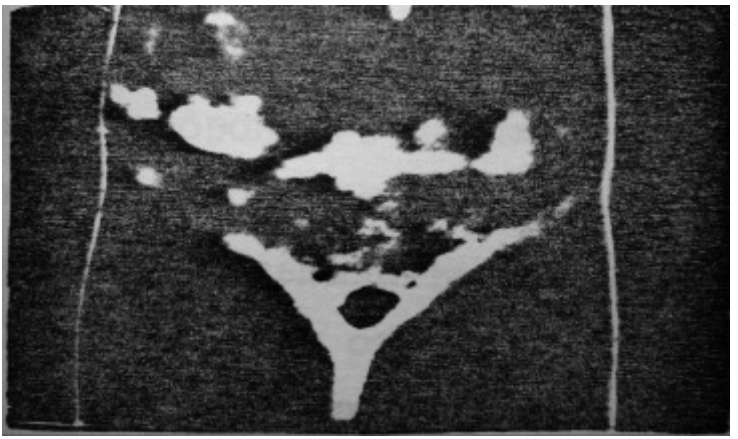


Patient C:

- Chart No. 903—National Center of Oncology, Tbilisi, Georgia
- Clinical Diagnosis: Ovarian Cancer
- Postoperative Histological Diagnosis: Papillary Cystadenocarcinoma
- Thermographic Diagnosis: Malignant Bilateral Ovarian Tumor

On the projection of the left ovary, the atypical local increase of thermogenic activity is determined.

T1 = + 1.7°C, T3= +1.0°C

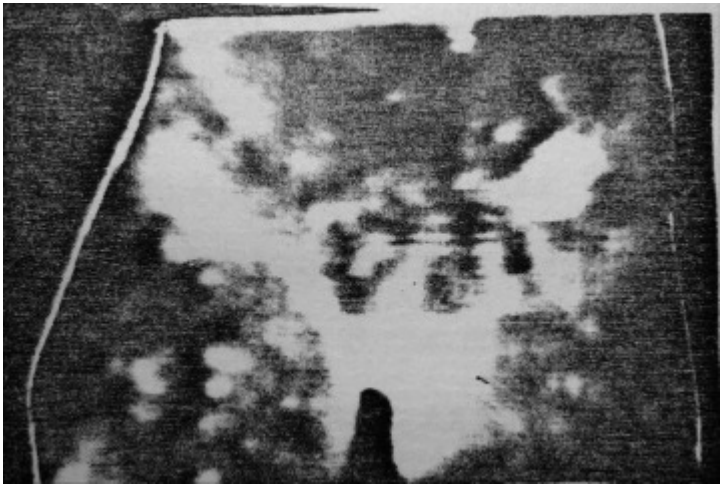


Patient T:

- Chart No. 57—National Center of Oncology, Tbilisi, Georgia
- Clinical Diagnosis: Left Ovarian Cancer
- Postoperative Histological Diagnosis: Adenocarcinoma
- Thermographic Diagnosis: Malignant Ovarian Tumor

ON THE PROJECTION OF the left ovary, the atypical local increase of thermogenic activity is determined.

T1 = + 2.0°C, T3= +0.6°C

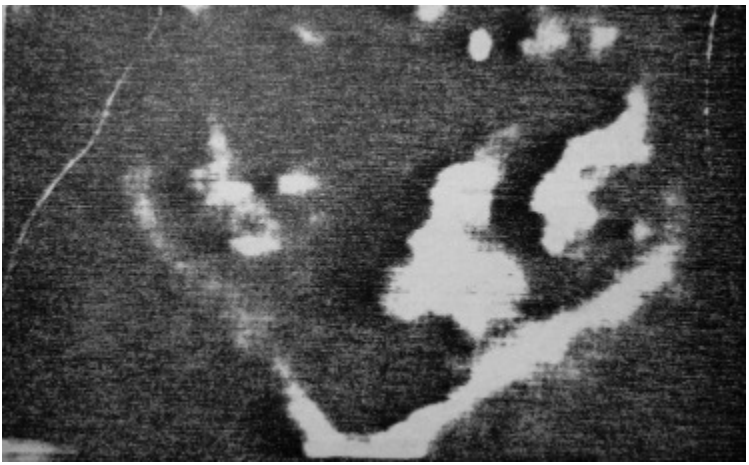


Patient B:

- Chart No. 919—National Center of Oncology, Tbilisi, Georgia
- Clinical Diagnosis: Ovarian Cancer
- Postoperative Histological Diagnosis: Cystadenocarcinoma
- Thermographic Diagnosis: Malignant Ovarian Tumor

On the projection of the left ovary, the atypical local increase of thermogenic activity is determined.

T1 = + 2.3°C, T3= +0.2°C



CATEGORIES OF THERMOGRAMS
OF OVARIAN CANCER

CONVINCING – 72.9%:

• Characterized by pronounced qualitative and quantitative traits.

• Atypical areas of increased thermogenic activity are clearly demarcated from the surrounding thermal background.

• Fluctuations in the value of T1 = + 1.3-2.5°C, T3 = +0.2-1.5C.

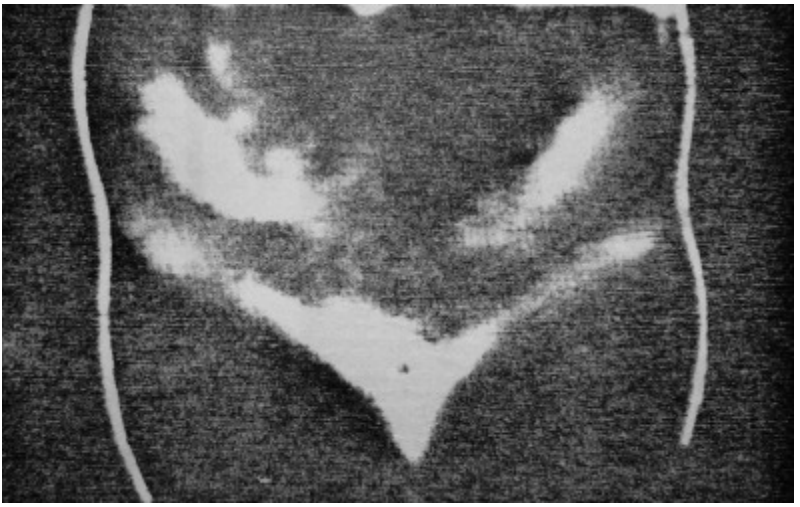
• With this type of thermal image, it is possible not only to detect ovarian neoplasms, but to make a differential diagnosis.

