CLINICAL EVALUATION REPORT

prepared by

Jusko Peter, ONKOCET Ltd., Bratislava, Slovakia

Vesnin Sergey, RES Company, Moscow, Russia

GENERAL DETAILS

IDENTIFICATION OF MD:

Microwave Radiometer-Internal Temperature Diagnostic Computerized Imaging System RTM-01-RES

The Commission on Devices and Technical Support of Oncology and Medical Radiology of the Committee on New Medical Techniques of the Ministry of Public Health and Medical Industry of the Russian Federation recommends (4th Juny 1998) the serial production and the use of the radiometers, developed by RES Ltd., in medical practice. The refined name of the radiometer is "The RTM-01-RES computer based radiometer for measuring the integral internal temperature of soft and bone tissues."

Д –В. Code- 94 4125 0003. Code – ОКДП (ОК 004-93) 3311222.

КЧ – 04.

Name – RTM-01- RES Medical Radiometer

ID Number - ТУ 9441-001-39549185-98 (ДКТП.942232.001 ТУ)

PATENT: the scheme of the device is protected by RF patent № 2082118 and application number № 205133624/14 (037 633) from 31.10.2005.

PATENT: №2306009 Name Antenna-applicator for non-invasive temperature measurement of internal tissues of a biological object.

PATENT: №2407429 Antenna-applicator and apparatus for determining the internal temperature changes of biological tissues and methods for determining the object temperature changes and detect the risk of cancer.

PATENT: №2510236 Antenna-applicator and apparatus for determining the internal temperature changes of biological tissues of an object by measuring the brightness of simultaneous non-invasive internal tissue temperature at various depths.

INTERNATIONAL APPLICATION: PCT/RU2009/000694 Antenna-applicator and apparatus for determining the internal temperature changes of biological tissues and methods for determining the object temperature changes and detect the risk of cancer.

In accordance with the Order of the Ministry of Health and Social Development of the Russian Federation № 744 of December 1, 2005 radiometry breast "is included in the standard of care of patients with malignant neoplasm of the breast, A05.20.002 code.

PRODUCER OF MD:

RES Company Ltd., placed by address: Bolshaya Pochtovaya 22, Moscow, 105082, Russia (Certificate Holder of the EC Certificate No. 09 0918 QS/NB, in process of recertification)

In 1997 RES, Ltd. under the All-Russian Research Institute of Radio Engineering developed the RTM-01-RES microwave computer-based radiometer. The system includes a microwave sensor to non-invasively measure the temperature of internal tissue and a non-contact infrared sensor to the measure skin temperature. Information about the skin temperature allows to obtain more reliable results

The device is manufactured and sold by RES, Ltd. (22, Bolshaya Pochtovaya, Moscow, 107082, Russia). First EC verification of radiometer on the requirements of the Directive 93/42/EEC has been carried out by NB 1293, which issued in February 09th, 2006 EC Certificate No. 40028/101/1/2005/CE. In 2007 Australian Therapeutic Goods Administration issued Certificate for inclusion of a medical device (ARTG No.: 141979) Microwave radiometer RTM-01-RES in the Australian Register of Therapeutic Goods. In 2009 EU Representant company Onkocet Ltd., applied for new recertification. The Notified Body No. 1023.

Today microwave radiometer RTM-01-RES is in service at 30 countries, in Russian Federation radiometer is using in 308 medical centers.

PEFERENCES

1	Directive 93/42/EEC, as amended by Directive 2007/47/EC	Concerning medical devices
2	MEDDEV 2.4/1 Rev. 9 June 2010	MEDICAL DEVICES: Guidance document - Classification of medical devices
3	MEDDEV 2.7.1 Rev. 3 December 2009	CLINICAL EVALUATION: A Guide for Manufacturers and Notified Bodies
4	ISO 14971:2012	MEDICAL DEVICES – application of risk management to medical devices
5	ISO 14155-1:2003/GOST R ISO 14155-1-2008*	Clinical investigation of medical devices for human subjects – Part 1 General requirements
6	ISO 14155-2:2003/GOST R ISO 14155-1-2008*	Clinical investigation of medical devices for human subjects – Part 2 Clinical investigation plan
7	MEDDEV 2.7/4 December 2010	Guidelines on Clinical investigation: A Guide for Manufacturers and Notified Bodies
8	MEDDEV 2.12/2 May 2004	Clinical Evaluation – Post Market Clinical Follow-up
9	World Medical Association	Declaration of Helsinki – Ethical principles for medical research involving human subjects

*Russia: Russian Ministry of Health Roszdravnadzor – ISO 14155 was included in Russian system of standards only in 2008.

ROUTE OF CLASSIFICATION

Microwave radiometer RTM-01-RES is Active Medical Device IIa class according the Rule 10 Annex IX Sect. I clause 1.4 of the Directive 93/42/EEC

DESCRIPTION OF DEVICE AND ITS INTENDED APPLICATION

a.) Description of device: Microwave radiometer RTM-01-RES techniques involve the measurement of the passive electromagnetic thermal radiation emitted from human body using suitable combination of microwave antenna internal temperature sensor (ITS) and infrared surface temperature sensor (STS), with an appropriate configuration to determine the temperature profile of the concerned area of the body. Microwave radiometry principles can be employed to obtain sensor information from subcutaneous tissues up to a few centimetres in depth. Briefly, the essential basis for developing a microwave imaging technique is the significant contrast in the dielectric properties, at microwave frequencies, of different tissues. The depth of penetration depends on the wavelength, the dielectric properties and the water content of the tissue.

Principle of Radiometer RTM-01-RES

Radiometers have constructions similar to receivers used in communication, radar and wireless local area network. The RTM-01-RES device is a modulated null balancing radiometer with a slipping circuit for

compensating reflection between the biological object and the antenna. The used wavelength is 8 cm. The scheme of the device is protected by the patent of the Russia Federation [Patent РФ № 2082118, 1994].The functional scheme is illustrated in Fig. 1.

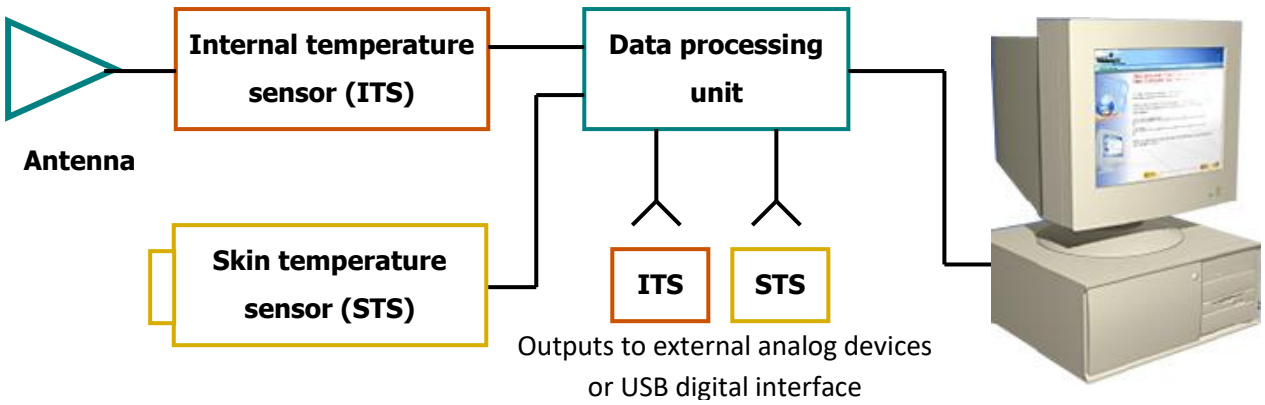


Figure 1. Functional scheme of RTM-01-RES

When the temperature is measured, the antenna's position on the patient's skin is in accordance with the computer diagram of the examined organ. The antenna receives microwave radiation from the examined organ as noise at microwave frequencies and the signal is amplified in ITS.

Passive Microwave Remote Sensing

Infrared (IR) thermography together with microwave radiometers belongs to passive remote sensing systems that measure the natural radiation emitted by objects. If an object is in thermal equilibrium with its surroundings, it emits all the energy that it absorbs. A perfect absorber that does not reflect any energy is known as a "blackbody".

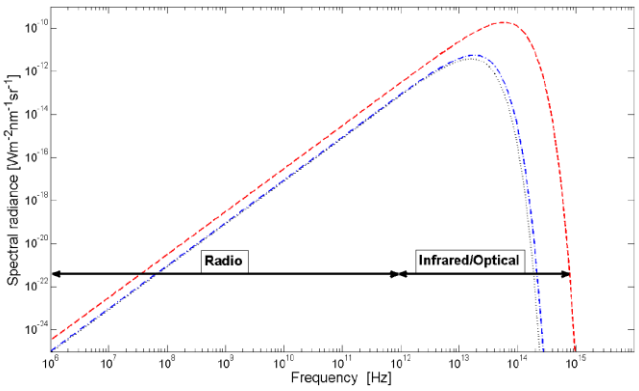


Figure 2. Black body radiation at 273 K (black line), 310 K (blue line) and 1000 K (red line) for the radio and infrared/optical frequencies.