QUESTIONABLE – 11.9%.

• This group includes the thermograms with qualitative and quantitative attributes expressed in a much lesser degree.

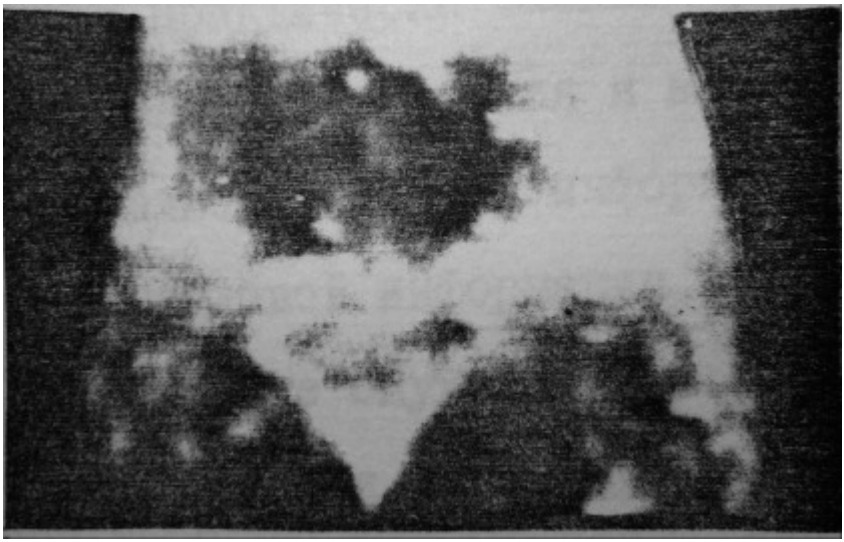
• Fluctuations in the value of T1 = + 0.9-1.2C, T3 = + 1.6-1.9C.

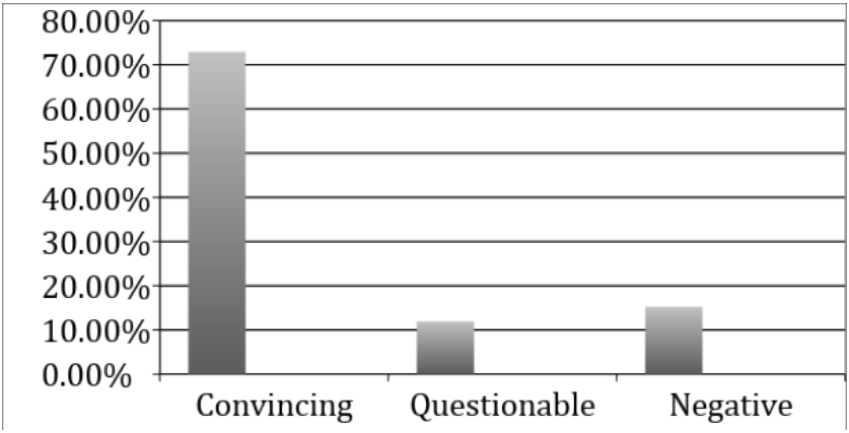
• On the basis of this type of thermogram, it is possible to assume the existence of cancer.



NEGATIVE – 15.2%.

• This group includes thermal images that have no pathological thermological signs.





THERMOGRAPHIC SCREENING
OF OVARIAN CANCER

AT A LEADING CHEMICAL plant in Rustavi, Georgia (48,936 workers), a thermal imaging study of 18,235 women was held.

Age of the studied women: 25 -66 years.

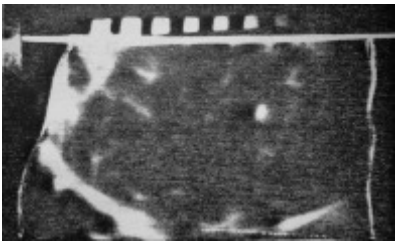
Duration of the project: 4 weeks.

Researchers: doctor/ interpreters - 2, laboratory technicians – 3.

TYPE OF THERMOGRAM:

18,235 WOMEN SCREENED

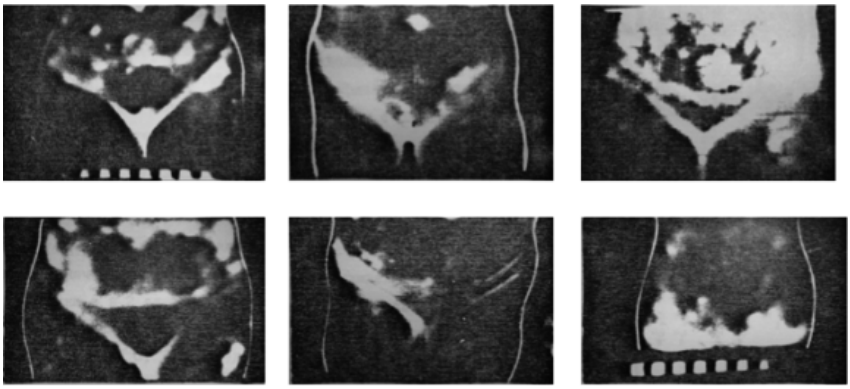
Convincing Thermograms	419	2.3%
Questionable Thermograms	1,021	5.6%
Negative Thermograms	16,795	92.1%



FROM 18235 WOMEN :

	THERMOGRAPHY	SONOGRAPHY	CYTOLOGY
Convincing	419	326	257
Questionable	1021	664	732

	FALSEPOSITIVE IN CONVINCING GROUP	FALSEPOSITIVE IN QUESTIONABLE GROUP
THERMOGRAPHY	162 (38.6%)	289 (25.3%)
	FALSEPOSITIVE IN CONVINCING GROUP	FALSENEGATIVE IN QUESTIONABLE GROUP
SONOGRAPHY	69 (21.1%)	68 (6.6%)



Contemporary Evaluation of Thermal Breast Screening

ANTHONY PIANA, DC
Alexander Sepper, MD, PhD

Background

Breast cancer is one of the major problems of modern oncology, and has certainly received the most attention. The World Health Organization (WHO) estimates that by 2030 there will be 26.4 million new cases of breast cancer annually worldwide, and 17 million people will die from this terrible disease.

Breast cancer is frequently found in women predominantly between the ages of 32-38 years old who are pregnant or have just given birth. According to statistics, breast cancer occurs 1 in 3000 pregnancy cases. About 3% of all cases are diagnosed during pregnancy, and 25% are seen in women less than 45 years of age. It is these women who currently do not have a method of annual screening, and in turn leave behind young families when they die. Adding a valid method of screening for these mothers will allow for a greater survival rate as well as a decrease in overall healthcare expenses. Early detection of breast cancer implies earlier treatment, therefore saving more lives, which the current system of conventional screening mammography has not achieved.

Earlier diagnosis will aid in decreasing the cost of overall healthcare in several areas. First, the number of full radical mastectomies will be reduced and more lumpectomies will be performed. This will cut down on the cost of not only the hospitalization stay, but the time of disability. There would be less reconstructive procedures required as breast integrity can be maintained. Finally, the need for costly chemotherapy could be lessened in the absence of lymph node involvement.

The FDA officially cleared thermography in 1982 as an adjunctive method for the diagnosis of breast cancer. Thermography is a complementary method of the screening process for breast cancer with no contact and allows for multiple screenings of women at any age, including pregnant women. The level of development of thermographic engineering is currently very high. This level in technology allows for mobility to serve remote locations with the added benefit of less cost. The information displayed in the images and user-friendly systems are far superior to previous medical thermographic equipment. The *No Touch Breast System* developers of the thermographic technology have recently been recognized for their work by the Government with a $900,000 grant to continue development.

This discussion establishes that thermography has its own niche in the methods of diagnosing breast cancer when used as an adjunct to mammography, and can improve the efficacy of such a diagnosis.

Brief History of Medical Thermography

THE SCIENCE OF MEDICAL thermology was first published in 1956 with an analysis of 26 breast cancer cases by Dr. Robert Lawson (1). Over 800 peer-reviewed articles have been published since that time including several contemporary pieces. While the nature of science is to build on past research, the challenge is that older information was dependent upon analog equipment, and not the improved technology utilized today. Modern digital equipment is noted to be far more sensitive than equipment employed when older studies were performed.

Many of the current methods of interpretation are utilizing a historical system of TH risk factor ratings. This originated from studies performed in the late 1970's with the use of analog equipment on statistically small groups of patients. The patients were monitored over time and their rate of breast cancer development was studied with assigned corresponding risk factors. Several problems existed within this

study including the fact that 10% of TH1 cases (lowest risk factor) went on to develop clinically confirmed breast cancer in mammograms with subsequent biopsies.

The use of the term "risk factor" in Thermology is invalid. The thermal patterns seen are not "risk factors", but actually early signs of cancer due to inflammation, neoangiogenesis, or estrogen related activity. A mammogram detects tumors dense enough to be visualized onradiographs. Physiologically, before a dense mass appears, heat is generated in and around the cells where the cancer is developing, which is rendered on thermal images. A potential use for "risk factor" prediction may lie in the thermal identification of estrogen dominance.

Using mammogram technology to initially screen for cancer rather than thermal imaging is like waiting for a tire to blow out instead of inspecting its' treads. Thermography sees the metabolic indicators of cancer earlier, therefore being a great adjunct to anatomical screening.

Risk factor assessment should be abolished. The use of thermal imaging for breast cancer screening should be utilized for initial analysis and establishing baselines for each patient. Changes in thermal activity must then be investigated and assigned appropriate clinical investigation including an ultrasound and diagnostic mammogram.

Current Screening Methods of Breast Cancer

THE US NATIONAL CANCER Institute recommends mammography screening for breast cancer only in women older than 40-50 years because the mammary glands of young nulliparous women have a high density. Tumors are not easily distinguished from the dense breast tissue resulting in many false negatives. Furthermore, the NCI states that X-ray radiation itself is a risk factor for the development of malignant tumors. Frequent radiation is not advised by any medical institution. Gotzsche and Olsen (2) studied a meta-analysis of more than 500,000 screening mammographic images that showed mammography causes more cancer cases than it prevents. Statistics show that for every 1,000

mammography examinations performed only one death was prevented, but six were caused.

A screening study in the former Soviet Union (USSR) of 18,000 women diagnosed 3.5 breast cancers per thousand (3). This study used a Barnes Thermovisual device where only a few staff members screened all women in one week. This rate of detection is comparable to screening with mammograms, but with less expense and more efficient testing.

Metabolism of Tumors and Tumor Growth

It is well understood that cancer cells, through the release of Vascular Endothelial Growth Factor (VEGF), develop a blood supply through a process called angioneogensis. Growing cells and increased blood supply produce measurable amounts of heat that can be detected by thermometric devices. The scientific community employs the uses of infrared thermal imaging to accurately measure heat both quantitatively and qualitatively, which are useful in evaluating skin temperatures of the human body; and therefore the skin overlying breast cancer.