If an ideal receiver of bandwidth B were to measure the power radiated by a blackbody, the received power would be equal to:

$$\mathbf{P = kT\ B} \qquad (1.1)$$

where **k** is Boltzmann's constant and **T** is the physical temperature of the blackbody in Kelvin. On the other hand, radiated power by a non-absorbing material (i.e. a perfect conductor) would be zero. The materials in real life fall in between these two extremes; hence, the power radiated by them is bounded by 0 and kT B at a certain temperature T. Therefore, if **P** is the power radiated by the object and **B** is the bandwidth of the receiver again, an equivalent temperature called the "brightness temperature" (TB) can be defined as:

$$\mathbf{T_B = P / kB} \qquad (1.2)$$

If external calibration techniques are not present, the power measured by a receiver is also affected by its

antenna's radiation pattern. In that case, the ratio measured in Equation 1.2 is called the "antenna temperature" rather than the brightness temperature. The ratio of the brightness temperature of an object to its physical temperature is called the "**emissivity**" (ε) which has a value between 0 for a non-absorbing medium and 1 for a blackbody:

$$\varepsilon = T_B / T \qquad (1.3)$$

Emissivity (ε) is a parameter used to indicate the ability of a body to emit heat radiation. Emissivity of all other bodies is given relative to the emissivity of a black body, which is set as 1. Although infrared radiation emitted from the surface of a human body ranges from 3-50 μm, maximal emission occurs around 8 to 10 μm with a peak at 9.3 μm

Radiation of biological object

Living organism including human represents build up heterogeneous scaffold designs by selectively adding cells that represents tissue complex of three-dimensional structu. Our intuitive daily experience notice that our hair falls out regularly, we donate blood or give blood samples without gradually draining our circulatory system. All of these examples point to a replacement rate of cells, that is characteristic of different tissues and in different conditions, but which makes it abundantly clear that for many cell types renewal is a part of their story. Normal cell proliferation in tissues is controlled by the availability of growth regulating factors and by the interaction with surrounding cells. The availability of nutrients and oxygen are necessary for cell proliferation and metabolism.

cell type	turnover time
small intestine epithelium	2-4 days
stomach	2-9 days
blood Neutrophils	1-5 days
white blood cells Eosinophils	2-5 days
gastrointestinal colon crypt cells	3-4 days
cervix	6 days
lungs alveoli	8 days
tongue taste buds (rat)	10 days
platelets	10 days
bone osteoclasts	2 weeks
intestine Paneth cells	20 days
skin epidermis cells	10-30 days
pancreas beta cells (rat)	20-50 days
blood B cells (mouse)	4-7 weeks
trachea	1-2 months
hematopoietic stem cells	2 months
sperm (male gametes)	2 months
bone osteoblasts	3 months
red blood cells	4 months
liver hepatocyte cells	0.5-1 year
fat cells	8 years
cardiomyocytes	0.5-10% per year
central nervous system	life time
skeleton	10% per year
lens cells	life time
oocytes (female gametes)	life time

Table 1: Cell renewal rates in different tissues of the human body.

Metabolism is the set of life-sustaining chemical transformations within the cells of living organisms. The three main purposes of metabolism are the conversion of food/fuel to energy to run cellular processes, the conversion of food/fuel to building blocks for proteins, lipids, nucleic acids, and some carbohydrates, and the elimination of nitrogenous wastes. These enzyme-catalyzed reactions allow organisms to grow and reproduce, maintain their structures, and respond to their environments. The word metabolism can also refer to the sum of all chemical reactions that occur in living organisms, including digestion and the transport of substances into and between different cells, in which case the set of reactions within the cells is called **intermediary metabolism** or **intermediate metabolism**.

Metabolism is usually divided into two categories: catabolism, the *breaking down* of organic matter, for example, by cellular respiration, and anabolism, the *building up* of components of cells such as proteins and nucleic acids. Usually, breaking down releases energy and building up consumes energy.

The chemical reactions of metabolism are organized into metabolic pathways, in which one chemical is transformed through a series of steps into another chemical, by a sequence of enzymes. Enzymes are crucial to metabolism because they allow organisms to drive desirable reactions that require energy that will not occur by themselves, by coupling them to spontaneous reactions that release energy. Enzymes act as catalysts that allow the reactions to proceed more rapidly. Enzymes also allow the regulation of metabolic pathways in response to changes in the cell's environment or to signals from other cells.

Normal proliferating mammalian cells, which are exposed to a continual supply of oxygen, glucose and other nutrients in circulating blood generate the energy needed for cellular processes throgh mitochondrial oxidative phosphorylation. Glucose metabolism is a primary source of energy and biomaterials for the

maintenance of life. In the first rate-determining step of the metabolism, glucose is transported across the plasma membrane by the facilitative glucose transporter (Glut) down its concentration gradient. Hexokinase (HK) on the mitochondria then phosphorylates glucose to glucose-6-phosphate (G6P). The product generally enters the glycolytic pathway, generating NADH, ATP, and pyruvate, or the pentose phosphate pathway (PPP). In the presence of sufficient oxygen, pyruvate from glycolysis can be fed into mitochondria and fully oxidized to produce more ATP. When oxygen is limited, however, pyruvate is disposed in the form of lactate and glycolysis becomes the main source for ATP production [1]. PPP plays an important role in the synthesis of nucleic acids for DNA and RNA, as well as generation of NADPH for the synthesis of lipids and maintenance of intracellular redox homeostasis.

To produce two viable daughter cells at mitosis, a proliferating cell must replicate all of its cellular contents. This imposes a large requirement for nucleotides, amino acids, and lipids. During growth, glucose is used to generate biomass as well as produce ATP.

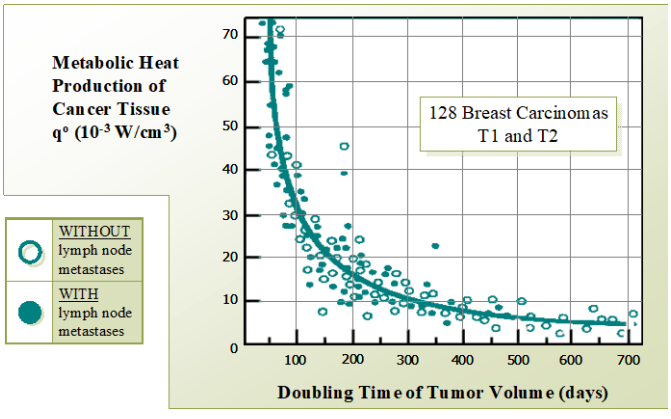
In 1930s, Otto Warburg observed altered metabolism in cancer cells. In 1956, Otto Warburg [2] originally described his observation that cancer cells exhibit high rates of glucose uptake and lactic acid production. By using Warburg manometer, Warburg and his colleagues found that cancer cells did not consume more oxygen than normal tissue cells, even under normal oxygen circumstances [3], and it seemed that cancer cells preferred to aerobic glycolysis than to oxidative phosphorylation. After more than half century's research, the Warburg effect stands true for most types of cancer cells.

Due to uncontrollable growth, the metabolism of cancer cells, like all proliferating cells, have to be adapted to facilitate the uptake and incorporation of nutrients into the biomass that are needed to produce a new cell: amino acids for protein synthesis, nucleic acids for DNA duplication, and lipids for cell biomembrane synthesis. Alternatively, cancer cell adopting glycolysis is to gain growth advantages as compared with normal cells: glycolysis provides acidic environment, which is harmful to normal cells but has no effect to tumor cells [4], underlining the importance of glycolysis as a cellular defense mechanism for cancer cell growth.

Cancer cells are different from most normal tissues in the energy metabolism and they take up glucose and glutamine at a high rate for aerobic glycolysis. It is widely accepted that glucose is the dominant energy fuel for most cancers. Uncontroled growth of cancer cell on the one hand is conected with high consumption of glucose and on other hand degradation of glucose is accompanied with large production of heat.

As when the cancer grows rapidly, energy consumption increases and so heat generation rises. This relationship is shown in Fig. 3

Fig.3



Therefore most of dangerous tumors (tumors with short DT) can be detected by thermal methods first of all. It means that thermal methods allow to select patients with rapidly growing tumors. According to current data these patients are a quarter of breast cancer patients.

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Heat **Transferring in the Bio-object**

Heat transfer within breast tissues. The best explanation of heart transfer was made by Gautherie. Therefore I will quote his work [7]. According to

M. Gautherie "temperature and blood flow pattern in cancerous mammary tissues", result from two phenomena: heat transfer from the cancer into the surrounding tissues, and vascular reactions.

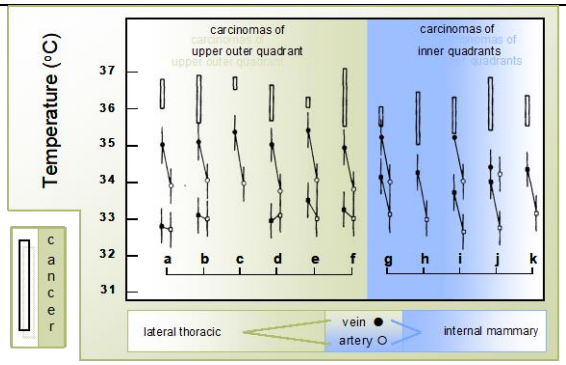
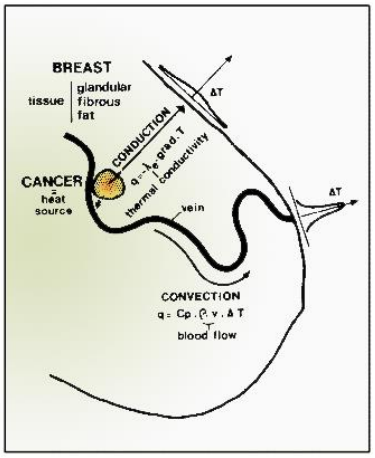


Fig. 4 *Tumor and blood temperature in breast carcinomas. An example of a series of measurements of tumor temperature and venous and arterial blood temperature taken during surgical management (mastectomy) of mammary carcinomas with various localizations. Measurements were carried out by means of thermometric fine-needle probes, five times for each temperature (the vertical segment indicates standard deviation from the mean value). In all cases investigated, tumor temperature was significantly higher than blood temperature, and venous blood temperature was higher than arterial blood temperature.*

Heat transfer occurs by tissue conduction as well as blood convection. However, from the physiologic viewpoint, it seems to be more appropriate to distinguish between the two following processes (Fig. 5): 1) "effective" conduction, including conduction in the physical sense (Fourier's law) and convection by the capillary vessels assumed to be distributed isotropically (see above); 2) convection through the relatively large vessels, the veins essentially, according to Newton's law. It is noteworthy that maximal capacity of heat transfer by convection through large vessels is much higher than by tissue conduction and capillary convection, up to 100 times, approximately. Nevertheless, the relative contribution of the various processes depends on the actual vascularization, which is largely different from one breast to the other, particularly under malignant conditions. Furthermore, conduction of_heat is easier along the galactophorous ducts as was demonstrated by intramammaryjnea-surements too. This anisotropy of thermal conductivity may explain the relative hyperthermia of the nipple observed in some carcinomas, depending on tumor_localization.

Fig. 5.

Breast thermokinetics. The metabolic heat produced by the tumor is transferred to the surroundings tissues, particularly towards the skin, through two pathways: 1) by conduction and capillary convection according to Fourier's law (the quantity of heat transported is a function of the thermal conductivity (λe), which depends on the type of mammary tissue either glandular, fibrous or adipous); 2) by convection by large vessels according to Newton's law (the quantity of heat transported is a function of the blood flow; Cp., heat capacity; P, density; v, rate of blood). Through these processes of heat transfer, as well as from vascular reactions, increase in skin temperature (ΔT) is generally associated with cancer.