TUMOR GROWTH VARIED considerably between subjects, with 5% of tumors taking less than 1.2 months to grow from 10 mm to 20 mm in diameter, and another 5% taking more than 6.3 years. The mean time a tumor needed to grow from 10 mm to 20 mm in diameter was estimated as 1.7 years, increasing with age.

Hobbins (4) at the University of Wisconsin showed that 70% of tumors are found up to 10 years prior to identification on a mammogram with thermal imaging. This study was paralleled in a study performed in the USSR showing the ability to detect tumor development in the preclinical phase.

Temperature Measurements

WITH THE USE OF SCIENTIFICALLY calibrated thermal imaging equipment, a quantitative measurement is possible. These same infrared cameras are utilized throughout the scientific community and have been established as reliable devices of accurate measurement. It is important to maintain room temperature at a consistent level. Patients' metabolic rate on the particular day of study may fluctuate. *Emissivity*, an objects ability to radiate infrared radiation is a consideration. Lotions, deodorant, and other factors can change the infrared readings due to emissivity differences. Qualitative measurement provides a relative temperature difference and is an extremely effective way to analyze vascular patterns independent of identical temperature and emissivity. Delta T measurements are used by the thermographer to analyze relative differences in body heat. This is done using symmetrical points for quantitative measures independent of the patient's base thermal state. Established protocols must be followed in order to receive reliable data.

Automated Interpretation

SOME RESEARCHERS (5, 6) have attempted to use automated interpretation software for breast screening. The drawback is that computerized programs have not been successful in the evaluation of vascular heat impressions used to locate probable pathologies through inverse grayscale imaging. Automated software is limited to delta T measurements. These studies show a comparison between the percent of success at finding malignancies compared to that of mammogram technology and not from a screening standpoint. The 97% sensitivity in a Cornell study concluded that 58 of 60 tumors were identified from a suspect mammogram and were confirmed after further biopsy. This is not saying it found 58 of 60 tumors in a screening population, but 97% of what mammography screening found. While these numbers are im-

pressive, thermography offers further potential as an initial screening, independent of mammographic screening.

Anatomy versus Physiology

NO CURRENT SCREENING test can diagnose breast cancer. Current anatomical tests include: ultrasound, mammography, and MRI. Thermography is a physiologic heat detection exam. Anatomical tests identify structures, which cannot lead to a complete understanding of the pathological process. Thermography, as a study of physiology, does not assess anatomy or structure, but senses the thermal radiation from the surface of the body (breast), revealing the metabolic activity of the area studied.

Thermography is a method of objectification of physiology with its inherent advantages and benefits. It does not replace the x-ray and ultrasound, but allows clarification of physiological processes.

Thermography benefits include: the early detection of disease in cases that are too small to be visualized on anatomical testing; following the effectiveness of therapeutic interventions (where is the benefit in this statement?); aid in decision making for the need for surgery, or what type of surgery to perform. Anatomical tests are unable to find: densities of tumors 1-5mm and smaller; metabolic activity of the cancer cells; the change in activity of the disease process in response to treatment. Thermal imaging fills these needs.

New Model of Thermographic Analysis

Current methods of assessment used to interpret thermal images for risk analysis do not reference any contemporary studies, but rather are based on prior research using analog equipment. The authors believe that the categorization of breast cancer risks is a strength of breast thermal imaging. The strength of modern thermology lies in the ability to evaluate vascular heat patterns and their deviation from baseline

studies. The risk factors previously used are taken into consideration, not as risk factors, but as abnormal physiology of the breast. The thermologist acts more as a radiologist in identifying abnormal versus normal; yet the former focuses on physiology while the latter analyzes anatomy. Baseline studies are important for periodic comparison.

Normal Thermal Breast Physiology

IT IS IMPORTANT FOR the thermologist to become familiar with normal breast patterns. Normal breast physiology will vary in women at different phases of life. Hormonal mottling patterns will be seen in premenopausal women after puberty. Normal physiology will show fairly symmetrical vascular bundles.

Post-menopausal women will show signs of hormone expression diminishing with the aging process.

Abnormal Thermal Breast Physiology

INFLAMMATORY CONDITIONS in the breast are represented by darker patterns in the inverse grayscale and usually white or red in color palette. This is dependent upon the scaling and range used by the individual thermographer. These may represent different forms of pathology, which includes breast cancer, mastitis, injury, and any other condition that would raise the temperature of the breast locally. In traditional analysis, the threshold for two bilateral points was 2.0 degrees Celsius. The studies were designed in a pre-mammographic era where DCIS was not as prevalent. We have found when less metabolically active tumors, such as DCIS, show on thermographic images, that the delta T is typically lower than 2 degrees. Another challenge, is that measurements over two degrees are commonly seen with fibrocystic breasts. Using this threshold value poses a problem of missing many cancers, as well as creating a substantial degree of over diagnosis with fibrocystic breast syndrome.

Frequently, we find areas of hypothermia in the breast unilaterally. These cold areas may represent lipomas or a sympathetic nervous system response. Nerve related findings might be the result of a spinal lesion, local CRPS, or trauma to the breast. Several cases are noted where biopsy trauma created hypothermic temperatures that masked underlying heat. Cold areas also affect the different temperature readings creating a much higher delta T on the opposite side, which may lead to false suspicion. We also identified viscera-somatic reflexes from contralateral pathologies that create a cold area. It is also possible to have similar reflexes from another more remote origin.

Bilateral nipple differences in early studies claim that a difference of 1.0 degree Celsius is considered a risk factor. We believe that any significant difference in nipple temperature is cause for suspicion. Heat from deep within the breast is conducted to the nipple. Some previous authors have separated the temperature difference between the areola and the nipple. The threshold of the areola has traditionally been 1.5 degrees Celsius. Until further mass studies are performed, these differences should be ignored and any heat difference in the areola and nipples should weigh heavily in the Thermologist's assessment. It is common to see hormone expression surrounding the nipple and areola. These findings are typically bilateral and are benign.

The axillary tail of the breast should be inspected very carefully for not only vascular patterns, but lymph node inflammation as well which may be metastatically related to a breast cancer, or an independent lymphoma. Small oval focal points of hyperthermia are pathognomonic for lymph node involvement. Lymph node heat may arise from metastatic origin or a primary tumor.

The axilla itself normally produces increased infrared readings compared to the neighboring breast tissue. This is partly due to its cavity radiator effect as well as being a warmer body area. It is important to note the relative and quantitative temperature differences. There is a

significant difference in temperature with inflammatory breast cancer and other aggressive metastatic cancers.

Inflammatory breast cancer appears as global heat in the breast, but usually starts more locally in the upper outer quadrants. Significant differences in global heat warrant immediate further investigation, while early signs require a short-term follow-up. The traditional threshold of 1.5 degrees Celsius for global heat should be ignored, as this serious disease requires immediate attention at thresholds lower than 1.5C, especially with any symptoms of skin irritation. A case study has been provided for visual clarification (Fig. IBC).

The authors concur that there are an abundance of breast cancer cases discovered with thermal imaging that are not easily detected with mammographic studies. These include inflammatory breast cancers and tumors in body regions hard to visualize with mammographic screening. For example, tumors alongside the rib cage and near the sternum are not easily identified, as well as cancers in women with small or excessively large breasts.

Identifying Breast Tumors with Thermography

NEITHER THERMOGRAPHY nor mammographic screenings are able to diagnose breast cancer. Tissue biopsy is the only method adequate to give a conclusive pathology report. One mechanism of improved accuracy was used in the USSR; it involved injecting a glucose solution into the patient, then waiting 60 minutes for a follow-up exam. This worked much in the same way as injecting radioactive glucose into a PET scan patient. Areas of increased metabolic activity were identified in the patients that were frequently referred for biopsy.

Fibrocystic Breasts

THERMAL PATTERNS INDICATIVE of fibrocystic breasts show extreme mottling patterns throughout the breast and into surrounding

adipose. The delta T of these patients is typically in the 2.0C range, but not usually over 2.5C. Hormonal balancing and lifestyle changes should be implemented resulting in a reduction of the mottling as well as temperature, indicating successful treatment. This underutilized method may be an effective way to prevent cancer. Patients express interest in prevention over cure. More focus on research in this area is required.

Vascular Networks

ANALYZING VASCULAR networks is the most valuable aspect of thermal imaging in detecting breast cancer. Vascular images are like a fingerprint in that they are similar from test to test. Any change in this vascular network creates immediate suspicion upon follow-up baseline comparison. On initial testing, a trained thermologist would be highly accurate in the recognition of suspicious patterns through inverse grayscale imaging. Early thermographers created names for various vascular findings, these included: *Closed Vascular Anarchy, Star Vascular Anarchy, Moya-Moya Sign, Edge Sign, Bite Sign, Transverse Vascular Anarchy, Inferior Vascular Anarchy,* and several more. These were considered *risk factors* and were added to the TH rating.

The trained eye easily identifies abnormal or asymmetrical vascular patterns. These patterns may represent the individual's normal vascularity or neoangiogenesis of a pathological process. Older interpretation methods of vascular risk factors should be studied and used in context of identifying suspicious areas rather than risk assessment. Closed vascular patterns frequently identify underlying cancer with or without high delta T measurements. Serpentine, transverse vascular patterns and star vascular patterns also frequently locate malignancies. The *bulge sign* originates from underlying heat expanding the infrared image outline of the breast, and should be weighed heavily. Many vascular patterns are also the result of a patient's normal thermal imprint and show up more frequently with modern equipment than in previous

years with less sensitive equipment. Some patterns may originate from injuries to the breast. For example, a common benign finding is seen in the lateral breast from seat belt injuries in a car accident.

The authors believe that these patterns in many cases are considered to be suspicious, however more importantly an abnormal pattern is recognized. It is important to recognize normal versus abnormal patterns.

Calcification and DCIS

THERMOGRAPHY DOES NOT use radiation, nor does it test for density in any way, thus, does not detect calcifications present in the breast. Calcifications may be associated with ductal carcinoma in situ, and may be missed in some cases with thermal imaging if there is no associated inflammation or neoangiogenesis. The beneficial aspect to this is that there will be less over diagnosis as cited in the New England Journal of Medicine article of 2012, by Dr. H. Gilbert Welch of Dartmouth Medical School (7), regarding the failure of screening mammography. It is estimated that as many as 50 percent of breast cancer diagnoses are over-diagnosed. Thermography will commonly identify the more serious cases displaying higher vascularity.

Monitoring Temperature Changes

INCREASED DELTA T DOES not always accompany a growing tumor. In some cases, we have seen progressing tumors with lower delta T measurements on follow-up exam. The growth is not linear and may be a result of immune system function, hormone imbalance, or inflammation. The lack of Delta T increase does not guarantee lack of pathology. In case MK-1 (Fig. MK-1) it is apparent that tumor metabolism was not linear.

Metabolic Rate of Cancer

THERMOGRAPHY SCREENING will be predominantly more aggressive with cancers that have higher metabolic rates, and therefore is a better screening test to assess which cancers may be life threatening. A developer of the *No Touch Breast System* commented that their system will be used primarily in India where they do not care about less aggressive forms of cancer like DCIS and will focus more on serious cases.

Metastasis of Breast Cancer

IN ADDITION TO THE diagnosis of breast cancer, thermography is very useful in the detection of regional metastases of cancer, particularly metastatic involvement of axillary and subclavicular lymph nodes. The main factor determining the prognosis of breast cancer is the presence of metastases in regional lymph nodes of the axillary and supraclavicular region. Five-year survival rates of patients without metastases is 82-90%, while with metastases is only 50-70% (8). Current diagnostic testing of these areas is challenging.