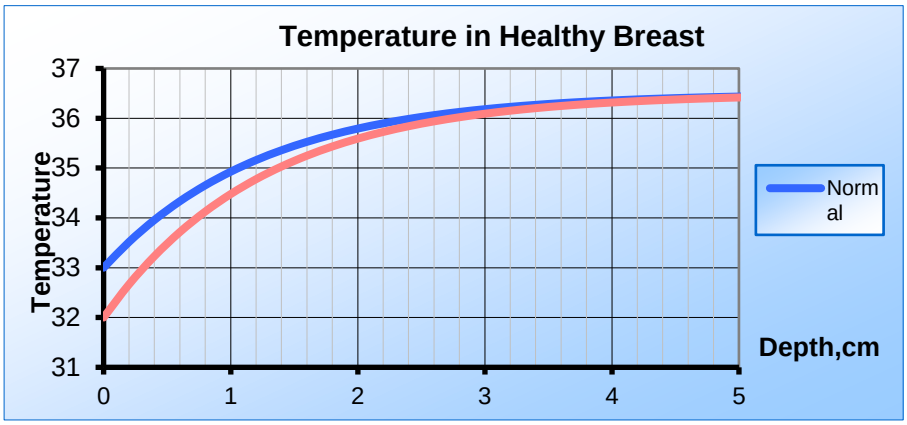
Temperature Pattern in Human Tissue

In some parts of a human body the temperature is constant due to homeostasis. This temperature is approximately equal to the temperature measured in axial, oral and rectal areas (36.5°C – 37.0°C). The central nervous system, thorax organs, the abdominal area, all have a constant temperature.

When the room temperature is 20-25°C the skin temperature lowers to 32-33°C so there is a temperature gradient between the skin temperature and the internal temperature.

This temperature gradient and its dynamics, depending on room temperature, are shown in Fig. 6.

Fig. 6



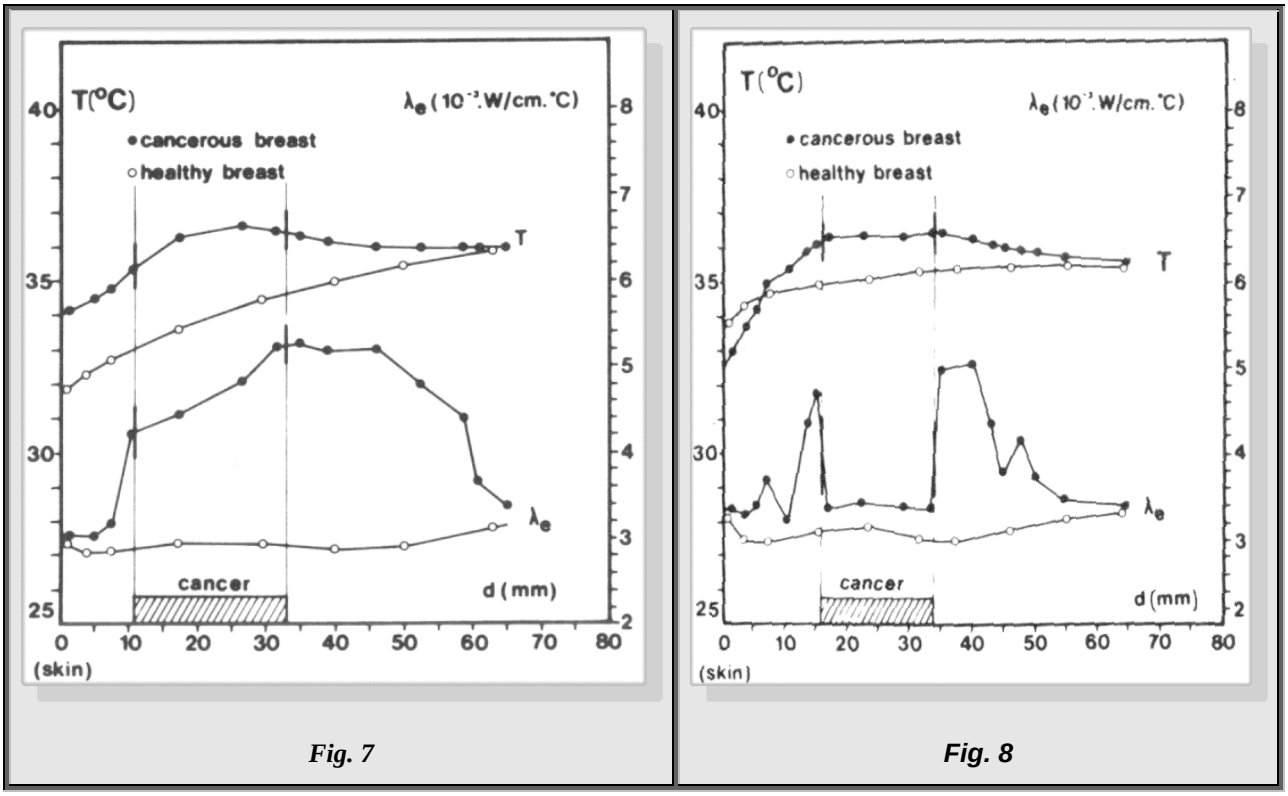


Fig. 7 *Fig. 8*

Fig.7 shows results obtained by Gautherie [7] with the help of fine-needles.

We can see that the temperature in cancer is three degree higher than the temperature in the healthy breast. In this example the skin temperature near the tumour is 2 degree higher than the skin temperature in the healthy breast too.

Also, Gautherie published the diagram, when the skin temperature near the tumour is less than it is in the healthy breast (Fig. 8).

Cancer cell temperature.

Cancer cells produce increased amounts of thermal energy.

This fact is confirmed by the researches of the French scientist M. Gautherie, which was held for 16 years. Based on clinical data 85000 patients clearly demonstrated that the dissipation of the tumor is directly proportional to the speed of its growth. Based on the results of his research, he showed that fast growing tumors with low doubling time are characterized by high specific heat, due to the fact that with the rapid development of tumors increased energy consumption, and the temperature rises. Gautherie in [5] published his data of the cancer. These data you can see in Fig.8.

On the base of these data we have written a very simple equation of the tumour temperature.

$$T = k \cdot \frac{R^2}{D_T} \cdot B \text{, where}$$

k – constant, **R** – tumour radius, $\mathbf{D_T}$ – doubling time of the tumour, **B** - BIOT'S number.

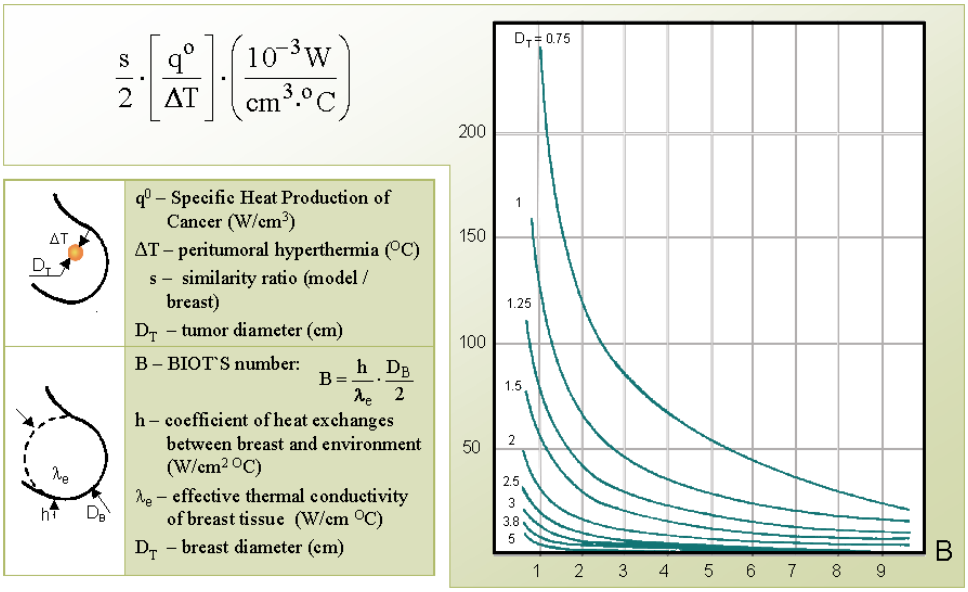


Fig. 8. *Rheoelectric simulation of heat transfer conditions in cancerous breasts: Experimental chart giving the specific heat production of cancer tissue (q^0) versus peritumoral hyperthermia (ΔT = temperature difference between the periphery of the tumor and the symmetrical area on the contralateral healthy breast), Biot's number (B), and tumor diameter (D_T). These curves, fitted by hand from the analog model of heat transfer, allow direct evaluation of q^0 from measurements of geometric parameters on mammography (s, D_T, and D_B), and thermal parameters (ΔT and λ_e). On account of the ranges of variations of λ_e and D_B, q^0 does not depend on tumor depth. The coefficient h may be assumed to be constant and equal to 1 x 10^{-3} W/cm²/ °C under controlled conditions (room temperature at 21 ± 1°C, no air draughts).*

Electromagnetic Radiation from Heated Objects

According to the law of physics, any object above zero degrees Celsius emits radiation at all frequencies and, in particular, in the microwave region, that is used in microwave radiometry.

This feature of heated objects is used for measuring averaged internal tissue temperature and detecting thermal abnormalities (higher or lower temperature of internal tissue).

The noise power received by the antenna contacted an evenly heated absorbing object is:

P= kT Δf , where

k - Boltzmann's constant (1.38 x 10^{-23} Dg/°K)

Δf - System bandwidth,

T – Temperature of the biologic object

Therefore the power noise received by the antenna is proportional to the tissue temperature.

When the object temperature is 309°K, i.e. 36°C the noise power received by the antenna is 3x10^{-13} Watt. This value corresponds with the noise generated by the antenna. Special methods are applied for receiving and processing signals.

Propagation of Electromagnetic Waves in The Body

Bio-objects usually examined consist of several layers (e.g. skin – fat – muscle). The radiation power passes through all parts of tissue with different losses and different temperatures, so the temperature measured by the antenna is not equal to the physical temperature of the examined organ, but depends on the temperature of other parties of the body and losses in these parts.