The most common method of locating metastases in the axillary lymph nodes and supraclavicular area are fine needle biopsies after palpating a lump. A negative biopsy does not guarantee the absence of metastasis since biopsies do not reveal more than 33% of metastases. (9) A Biopsy is an invasive method, which may increase the risk of dissemination of a tumor. As a result it is recommended that it not be over utilized. Thermography can lessen the use of this harmful and expensive procedure.

Using mammography for diagnosis of metastatic axillary lymph nodes is only 37% effective (5). This is due to poor radiological indicators in early forms of metastases, and the methodological difficulty of obtaining images in the upper part of the axilla. The value of ultrasound diagnosis in this area is slightly better, and excellent when combined with thermal imaging. The assessment of thermographic analysis

of the axilla has a sensitivity of 95%, specificity 88%, positive predictive accuracy of 87.5% and a negative predictive accuracy of 95.6%. (10)

Supraclavicular images should look isothermal in lean patients and may show a small degree of hyperthermia in the medial clavicle due to the concavity of the surface being a cavity radiator. Angling the camera perpendicularly to this area will improve detection of pathology.

In metastatic lesions of the supraclavicular lymph nodes, the images appear hyperthermic and bilateral temperature gradients can reach 2°C or greater. These thermal signs can be detected at the earliest stages of metastasis development when it cannot yet be determined by other available diagnostic methods. A thermogram cannot accurately determine the location of the lesion in the lymph node to puncture, but when it detects such signs, the need for radiation therapy in the postoperative period is warranted.

Baseline Comparison

MANY WOMEN HAVE NORMAL asymmetrical physiology of heat patterns in the breast. Each pattern again is like a fingerprint, and will be similar year after year. At times these patterns are acquired through traumatic origin and a new benign pattern will emerge; however, all new findings should be considered suspect until proven otherwise. It is important to realize that some Thermologists not current in training claim when patterns become "stable", it is a normal thermal variant. In some instances, the delta T values of patients with cancer do not increase, and in some cases may decrease. Whenever questionable patterns are seen, they should be monitored semi-annually until the thermologist is convinced the condition is non-pathological.

Implants and Large Breast Size

PATIENTS WITH LARGE breast tissue size and large implants can decrease the accuracy of thermal screening as the thermographic image

becomes cold and the risk of false-negative findings becomes greater. The heat from deeper lying pathologies does not conduct well enough to be seen as a concern for these women. Lower delta T measurements in these patients should be considered suspicious.

Follow-Up Recommendations

THE MOST IMPORTANT job of the thermologist is to assign proper follow-up intervals. Normal breast studies are evaluated and compared to previous baseline studies annually. Studies with mild questionable patterns should be rechecked in six months with more suspicious cases checked in three months. If IBC is suspected, one month is advised. Women with higher risk factors can be screened every six months including those with extensive fibrocystic findings.

Women under Age 50

RECENT GUIDELINES IN mammography are being challenged for efficacy and safety. Researchers note in the NEJM (7) that over diagnosis is seen in almost 50% of women overall. Other organizations state that mammograms should be reserved for women over 50. This leaves a large percentage of the cancer population to fend for themselves without access to any method of breast screening. 40,000 women under the age of 40 will die from breast cancer each year. This demographic should not be overlooked.

Combining Technologies

COMBINING THE USE OF modalities generates better outcome measurements. We have been working to incorporate sonography with thermography for screening. These tests are both free of radiation and the initial results prove to be very promising.

Keyserlingk (11) and associates published a retrospective study reviewing the relative ability of clinical examinations, mammography, and infrared imaging to detect 100 new cases of ductal carcinoma in situ, stage I and 2 breast cancers. Results from the study found that the sensitivity for clinical examination alone was 61%, mammography alone was 66%, and infrared imaging alone was 83%. When suspicious and equivocal mammograms were combined, the sensitivity increased to 85%. A sensitivity of 95% was achieved when suspicious and equivocal mammograms were combined with abnormal infrared images. However, when clinical examination, mammography, and infrared images were combined, a sensitivity of 98% was reached.

The potential of lowering the rate of false positives on biopsy is favorable with thermal imaging. All BiRad 3 and 4 mammograms should be thermally screened prior to the decision for biopsy. If Bi-Rad 3 findings were hyperthermic, the need for biopsy would be indicated. If a Bi-Rad 4 were not hyperthermic in the area of significance, then this would not indicate the need for biopsy at that time. This approach has been tested on small samplings of women and requires a larger study design.

Conclusions

THE IMMEDIATE IMPLEMENTATION of thermography into the arena of breast cancer screening is obvious. Evidence based research shows it is drastically needed to reduce the mortality rate of breast cancer as well as false positive rates and thus the over-diagnosis found with mammography.

This combination of technologies would have an enormous reduction on the expense on healthcare in the area of biopsy and unnecessary surgeries. Previous biases to this method with older technologies need to be abandoned and physicians should become more familiar with this non-destructive form of testing to better serve their patients.