The exponential law of distribution describes propagation of plane waves in the body.

$$P = P_0 \cdot \exp^{-G \cdot z}; \qquad G = i\beta + \alpha$$

where α- attenuation per unit in environment

β- propagation factor of electromagnetic wave;

$\mathbf{P}_0$ – input power

The attenuation per unit in tissue depends on the water content of tissues. The tissues may be divided into two groups. The first group includes low water content tissue, which is represented by fat and bone. The attenuation per unit of the tissue is low. It is 20-30% (0.5-0.7dB/cm).

The attenuation per unit of skin and muscle (high water content tissue) is greater. It is about 50% (3 dB/cm).

For infrared, bio-tissue is not transparent thus radiation attenuates at a depth of several microns.

Brightness Temperature

The power of radiation from all tissues passes through layers with different losses and different temperatures, so the temperature measured at the output of the antenna is not equal to the physical temperature of the investigated organ. This temperature depends on temperature of several layers of the body and losses in these layers.

This measured temperature is called brightness temperature. The brightness temperature is the averaged temperature in volume (cylinder) under the antenna. The diameter of the cylinder is 5 cm; the depth is 3-7 cm, depending of water content.

Fig. 10 shows the area in which RTM measured the temperature.

We can sea that 30% of energy is placed in the volume 16cm^3. The size of the area is 3 x 2 x 3 cm, 70% of energy is placed in the volume 120cm^3. The size of the area is 3 x 2 x 3cm.

Widths of Antennas

ENERGY	Dx_0, cm	Dy_0, cm	Dx_{max}, cm	Dy_{max}, cm	Z_{max}, cm	V, cm^3
11,0	2,0	1,7	2,0	1,7	8,0	1,5
20,8	3,0	4,2	3,0	4,2	15,0	6,0
30,8	3,5	4,5	3,5	4,5	22,0	15,8
40,1	3,5	5,4	3,5	5,4	30,0	32,9
48,9	4,0	6,5	4,0	6,5	39,0	64,3
58,6	4,5	8,7	4,5	8,7	49,0	133,6
70,6	6,0	15,4	6,0	15,4	74,0	321,4
78,8	8,0	15,1	8,5	15,5	94,0	616,9
92,6	14,0	14,2	14,0	15,5	120,0	1991,0

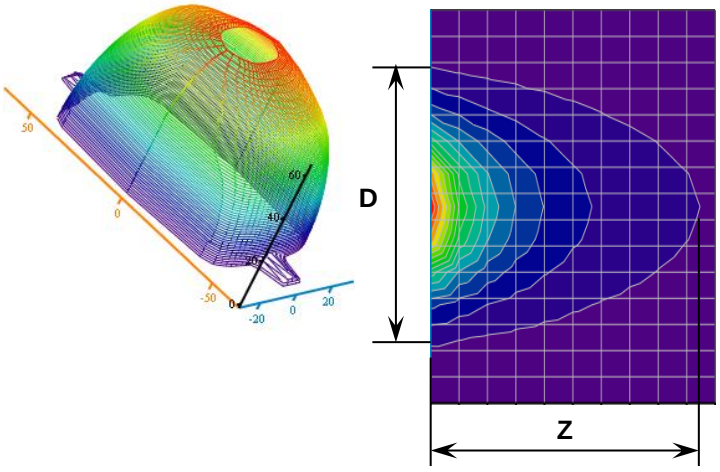


Fig. 9 *Energy distribution*

Also, Fig. 9 shows that the measured volume is rather large. That's why breast RTM-examination very often reflects lung inflammation (especially if the breast is small)

Device Structure

Fig. 10 RTM-01-RES
microwave computer based system

In 1997 RES, Ltd. developed the RTM-01-RES computer based microwave radiometer. The system is shown in Fig. 10.

RTM-01-RES is safe and simple in operation. It does not require a calibration procedure and is always ready for measurements.

The system consists of the following items:

- Internal Temperature Sensor with the antenna (ITS)
- Skin Temperature Sensor (STS)
- Data Processing Unit (DPU)

The system includes a personal computer and a printer. The device is connected to a PC through a serial port. The results of RTM-diagnosis are shown on the monitor of the computer or printed as a thermogram and temperature field on the projection of the investigated organ.

The advantage of the method is the expert system for breast cancer detection. The expert system analyzes several parameters, including thermal asymmetry, dispersion of the temperature within the breast, etc.

b.) Intended application: The device based on the microwave radiometry principles can provide an early inflamation or cancer detection/warning technique that is simple and quick.

INTENDED DIAGNOSTIC INDICATIONS AND CLAIMS

The RTM method captures changes of temperature inside the soft and hard tissues and on the skin surface that reflect functional processes in many organs of human body. Device is intended for noninvasive detection of inflamation processes and cancer depending thermal changes.

Diagnostic indication:

- Inflamation of any organs and tissues
- Cancer of any organs and tissues

CONTEXT OF THE EVALUATION AND CHOICE OF CLINICAL DATA TYPES

Microwave thermometry (MWR) was developed in the 1940s as a technique for sensing thermal emission, with applications in radio astronomy and remote sensing of the earth and its atmosphere. Its application in medicine was first proposed in early 1970s (see reviews in Gautherie[1] and Ryan[2]) when a contacting waveguide antenna was employed to couple MW radiation emitted by tissue into a comparison or "Dicke" radiometer working at a central frequency of 3.3 GHz. In the same period, a millimeter-wavelength scanning system employing a remote dish antenna was used to study images of superficial thermal distributions. Originally, the primary application envisaged was in

screening for breast cancer. Then this technique was applied to a wide range of pathologies with associated elevated temperature, such as joint inflammation or rejection of a kidney transplant. More recently, the technique has been investigated for monitoring hyperthermia treatments.

The principle of MWR diagnostics was based on the detection of small temperature changes (range, 0.1-1.8°C) due to increased cancer-cell metabolism. [3]

Theoretical basis of MW: Temperature resolution

It is known that in the MW region where $\nu << kT/h$, Planck's expression for power emitted from a black body can be approximated by the Rayleigh-Jeans expression: [1]

$$P = 2kT\,\nu^2/c^2, \qquad (1)$$

that is, in the MW region, the power emitted by a black body is proportional to its physical temperature T. Hence, me interpretation of external measurements in terms of internal temperature distribution and calibration procedure is potentially easy, compared with that in the IR range, where at recording integrated radiation in relatively broad-spectrum signal is proportional to T^4 according to Stephan-Boltzmann's law. The internal temperature is measured by contacting a patient's skin with the antenna at the point of the organ under investigation or of its part projection. Noise signal power at MW frequencies received by the antenna in the first approximation is calculated as[1]

$$P = \varepsilon kT\,\Delta f, \qquad (2)$$

where ε is emissivity, and Δf frequency bandwidth. When me frequency band Δf is 100 MHz, the tissue temperature is T = 310K, and when ε = 1, this power is 4×10^{-13} W. According to Gautherie, [1] the temperature resolution depends on the system noise temperature, the temperature of the body, the bandwidth of the radiometer, the receiver, and the integration time constants. For optimal MWR parameters at room temperature and the above mentioned parameters, temperature resolution of 0.1°C is achievable with a time constant of 1 s.

LITERATURE

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7.

SUMMARY OF THE PRE- & CLINICAL DATA AND APPRAISAL

Clinical Evaluation and the Clinical Evaluation Report

Clinical evaluation is the assessment and analysis of clinical data pertaining to a medical device microwave radiometer RTM-01-RES to verify its clinical safety and performance. The evaluation is based on comprehensive analysis of pre- and post-market clinical data relevant to the intended use.
This includes data specific to the device as well as any data relating to devices claimed as equivalent by the manufacturer. The whole process is documented in a clinical evaluation report (CER).

Clinical data sources for a clinical evaluation

Clinical Data Source	Manufacturer's Device	Equivalent Devices*
Published Data	X	X
Clinical Investigation	X	
Post-Market Surveillance Data	X	
Public Adverse Effect Databases	X	X
Compassionate Use Data	X	
Internal Corrective and Preventive Actions (CAPAs)	X	

* Devices that are demonstrated by the manufacturer to be equivalent in some or all aspects to the manufacturer's own device

The clinical trials were held under the direction of leader Russian specialists at six Moscow medical centers. As follows:

#	DATA	NAME OF PRECLINICAL TRIAL
1	2014	A new non-invasive method for detection of local inflammatory activation in atherosclerotic plaques: Experimental application of microwave radiometry. First Department of Cardiology, Hippokration Hospital, Athens, Greece. Department of Pathology, Athens Medical School, Athens, Greece Centre for Materials Research & Innovation, University of Bolton **/www.thecdt.org/article/view/1287/1733**
#	**DATA**	**NAME OF CLINICAL TRIAL**
1	2005.12.16 - 2006.04.22	Report on the scientific research work conducted on the assessment of the factors influencing upon the efficiency of radio-thermometric measurements with the use of the diagnostics complex RTM-01-RES (company RES, Russia) *Russian Scientific Center for X-ray-radiology of the Federal Agency foe Healthcare and Social Development Academician of RAMN*
2	1998.01.21 - 1998.03.31	Clinical Trial Protocol of the RTM-01 Microwave Radiometer Developed by RES Ltd. *The Branch #1 of the Moscow Mammology Health Center*
3	1995.10.08 - 1997.12.26	Clinical trial protocol of the RTM-01 radiometer (RES Ltd.) *The Municipal Hospital #40*
4	1998.02.10 - 1998.05.14	Clinical Trial Protocol of the RTM-01 Radiometer, Developed by RES Ltd. *Blokhin Scientific Research Institute of Clinical Oncology*
5	2000.10.17 - 2000.12.21	Clinical trial protocol of the RTM-01 *Burdenko Major Military Hospital*
	1996.05	Clinical trial protocol of the RTM-01

6	- 1996.08	*Central Dermatology and Venereology Research Institute of Medical Industry and Public Health Ministry*
7		Radiothermography for theDetection of Breast Cancer in Patients with Palpable or Mammographically Detectable Breast Masses *University of Arkansas*
8	2014 - 2015	Bilateral Symmetry of Local Inflammatory Activation in Human Carotid Atherosclerotic Plaques *First Department of Cardiology, Hippokration Hospital, Athens Medical School, Athens, Greece; Centre for Materials Research and Innovation, University of Bolton, Bolton, UK,* Hellenic J Cardiol 2015; 56: 118-124
9	2014 - 2015	Comparative Study of Microwave Radiometry and Ultrasonography for the Diagnosis of Acute Appendicitis *https://clinicaltrials.gov/ct2/show/NCT02108340*
10	2012 - 2013	Detection of Subclinical Synovial Inflammation by Microwave Radiometry *First Department of Propedeutic and Internal Medicine, Athens University Medical School, Athens, Greece, Rheumatology Department, Asklepion General Hospital, Athens, Greece, First Department of Cardiology, Athens University Medical School, Athens, Greece, 4 Institute for Materials Research and Innovation, University of Bolton, Bolton, United Kingdom*
11	2013 - 2014	Efficacy and safety of breast radiothermometry in the differential diagnosis of breast lesions *Department of Radiology, Dokuz Eylül University, Izmir, Turkey Çanakkale Onsekiz Mart University, Çanakkale, Turkey Department of General Surgery, Dokuz Eylül University, Izmir, Turkey Department of Pathoology, Dokuz Eylül University, Izmir, Turkey*
12	2015	Microwave Radiometry for the Diagnosis and Monitoring of Breast Cancer (RTM) *https://clinicaltrials.gov/ct2/show/NCT02514837*
13	1998	Testimonial on the diagnostic trial of the RTM-01 medical radiometer (RES Ltd.) *Cybernetic Medicine Institute*
14	2002	Test protocol of diagnostic computerized radiometer integrated internal temperature RTM-01-RES *Moscow mammology dispensar*
15	2013	In vivo measurement of plaque neovascularisation and thermal heterogeneity in intermediate lesions of human carotid arteries *Heart 2012;98:1716–1721. doi:10.1136/heartjnl-2012-302507*

DATA ANALYSIS

During the period from 1994 to 2015 has been held a scientific research work with the use of the radio thermometric method (RTM method) on the diagnostic complex RTM-01-RES with high-frequency receiver and noise-protected antenna (company RES, Russia).

Objectives and tasks

The main objective of the tests has been the revelation of the main criteria influencing upon the diagnostics efficiency of the RTM method.

The main tasks of the clinical tests were:

a) To estimate the ability to use the RTM-01 microwave radiometer in medical practice
b) To estimate sensitivity, specificity of RTM depending on the degree of the malignant tumor.

c) To estimate the correlation of results of standardized regular equipment (X-ray mammography, US, puncturing biopsy, radionuclide research) of mammary glands with the results received with RTM.
d) To identify and evaluate side effects

PERFORMANCE OF

Clinical trial # 1: Objectives and tasks

a.) The main objective of the tests has been the revelation of the main criteria influencing upon the diagnostics efficiency of the RTM method.

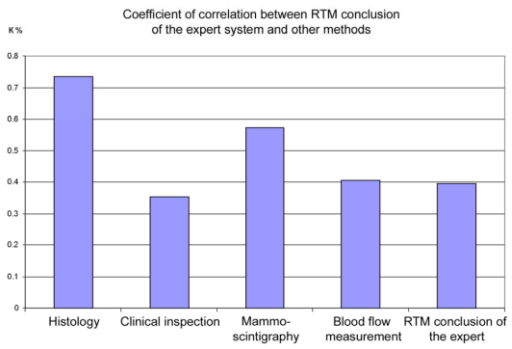
b.) The main tasks of the clinical tests were:

1	To estimate the correlation of results of radionuclide study of mammary glands based on the study of vascularization, and on the change of the transmembrane potential with the results received with RTM.
2	To estimate the correlation of results of color dopplerography of mammary glands based on the study of distinctive features of the blood flow and RTM.
3	To estimate sensitivity, specificity of RTM depending on the degree of the malignant tumor.

- **Results**

  - 79 patients with various pathologies of mammary glands were examined
  - 30 (38%) of them were cancer patients
  - Sensitivity 87.0%
  - Specificity 90.5%
  - Qualitative index of the efficiency of RTM in revealing cancer of mammary glands was at 79.2%

The authors give the results of radiothermometric studies in 79 patients with various breast diseases (6 with cancer in situ, 24 with invasive carcinoma, 15 with proliferation with atypia, 34 with other benign diseases). The radiometric study involved the measurement ot internal breast temperatures and skin temperatures with a RTM-01-RES radiometer. Thermal changes were rated by a 6-score scale from Th0 to Th5.
A relationship of the level of the thermal changes to the grade of tumor malignancy. The maximum thermal changes (Th5) occured in 85% of the patients having a high malignancy grade. Pronounced thermal changes were observed in 83, 96.6, 80, and 44.5% of the patients with cancer in situ, invasive carcinoma, atypia, and ductal hyperplasia, respectively. At the same time, color Doppler study reveald no blood flow changes in any patients with cancer in situ. It is concluded taht the methods is recommended for screening and differential diagnosis in bordeline breast conditions.



SAFETY

No side effects were mentioned.

CONCLUSION

- The RTM method captures changes of temperature inside the mammary gland and on the skin surface that reflect functional processes in mammary glands.
- In 90% of patients diseased with the mammary gland cancer there are noted significant thermal changes.
- With the noninvasive cancer and the cancer in situ in 80% thermal changes are revealed of mammary glands captured with the use of RTM-01-RES.
- In 50% of cases the noninvasive cancer and the cancer in situ are accompanied by very strong thermal changes (Th5).
- The thermal changes of at the cancer of mammary glands are also registered in the absence of change of blood flow.
- At the stage of atypic changes and the heightened cells proliferation in 80% of patients there are manifested thermal changes of mammary glands that are captured with the use of RTM-01-RES.
- In 44.5% of patients with simple duct hyperplasia of cells there are significant thermal changes.
- Application of computer processing of the results allows to increase the specificity of the RTM method (90% with simple duct hyperplasia, 70% with proliferation and atypia) at the sensitivity of 87%.
- At the high degree of malignance predominate the maximal thermal changes (Th5), at the modest degree of malignance predominates the index (Th4), at the low degree of malignance over half of the patients have the index Th3 and Th2.
- The RTM method allows to reveal patients having high risk of malignization and needing further complex examination.

The results of the conducted research allow to recommend the RTM method for the screening and differential diagnostics at the boundary states of a mammary gland.

PERFORMANCE OF

Clinical trial # 2: Objectives and tasks

a.) The main objective of the trial was investigation of diagnostic abilities of the RTM method.
b.) The main tasks of the clinical test was: differential diagnosis of breast cancer the following basic criteria

1	significant thermal differentials between corresponding points on the right and left breasts
2	an increase in nipple temperature
3	an increase in temperature diversity within one breast

and detection where a tumour is locates.

- **Results**

- 771 patients were examined
- 101 (13%) of them are cancer patients
- Sensitivity 85.1%
- Specificity 76.5%

- The radiometer has small dimensions, weight and power consumption. It can be easily transferred within a hospital.
- It is easy to operate the RTM-01 microwave radiometer and the secondary medical staff can operate it. There are no external adjustment elements on the device.

- Utilization of the device is absolutely harmless for patients and the physicians, therefore the tests can be repeated for the monitoring of treatment.
- The device was being used for more than 800 hours. Over this period there were no failures.
- In 86 of 101 studies RTM-results of breast cancer were confirmed by the data of clinical and mammography tests (85 %). 15 cancer patients had no significant thermal abnormality (15%).
- 157 of 771 patients had all RTM-features of breast cancer (criteria mentioned above), but they were not confirmed by clinical and mammography tests. They are 20.3% of all examined patients.
- It is necessary to emphasize that the patients were diagnosed with breast cancer basing only on the data of temperature field measurements. At the same time the use of data received by clinical and mammography examinations in conjunction with radiometry methods will improve the efficiency of the microwave radiometry method.
- Imaging when the temperature values are linked with measured sites and isotherm lines are drawn through sites having the same temperature help physicals to diagnose.
- The imperfection of RTM-diagnosis is the RTM-features of acute mastitis are similar to RTM-features of inflammatory cancer (the significant thermal differential). However for clinical practice this imperfection is not essential, as physicians may order a conservative treatment if there are any suspicions of acute mastitis and then repeat RTM-diagnosis. This allows to compare results and analyze dynamics.

SAFETY

No side effects were mentioned.

CONCLUSION

The RTM-01 radiometer developed by RES Ltd. is recommended to be used in medical practice for screening at consulting and oncology rooms and at specialized oncology and mammalogy centers for detection of breast cancer and the monitoring of treatment.

PERFORMANCE OF

Clinical trial # 3: Objectives and tasks

The purpose of the trial is to estimate the ability to use the RTM-01 radiometer in medical practice. In this case the ability to detect breast cancer was checked.

Results

- 43 patients were examined
- 35 (76%) of them are cancer patients
- Sensitivity 94.2%
- Specificity 77.7%

- The RTM-01 radiometer has small dimensions, weight and power consumption. It can be easily transferred within a hospital.
- It is easy to operate the RTM-01 microwave radiometer. There are no external adjustment elements on the device.
- 33 of 35 verified breast cancer were confirmed by radiometric examination, i.e. the detective ability of the method exceeded 94 %.
- 2 of 42 patients had false positive results that is less than 5 %.
- Imaging when temperature values are linked with measured sites and isotherm lines are drown through sites having the same temperature help physicals to diagnose.

SAFETY

- The utilization of the device is absolutely harmless for patients of any ages and with any diseases as well as for physicians. So examinations may be repeated to analyze dynamics of disease.
- The device was being used for more than 50 hours. Over this period there were no failures.

CONCLUSION

The RTM-01 radiometer developed by RES, Ltd. is recommended to be used in medical practice for screening at consulting and oncology rooms and at specialized oncology and mammology centers for detection of breast cancer and the monitoring of treatment.

The serial production of the device is recommended.

PERFORMANCE OF

Clinical trial # 4: Objectives and tasks

The purpose of the trial is to estimate the ability to use the RTM-01 radiometer in medical practice. In this case the ability to detect breast cancer was checked.

- **Results**

- 81 patients were examined
- 48 (60%) of them were cancer patients
- Sensitivity 89.6%
- Specificity 81.8%

- The RTM-01 radiometer has small dimensions, weight and power consumption. It can be easily transferred within a hospital.
- It is easy to operate the RTM-01 microwave radiometer. There are no external adjustment elements on the device.
- The utilization of the device is absolutely harmless for patients of any ages and with any diseases as well as for physicians. So examinations may be repeated to analyze dynamics of disease.
- The device was used for more than 100 hours. Over this period there was no failures.
- The sensitivity of the method (detective ability of breast cancer) is:

  TP/(TP+FN) x 100% = 43/(43+5) x 100% = 89,6%

  The accuracy of the method is:

  (TF + TN)/(Studies number) x 100% = (43+27)/81 x 100% = 86,4%

  The specificity of the method is:

  TN/(FP+TN) x 100% = 27/(27+6) x 100% = 81,8%

- Imaging when temperature values are linked with measured sites and isotherm lines are drown through sites having the same temperature help physicals to diagnose.