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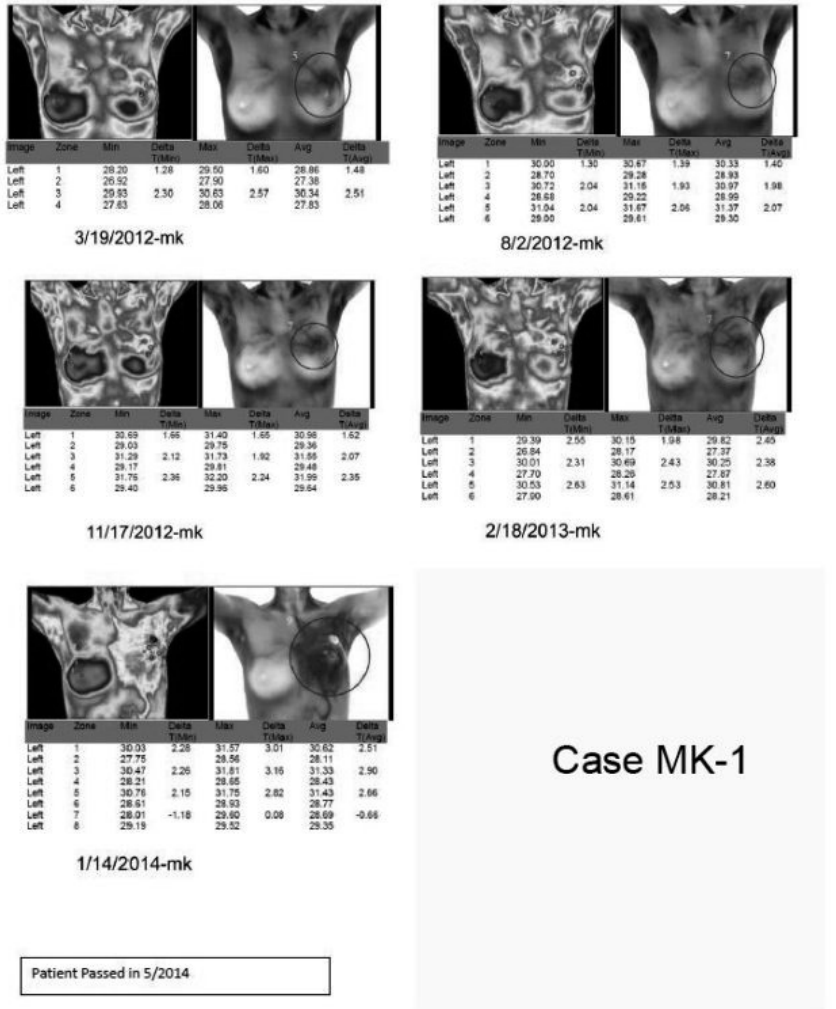

Fig. MK-1 Patient had a lumpectomy in 2009. The cancer returned and was seen on thermal imaging in March or 2012. The first annual re-exams were relatively unchanged. The fast progression was seen in January 2014.

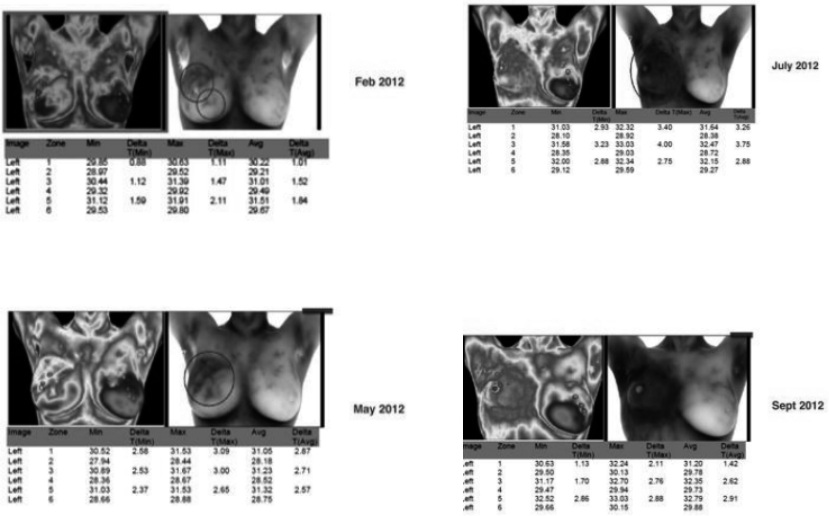

FIG. IBC- THIS IMAGE shows the progression of a patient with early thermal signs of Inflammatory Breast Cancer in Feb and a progression until September. The patient passed away in January 2013.

THERMOGENIC RESPONSE TO THE GROWTH OF SKIN TUMORS

Alexander Sepper, Anthony Piana

Abstract

Screening for Skin Cancer using thermal imaging has been sought after by many thermologists. This study uncovers research performed in the former Soviet Union in the diagnosis of skin cancer. An attempt to not only screening for the existence of a skin lesion was made, but also to classify as malignant. Conclusion The detection of skin tumors was effectively identified in 98.6% of the subjects. The ability to differentiate malignant versus benign tumors was 86.3%. The use for the identification and diagnosis of skin tumor pathology is accurate to use adjectively for general skin cancer identification. Discussion The day when every dermatologist has a small compact digital thermal camera should not be far off. Since every suspect skin lesion can not be sent for biopsy, the use of thermal imaging in a clinical setting is paramount.

Clinical and experimental research in oncology and thermal imaging found that the formation of thermogenic response to growth of skin tumors is mainly due to two factors: convective heat transfer by skin blood vessels and conductivity of tissue layers. Since the layer of subcutaneous fat tissue has prominent "shielding" properties to infrared radiation, the primary role in the transfer of heat from the tumors beneath the skin has a convective transmission. In regard to thermal imaging studies of superficial tumors, in addition to registering thermogenic manifestations of convective reactions, it is possible to analyze the "true" temperatures of tumors. Morphological studies of skin tumors identified a number of areas differing in intensity of the microvasculature: I - necrotic area without vascularization, II - semi-

necrotic area with few capillaries, III - area of stable microcirculation, IV - border zone penetrating and contacting with normal tissues, and V - area of normal tissue.