SAFETY

The utilization of the device is absolutely harmless for patients of any ages and with any diseases as well as for physicians. So examinations may be repeated to analyze dynamics of disease.

CONCLUSION

The RTM-01 radiometer developed by RES, Ltd. can be recommended to be used in medical practice for screening at consulting and oncology rooms and at specialized oncology and mammology centers for detection of breast cancer and monitoring of treatment.

The serial production of the device is recommended.

PERFORMANCE OF

Clinical trial # 5: Objectives and tasks

The purpose of the trial was to evaluate the possibility to use the RTM-01-RES diagnostic system to detect breast cancer and select risk patients in the military hospitals.

Results

- 51 patients were examined
- 16 (32%) of them were cancer patients

SAFETY

No side effects were mentioned.

CONCLUSION

RTM-01-RES is recommended to be used for screening, diagnosis of breast diseases and monitoring the treatment in hospitals and health centres of the Ministry of Defence.

PERFORMANCE OF

Clinical trial # 6: Objectives and tasks

The purpose of the trial was to evaluate the diagnostic abilities of the RTM-01-RES.

Results

- 18 patients with chronic adnexitis and 6 healthy volunteers
- The received data coincided with ultrasound investigation of uterus and oviducts.

SAFETY

No side effects were mentioned.

CONCLUSION

The clinical trial indicated that the RTM-01 radiometer could be used in cases of chronic adnexitis for diagnostic purposes (for example for primary examinations or check-up in observation room) as well as for the monitoring of treatment.

PERFORMANCE OF

Clinical trial # 7: Objectives and tasks

Radiothermography (RTM) has shown diagnostic value in the detection of breast cancer in international studies, but this data has not been reproduced in the United States. We evaluated the diagnostic efficacy of the BreastScan RTM device for the detection of breast cancers in patients with suspicious breast lesions on physical exam or breast imaging who were scheduled for breast biopsy. We measured the specificity, sensitivity, accuracy, positive predictive value and negative predictive value of RTM by comparing preoperative RTM findings with the resulting histology from biopsy.

Results

- 30 patients were examined
- 13 of them were cancer patients
- Sensitivity 84.0%
- Specificity 70.0%
- Positive predictive value 68.0%
- Negative predictive value 85.0%

SAFETY

No side effects were mentioned.

CONCLUSION

This study, with the aid of RTM, clearly demonstrated that the presence of both hyperthermia and hypervascularization within the tumor, as well as at its periphery in relation to the temperature and blood flow in the contralateral healthy breast tissue, are dominant signs for detection of a breast lesion.

The diagnostic efficancy of radiothermography in the detection of breast cancer is similar to that of mammography. Because RTM uses a completely distinct physical entity to detect breast cancer there is the possibility that a combination of RTM and diagnostic mammography may significantly enhance our ability to detect breast cancer.

PERFORMANCE OF

Clinical trial # 8: Objectives and tasks

In the screening process, was included 246 patients who were evaluated for coronary artery disease. Of these, 200 patients met the inclusion criteria and 400 carotid arteries were analysed.

The MWR measurements were performed with the RTM 01 RES microwave computer-based system that measures temperature from internal tissues at microwave frequencies. MWR measurements were obtained at least 10 minutes after the ultrasound examination in order to avoid any influence on temperature from palpation or the ultrasound study.

Significant carotid artery stenosis (≥70%) was found in 22 patients (11%).
Four patients (2%) had unilateral carotid artery occlusion.

SAFETY

No side effects were mentioned.

PERFORMANCE OF

Clinical trial # 9: Objectives and tasks

This study will evaluate the use of microwave radiometry in a population of patients diagnosed with acute appendicitis and treated with appendectomy. The main purpose of the study is to report the results of microwave radiometry as a diagnostic tool in acute appendicitis and compare those results with the commonly used ultrasonography.

ClinicalTrials.gov Identifier: NCT02108340

PERFORMANCE OF

Clinical trial # 10: Objectives and tasks

Microwave Radiometry is a non-invasive method which determines within seconds the in vivo temperature of internal tissues at a depth of 3–7 cm with an accuracy of ±0.2°C. In this proof-of-concept study, we tested the hypothesis that, in absence of relevant clinical signs, increased local temperature detected by microwave radiometry reflects subclinical synovial inflammation, using ultrasound as reference method.

Results

In 30 healthy and 10 injured knees the temperature was always lower than thigh (32.361.1 and 31.861.4 versus 34.160.9 and 33.661.2uC with a difference (DT) of 21.860.2 and 21.960.4uC respectively). Of 40 RA and 20 osteoarthritis knees examined, ultrasound findings indicative of subclinical inflammation (fluid effusion and/or Doppler signal) were found in 24 and 12, respectively, in which the temperature was higher than healthy knees and DT was lower (20.960.7 in RA and 21.060.5 in osteoarthritis versus 21.860.2uC, p,0.001). The 5 RA knees with power Doppler findings indicative of grade 2 inflammation had a DT 3 times lower compared to healthy (20.660.6, p = 0.007), whereas the 9 RA and the 7 osteoarthritis knees with additionally fluid effusion, had even lower DT (20.460.7, p,0.001).

SAFETY

No side effects were mentioned.

CONCLUSION

Using a safe, rapid and easy-to-perform method, such as microwave radiometry, thermal changes within the knee joint may reflect non-clinically apparent joint inflammation. Refinement of this method, including production of sensors for small joints, could result to the development of the ideal objective tool to detect subclinical synovitis in clinical practice.

PERFORMANCE OF

Clinical trial # 11: Objectives and tasks

The aim of this study is to research the contribution of radiothermometry (RTM) to the characterization of breast masses, the differentiation of malignant-benign masses and diagnosis of early stage breast cancer.

Results

- 237 patients were examined
- 182 of them diagnosed with a breast mass
- 55 control group

Diagnostic method	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)	κ value
RTM	90.9	20.8	61.2	62.5	0.129
Mammography	93.9	43.3	57.4	33.3	0.622
US	84.8	56.7	58.3	44.4	0.717
Mammography ve US	96.7	60.8	47.7	65.8	0.915

Table 1. Diagnostic value of imaging methods according to histopathology results (n = 57)

Diagnostic method	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)	κ value
RTM	87.0	81.4	58.0	95.5	0.582
US	85.2	98.9	95.8	95.8	0.875

Table 2. Sensitivity, specificity, and positive-negative predictive values of diagnostic methods according to mammography results (n = 237)

Diagnostic method	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)	κ value
RTM (mass size ≥ 2 cm)* (n = 45)	88.9	83.3	88.9	83.3	0.722
RTM (mass size < 2 cm) (n = 123)	89.5	76.9	41.5	97.6	0.451
RTM (microcalcification – yes) (n = 20)	86.7	80	92.9	66.7	0.625
RTM (microcalcification – no) (n = 217)	87.2	18.5	50.7	49.3	0.536

Table 3. Sensitivity, specificity, and positive-negative predictive values of RTM according to mass size accepting mammography as gold standard
**In cases with more than one mass, the size of the largest mass was noted*

Diagnostic method RTM	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)	κ value
BI-RADS I (n = 52)	75	77.8	60	87.5	0.494
BI-RADS II (n = 116)	93.1	86.2	69.2	97.4	0.711
BI-RADS III (n = 34)	100	100	25	94.1	0.338
BI-RADS IV (n = 35)	85.7	71.4	42.9	95.2	0.416

Table 4. Sensitivity, specificity, and positive-negative predictive values of RTM for identifying lesions in different breast structures (n = 237)

Diagnostic method US	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)	κ value
BI-RADS I	87.5	100	100	94.7	0.906
BI-RADS II	89.7	97.7	92.9	96.6	0.884
BI-RADS III	50.0	100	100	97.0	0.653
BI-RADS IV	71.4	100	100	93.3	0.800

Table 5. Sensitivity, specificity, and positive-negative predictive values of US examination to identify lesions in different breast structures(n = 237)

In this study, as in other studies, suspicious cases not only on RTM, but also on mammography and US, were sent for histopathologic diagnosis. As a result, positive results were expected to be higher. In other words, sensitivity and positive predictive values in this study were higher than specificity and negative predictive values. Similar results are seen in Table 5 where the specificity and negative predictive values between mammography and histopathology are lower than sensitivity and positive predictive values This situation results from a higher proportion of malignant cases being directed for histopathologic diagnosis. When were compared RTM results with X-ray mammography results, the validity results for RTM (sensitivity, specificity,positive and negative predictive values) are 87.0%,81.4%, 58% and 95.5% respectively, with the consistency value at a good level of $\varkappa = 0.582$. This result indicates that there is a high level of compliance between both diagnostic methods.

In this study it was examined the sensitivity,specificity and positive-negative values for RTM according to mass size. RTM examination had sensitivity,specificity and positive-negative values for masses 2 cm and above of 88.9%, 83.3%, 88.9% and 83.3%. For masses below 2 cm in size the sensitivity, specificity and positive-negative values for RTM were 89.5%, 76.9%, 41.5% and 97.6%. In conclusion, the specificity and positive predictive value of RTM for masses 2 cm and above were higher than for those below 2 cm. For masses below 2 cm in size the negative predictive value of RTM was higher.Sensitivity in both cases was similar. There is no study in the literature evaluating according to mass size. Sensitivity, specificity and positive-negative values of RTM examination in the presence of microcalcification were 86.7%, 80.0%, 92.9% and 66.7%, respectively. In the absence of microcalcification the sensitivity, specificity and positive-negative values were 87.2%, 18.5%, 50.7% and 49.3%, respectively. The conclusion is that in cases with microcalcification the specificity, positive and negative predictive values were higher than in cases without microcalcification. The reason for this may be the possibility that the lesion is large or that it may be late stage.However, there is no study in the literature that evaluates based on the presence of microcalcification.Additionally, the sensitivity, specificity and positive-negative values of RTM in different breast structures were researched. The results for BI-RADS I breast density were sensitivity 75%, specificity 77.8%, positive predictive value 60% and negative predictive value 87.5%. For BI-RADS II breast density sensitivity was 93.1%, specificity 86.2%, positive predictive value 69.2% and negative predictive value 97.4%. BI-RADS III sensitivity was 100%, specificity was 100%, positive predictive value was 25% and negative predictive value was 94.1%. For BI-RADS IV breast density sensitivity was 85.7%, specificity 71.4%, positive predictive value 42.9% and negative predictive value 42.9%. The consistency of RTM for lesion diagnosis in BI-RADS II breast density was higher than for mammography. On mammography for dense breast tissue types such as BI-RADS III and BI-RADS IV values were moderate and low. The sensitivity,specificity, and positive-negative predictive values of US for lesion detection in different breast densities were higher than for RTM. There is no study in the literature with information on this topic.

Our study comprised 237 patients. Of these, only 57 were sent for histopathologic diagnosis of masses found on mammography and US. The low case number and low number of patients with histopathologic diagnosis by biopsy are important limitations.

SAFETY

No side effects were mentioned.

CONCLUSION

In conclusion, identification of lesions in the breast and presence of microcalcification by RTM shows that it is more trustworthy compared to mammography. Accepting mammography as the gold standard, the validity results for RTM show a good level of conformity between the two methods. When evaluated based on the area below the ROC cure and compared to mammography, RTM is sufficiently successful at evaluating positive and negative cases. These results show that RTM is not appropriate as a single scanning method. If this method is used, it is more appropriate to use it with basic scanning methods such as mammography and US.

PERFORMANCE OF

Clinical trial # 12: Objectives and tasks

The investigators would like to use the device in clinics in Scotland and later United Kingdom (UK) for breast diagnosis and monitoring treatment.

During 3 months the investigators aim to examine 150 patients with breast cancer and 150 patients without cancer who will be the control group. The results of temperature measurement will be compared with the results of histology, in particular, tumour cellulants p53 expression and other gene expression data for metabolic biomarkers and other tumor indicator. Statistical analysis of data will be performed. The device and initial training will be provided by RES Company (device producer).

ClinicalTrials.gov Identifier: NCT02514837

PERFORMANCE OF

Clinical trial # 13: Objectives and tasks

At the room for treatment and diagnostics of the State Clinical Hospital #124 the diagnostic possibilities of the RTM-01 for examination of the patients having pathology of the urinary-secretory system were explored by Cybernetic Medicine Institute.

- **Results**

- 186 patients were examined
- 72 of them diagnosed with various pyelonephritis types
- 10 control group

SAFETY

No side effects were mentioned.

CONCLUSION

Clinical trial showed that RTM-01 could be used to diagnose and monitor treatment of chronic disease kidney patients.

PERFORMANCE OF

Clinical trial # 14: Objectives and tasks

The purpose of the test - evaluation of the use of diagnostic RTM-01-RES in the algorithm of complex diagnostics of mammary glands.

The studies addressed the following tasks:

• Carrying out statistical analysis of the results for the RTM diagnostics of malignant and benign breast diseases.

• Comparative analysis of different instrumental methods included in the diagnostic algorithm for complex diseases of the mammary glands.

• Assess the possibility of using the RTM-01-RES for monitoring the treatment of benign diseases.

• Evaluation of usability of the device, its ergonomic features.

- **Results**

With the help of radio-thermometer were examined 155 women with different forms of breast pathology at the age of 26 to 79 years.

SAFETY

No side effects were mentioned.

CONCLUSION

1. RTM method has high sensitivity. The mutual use of classical methods of diagnosis and RTM method increases diagnostic efficiency surveys. The number of false-negative conclusions for complex survey decreases.

2. RTM method allows to determine the response of breast tissue to carry out treatment and can be used for dynamic monitoring of the treatment.

3. RTM procedure is absolutely harmless to the patient and the physician, and may repeatedly performed at any age group.

4. It should be noted high information and method of its versatility, ease of use and compact equipment.

Results of the visualization of RTM results in the form of heat fields are rather evident. Automated expert system allows you to focus medical attention to patients at risk.

PERFORMANCE OF

Clinical trial # 15: Objectives and tasks

Both neoangiogenesis and inflammation contribute in atherosclerosis progression. Contrastenhanced ultrasound (CEUS) provides visualisation of plaque neovascularisation. Microwave radiometry (MR) allows in vivo non-invasive measurement of temperature of tissues, reflecting inflammatory activation. Researcher assessed the association of carotid plaque temperature, measured by MR, with plaque neovascularisation assessed by CEUS in intermediate lesions.

Results

- 86 carotid arteries were examined
- 48 patients were included

SAFETY

No side effects were mentioned.

CONCLUSION

Carotid plaque neovascularisation on CEUS examination is associated with increased thermal heterogeneity by MR and ultrasound characteristics of plaque vulnerability in intermediate lesions. In vivo non-invasive assessment of the functional and morphological characteristics of carotid artery atherosclerotic plaques may serve as an additional screening tool to identify 'high risk' patients.

Avramenko *et al.* [6] studied non-palpable masses in 200 female patients using RTM scanning together with US and mammography. They concluded that the sensitivity of the three methods was 86.7%, 75.8% and 88.3% with specificity of 75.2%, 80.0% and 83%.

SUMMARY

SAFETY

Place the test	Year	# patient	# patient breast	Sensitivity %	Specificity %	Side effects

			cancer			
City Clinical Hospital №40 Moscow, Russia	1997	42	35	94.2	71.4	No side effects were mentioned
Mammology dispensary Moscow, Russia	1998	771	101	85.1	76.5	No side effects were mentioned
Russian Cancer Research Center Moscow, Russia	1998	81	48	89.6	81.8	No side effects were mentioned
Burdenko Hospital Moscow, Russia	2001	51	13	98		No side effects were mentioned
Branch №1 Moscow Mammology dispensary, Moscow, Russia	2002	155	28	95		No side effects were mentioned
Medical College, Arkanzas, USA	2003	30	13	84	70	No side effects were mentioned
Russian Scientific Center of Radiology	2006	79	30	96.6		No side effects were mentioned
University of Edinburgh United Kingdom	**2015**					**In process**

No side effects were mentioned.

Reviews of MD RTM-01-RES users

The word „Review“ is translated from the latin «recensio» and means "view, message, evaluation, review of anything." The main task of Reviews has been an expression of personal attitude to the product, reasoned assessment of device RTM-01-RES by its application in clinical practice at long period of using. In some Reviews a detailed analysis of safety and performance of device RTM-01 missing, but for argument evaluation recall includes a comparative analysis to the traditional devices (US, X-ray mammography). The writers created some Reviews in form of presentation some results in a highlight of a variety tasks: for instance, in impressions of using device RTM-01-RES in the pattern during the diagnosis or in the pattern during control of therapy.

In the period from 1998 to 2015 the producer of device RTM-01-RES received 21 Reviews from the users. The list of Reviews is presented. In Table, there are present results from application of device in clinical practice.

List of „Reviews“ issued by users of microwave radiometry RTM-01-RES

1) Feedback on the operator for radio-thermodiagnostics of diseases of the female breast//Medical Care Center, Dusseldorf, Grmany 1998-2009
2) City Hospital № 227//Moscow 1999
3) Sanatorium and spa complex DiLUCH//Rostov on Done 1999
4) Polyclinic № 1// Rostov on Done 2009
5) Clinical Hospital № 3//Volgodrad 2009

6) Sanatorium named after M.V. Frunze//Sochi 2009
7) Review on experience of the use of microwave radiometry in Samara Regional Clinical Oncology Center//Samara 2004-2009
8) Review № 889//Clinical diagnostic center „Haelth“ 2007-2009
9) Review of Mammology center//Izhevsk 2005-2009
10) Review Institution Educational Clinical Research Medical Centr//Biskek, Kyrgyz Republic 2008
11) Clinic of management//Samara 2006-2009
12) City polyclinic № 1//Norilsk 2006
13) Medical radiology education center//Obninsk 2007
14) The experience of using the method of microwave radiometry in a breast oncology dispensary № 5// Moscow 2007-2012
15) Reviewed for medical technology "The use of computer-RTM-01-RES to identify patients at risk and to evaluate the effectiveness of treatment of breast diseases//Moscow 2007
16) Reviewed for medical technology "The use of computer-RTM-01-RES to identify patients at risk and to monitor the treatment of benign breast disease//Moscow 2007
17) Reviews of the application of the RTM-01 in the medical center "HERA"//Tver 1997-2012
18) Analysis of the use of radiometry for the diagnosis of breast pathology//Belgorod 2010
19) Review on the application of RTM 01//Tver 2000-2012
20) Review on the application of medical radiometer RTM 01B Tver Clinical Oncology dispensare//Tver 2012
21) Review of testing RTM 01//Moscow 2008

Place of application of RTM-01-RES in clinical practice	**Period**	**# patient**	**Pathology or control of therapy**	**Sensitivity %**	**Specificity %**	**Side effects**
MEDICAL CARE CENTER Düsseldorf, Germany	1998 - 2009	unknow	Adjuvant therapy of CaMa	good corelation of RTM results with X-ray mammo and US		No side effects were mentioned
City Hospital № 227 Moscow, Russia	2008 - 2009	715	Diagnosis of CaMa and control of therapy	screening study helped improve the detection of early forms of breast cancer from 70.0% to 76.3%		No side effects were mentioned
"DiLUCh" - health resort Anapa, Russia	1999 - 2009	2742	Breast diagnosis a and control of therapy	diagnosis of tumor and pseudo tumor diseases		No side effects were mentioned
Road Clinical Hospital, Rostov-on-Don, Russia	2006 - 2009	1036	diagnosis	screening of breast pathology		No side effects were mentioned
Clinical polyclinic №. 3, Volgodrad Russia	2007 - 2009	530	control of therapy	control of therapy of benign pathology of breast		No side effects were mentioned
Sanatorium. M.V. Frunze, Sochi, Russia	2009 - 2012	813	diagnosis	to identify patients with a high risk of malignancy and requiring complex examination		No side effects were mentioned
Samara Regional Clinical Oncology Center, Samara, Russia	2004 - 2009	3830 mamma 376 thyroid gland 311 skin	diagnosis	86.0 CaMa	98.0	No side effects were mentioned