It is clear that the character of thermogenic skin reaction depends on the grade of microcirculatory processes. Zones of necrotic changes and poor vascularization will be presented on thermograms as hypothermic local entities which are transferred to the periphery into the isothermal background of surrounding tissues with normal microcirculation. At the same time, it should be noted that the detection of the mentioned hypothermic zones may depend on the size and extent (area) of tumors and formation of necrotic hypo-circulation processes. In cases of their non-significant grade, local hypothermia may not be detected. However, the formation of the thermovisual structure of the superficially located tumors, as has been observed, also depends on their geometrical shape. In objects of hemispherical shape with a curved surface, the process of thermoemission is outperforming the thermoemission of objects with a straight (flat) surface. In this regard, tumors protruding above the surface of the skin may be presented as localized hypothermic formations. Tumors with flattened shape in absence of large necrotic areas are identified on thermograms as foci of increased thermogenic activity. In many cases, the secondary inflammatory process associated with a sharp increase in the thermogenic activity of tissues may develop in and around the tumor. In such cases, the thermovisual structure of the skin has a contrast character of hypothermic local areas surrounded with hyperthermic perifocal zones of different lengths, reflecting the severity of the inflammatory reaction. Often the marked hyperthermia "covers" the low thermogenic activity of tumor sites themselves. There are observations when with morphologically proven absence of inflammatory changes in neoplasms, there are defined zones of enhanced thermogenic activity on thermograms and the intensity of infrared luminescence is considerably expressed in malignant tumors. Evidently, in such cases there is a reactive increase in in-

frared emission of surrounding tissue intact when the temperature increases in response to atypical metabolic and circulatory processes. Criteria for Qualitative Analysis of Thermal Information: the nature of the thermal structure is visually assessed. The presence of atypical foci of increased or decreased luminosity and perifocal thermal formations, their shape, homogeneity, dimensions and outlines are determined.

Criteria for Quantitative Analysis of Thermal Information:

1) The ratio of the perimeters of atypical thermal areas on the thermograms and tumors themselves (P1)

2) The ratio of the perimeters of perifocal reactive zones on thermograms with those around the tumors in patients (P2)

3) The value of temperature difference of "Local Thermal Area - Intact Tissue Zone" (T1)

4) The value of temperature difference of "Perifocal Thermal Area - Intact Tissue Zone" (T2)

The data of thermal analysis and thermovisual diagnostics are compared with the results of clinical and laboratory studies and in the case of surgical treatment are verified by histological analysis of the surgical specimens.

GLYCEMIC LOADING PROCEDURE: Patients are studied before and 30 minutes after intravenous administration of 20 grams of a 40 percent solution of glucose, taking into account the history of diabetes and blood glucose levels.

MALIGNANT TUMORS

Type	Qualitative Analysis of Thermal Information	Quantitative Analysis of Thermal Information
IA	Before glycemic load: the formation of non-homogeneous clearly contoured atypical localized areas of increased thermogenic activity that are detected on the relatively isothermal background of surrounding tissues.	P1 = 1.5 : 1 T1 = +1.3-1.6°C After glycemic load the ratio of P2 can increase to 2:1; T1 to +1.5-2.0°C
IB	Before glycemic load: marked hyperthermic local areas are surrounded with perifocal zones of enhanced infrared emission	P1 = 1.5:1 P2 = 2:1 T1 = 1.0-1.5°C T2 = +2.5-3.0°C After glycemic load the ratio of P2 can change to 2.5:1, T1 to +1.5-2.0°C, T2 to +2.9-3.3°C
II	Formation of atypical areas of irregular non-homogeneous decrease of thermogenic activity surrounded by perifocal zones of hyperthermia	P1 = 1:1 P2 = 1.5:1 T2 = +2.5-3.0°C After glycemic load the ratio of P2 can change to 5.5:1, T2 to ++3.2-3.5°C
PS	In addition to these types it is possible to obtain characteristic for melanoma thermostructure - the presence of atypical hyperthermic area and the formation of hyperthermic perifocal zone in the form of a "flame" with the top forwarded to the proximal direction of the limb	P1 = 1.5 : 1 P2 = 2.5:1 T1 = +3.5-5.0°C T2 = +2.5-3.0°C Test of glycemic load usually increases these numbers

THERMOSEMIOLOGY OF SKIN NEOPLASMS

BENIGN TUMORS

Type	Qualitative Analysis of Thermal Information	Quantitative Analysis of Thermal Information
IA	Before glycemic load: the formation of various forms of atypical local hypothermic areas with variable size and homogeneity, quite clearly contoured on a relatively isothermal background of the surrounding tissues. After glycemic load thermal characteristics do not change.	P1 = 1 : 1 T1 = 1.0-1.5°C
IB	Before glycemic load: the formation of various forms of atypical local hypothermic areas with variable size and homogeneity, surrounded with non-homogenous hyperthermic zones turning into the isothermal background of the surrounding tissues.	P1 = 1:1 P2 = 1:1 T1 = 1.0-1.5°C T2 = 2.0-2.5°C (if perifocal inflammation is present); +1.0-1.5 (in case of reactive hypertermia). After glycemic load the ratio of P2 can change to 1.5:1
II	Before glycemic load: the formation of homogeneous clearly contoured atypical localized areas of increase thermogenic activity that are detected on the relatively isothermal background of surrounding tissues. After glycemic load thermal characteristics do not change.	P1 = 1:1 T1 = +0.5-1.0°C

DISCUSSION

The shown above figures are based on an analysis of 376 thermograms of patients with benign and malignant tumors of the skin. According to our data the efficiency of the method of thermal imaging in the detection of skin tumors was 98.6% and in the differential diagnosis of benign and malignant nature of the disease in 86.3%. The erroneous conclusions of the differential diagnosis are accounted for false-positive results. This is primarily due to the similarity of qualitative indicators of thermographic types of benign and malignant forms of skin tumors. In this regard, for the implementation of thermal differential diagnosis, we have to first be guided by quantitative criteria of thermo-information analysis. In addition, it is important to use the application of active thermography techniques with the test the glycemic load. The formulation of thermal imaging diagnosis requires comparison of the infrared data with the results of clinical and laboratory observations.