Clinical and Diagnostic Center „Health“, Rostov-on-Don, Russia	2008 - 2009	1000	screening of breast	screening of breast pathology	No side effects were mentioned
Breast center Izhevsk, Rossia	2005 - 2009	2400	diagnosis	control of therapy of benign pathology of breast	No side effects were mentioned
Institution Educational Clinical Research Medical Center, Bishkek, Kyrgyz rep.	2008 – 2010	1000	screening of breast	screening of breast pathology	No side effects were mentioned
4 Control Clinic Samara, Russia	2006 - 2009	710	diagnosis and screening	breast examination in a complex algorithm study of mammary glands as a prophylactic and diagnostic purposes	No side effects were mentioned
City polyclinic №. 1 Norilsk, Rossia	2006 – 2009	1000	diagnosis and screening of therapy	study, both as a primary diagnostic method, and as the monitoring of treatment	No side effects were mentioned
Medical Radiological Research Center Obminsk, Russia	2007 – 2009	100	diagnosis and screening of therapy	radiometry carried out in conjunction with ultrasound and mammography, and helped identify the pathological processes and to conduct monitoring of treatment for benign processes in the mammary gland	No side effects were mentioned
Oncology Center №. 5 Moscow, Russia	2007 - 2012	2500	diagnosis	including radiometry method in comprehensive survey of breast	No side effects were mentioned
FGU "Herzen MNIOI of Russian Medical Technologies" Moscow, Russia	2007		diagnosis	use of radiometry for the detection of patients at risk and to evaluate the effectiveness of treatment of breast diseases	No side effects were mentioned
Russian Scientific Center of Radiology and the Federal Agency for Healthcare and Social Development Moscow, Russia	2004 - 2006		diagnosis	radiometry was used for identifying group of patients at risk and for monitoring the treatment of benign breast diseases	No side effects were mentioned
Medical Center „GERA“ Tver, Russia	2000 – 2012	10000	diagnosis	diagnosis of breast pathology	No side effects were mentioned
St. Joasaph Regional Hospital, Belgorod, Russia	2010 – 2012	953	diagnosis and screening of therapy	definition of radiometry possibilities in the diagnosis of breast diseases, as well as the conduct of controlled trials in benign mammary dysplasia at women, who received conservative therapy	No side effects were mentioned
Tver` regional clinical - oncological dispensar Tver, Russia	2000 – 2012	8 000	diagnosis of breasts, thyroid glands and genitals	diagnosis of breast pathology and MTS in spinal cord	No side effects were mentioned
Tver` regional clinical - oncological dispensar Tver, Russia	yyyy - 2012	6000	diagnosis and screening of therapy of the breasts	diagnosis of breast pathology and control of therapy	No side effects were mentioned
FSB Central clinic Moscow, Russia	-	30	breast diagnosis	diagnosis of breast pathology	No side effects were mentioned

∑ 21 medical centers	**1998 - 2012**	**cca 39 000**	**diagnosis and screening of therapy**	**Predominantly breasts pathology diagnosis**	**No side effects were mentioned**

CONCLUSION

Based on the processing of the data, we can conclude that Radiometer RTM-01-RES, designed by the RES company can be recommended for use in practice for breast pathology diagnosis and for the screening of the therapy. It was stated, that in ambulatory or polyclinical facilities may be using the device in the oncology and dispensar departments with high efficiency. Except traditious application of RTM-01-RES that is diagnosis of breasts pathology, the writers presents the results of application radio thermometer for diagnosis of thyroid glands pathology and skin pathology.

On the basis of comparing the results from radiometry to the results received by traditional methods of diagnosis (US, X-ray mammography) it was stated that results are comparable.

No one Review mentioned side effect. Many of them stated that device RTM-01-RES is safe for patient and staff.

THESIS

Introduction

From the open source (internet) it was collected 14 THESIS works of physicians which presents the results of microwave radiometer RTM-01-RES examination in clinical-hospital practice in period from 1999 to 2015.

LIST OF THESIS

A dissertation submitted in fulfillment of the requirements for the degree of Doctor of Medical Science.

1.) CLINICAL SIGNIFICANCE radiometry in the diagnosis and differential diagnosis of the pelvic organs diseases
TSOMAEVA Elena Aleksandrovna, Moscow 2012
2.) Microwave radiometry in the diagnosis and evaluation of effectiveness of neoadjuvant treatment of breast cancer
Sinelnikov Olga Aleksandrovna, Moscow 2013
3.) Management of breast pathology screening, based on computer radiometry
Popov Andrey Nikolaevich, Voronezh 2006
4.) DEEP INTEGRATED MICROWAVE RADIOTERMOGRAPHY in diagnosis of acute appendicitis
Daoud Hamada, Moscow 2001
5.) COMPARATIVE EVALUATION OF TREATMENT PATIENT WITH CARBUNCLES OF SKIN
GULMURADOVA NARGIS TASHPULATOVNA, Moscow 2004
6.) Radiologic methods in the diagnosis and monitoring of treatment of the thyroid gland diseases
Zimin Valeriy Valerievich, Nizhnii Novgorod 2004
7.) EXPERIMENTAL grounding for application of millimeter and centimeter radiometry in the diagnosis of intracranial pathology
DISTRIBUTION of contrasts in internal temperature and depth´s thermoprofiles in healthy volunteers
THERMAL AND RADIO THERMOMETRIC diagnosis of tumors and brain injuries
Preoperative thermovision and microwave radiometry diagnosis of tumors and spinal cord injuries
Thermovision and microwave radiometry diagnosis of lumbar osteochondrosis
Polydiapason thermo-radiometry - a new direction in the study and diagnosis of diseases of the central and peripheral nervous system
Kolesov S.N.

8.) EFFECT of the inducers of ovulation on condition of breast cancer in women with different factor of infertility
ALIBAHSHOVA Farhangez Kayhusravovna, Moscow 2010
9.) Cerebral blood flow and heart rate variability in persons with signs of premature aging
Nikitin Victor Sergeevich, Kirov 2007
10.) New approaches to the diagnosis and treatment of fibrocystic breast disease
Naumkin Natalia Genadyevna, Moscow 1999
11.) Optimization of early diagnosis of breast formations
Makieva Kiyal Bolotbekovna, Bishkek, 2010
12.) OPTIMIZATION APPROACHES TO THE DIAGNOSIS AND TREATMENT OF BREAST DISEASES
Kanevtsov Valery Viktorovich, Moscow 2004
13.) Brain radiometry with cranio-cerebral hypothermia in acute ischemic stroke
Cheboksarov Dmitry Vasilyevich, Moscow 2015
14.) The role of radiometry in the surgical treatment of unpalpable breast tumors
Avramenko Galina Vilyamovna, Moscow 2009

TSOMAEVA Elena Aleksandrovna, Moscow 2012– physician by specialisation: gynecology, reproductive system, obstetrician, gynecologist of reproductive system - she specializes in infertility problems. It is engaged in the treatment, diagnosis and overcoming female infertility with reproductive technologies, carrying out small gynecological operations. Performs maintenance of pregnancy after IVF, is involved in programs donation of oocytes and surrogate motherhood. She defended her thesis on the topic - "The clinical significance of radiometry", Moscow Regional Scientific Research Institute of Obstetrics and Gynecology Department Health of Moscow Region in 2012.

Objectives and tasks of thesis.

Perpose of the study

Improving the comprehensive diagnosis of diseases of a small basin with deep radiometry.

Objectives of research

1. Develop a methodology for microwave radiometry (RTM) research and identify particular thermometric picture pelvic organs healthy women.
2. Identify the importance of radiometry in conjunction with ultrasound and certain blood markers (proteins acute phase) in the diagnosis of inflammatory diseases of the internal genitals.
3. To study the clinical significance in the differential radiometry the diagnosis of diseases of the pelvic organs.

4. Assess the information content of radiometry in the evaluation of the effectiveness the treatment of inflammatory diseases of the uterus.

5. Determine the role of endoscopic techniques (laparoscopy, cystoscopy) in the diagnosis and differential diagnosis with external genital endometriosis.
6. On the basis of a comparative analysis of traditional methods imaging (ultrasound, cystoscopy, laparoscopy) and radiometry to develop recommendations for the diagnosis and differential diagnosis inflammatory diseases of the uterus, external endometriosis, benign ovarian tumors.

Scientific novelty of research

For the first time, on the basis of a detailed study of microwave radiometry data, it was highlighted features of the thermometric picture of pelvic by healthy women according topographic - anatomical landmarks and projections. Diagnostic value of RTM-study was carried out by vaginal probe. Based on these results of radiometry, in conjunction with clinical and laboratory (determination of proteins of acute phase) and ultrasonic parameters, it was

carried out the development of diagnostic criteria and the expediency of the microwave radiometry in the diagnosis of vaginal inflammatory diseases of the uterus. Comparing the results of the deep microwave radiometry with clinical and laboratory, ultrasound and endoscopic parameters in various pathological conditions of the pelvic organs. On the basis of obtained results it was received the Patent "Method for the differential diagnosis of subacute salpingoophoritis", Registration number №2440021 from 20.01.2012.

The practical significance of the work

The expediency and high efficiency inclusion of radiometry in the examination of patients with inflammatory algorithm diseases of the uterus and benign tumors ovaries has been shown. Presented efficiency of RTM in determining the severity and incidence of inflammation of appendages uterus, in assessing the effectiveness of the therapy. The degree of increase temperature gradient allows indirectly to judge the nature of the flow inflammation of the uterine appendages. The necessity changes in the traditional diagnostic approach of external genital endometriosis, given the frequent combination with interstitial endometriosis cystitis, which justifies the need to perform simultaneous laparoscopy and cystoscopy has been presented.

CONCLUSIONS

1. Deep microwave radiometry in healthy women were characterized by low temperature asymmetries in the uterus - 0,2-0,4 °C during transabdominal dimension and 0.1-0.2 ° C – by vaginal measurement.
2. In the RTM-study diagnostic value has presence thermoasymmetry a 0,5 °C (using transabdominal sensor) and 0,3 °C (using a vaginal probe) in the projection the uterus compared to healthy tissue, indicating that the presence of a pathological process in the study area.
3. Deep microwave radiometry is informative method of diagnosing inflammatory diseases the uterus and benign ovarian tumors and is unhelpful - for external genital endometriosis.
4. The use of modern clinical and laboratory (performance blood count and acute-phase proteins, biological, direct microscopic study, PCR diagnostics) and other instrumental methods of investigation (ultrasound, laparoscopy), with the inclusion of a comprehensive examination of the vaginal radiometry, allows for the most accurate and objective diagnosis, differential diagnosis of different forms of flow salpingoophoritis.
5. Informative vaginal radiometry above transabdominal: in the diagnosis of benign ovarian tumors descriptiveness vaginal thermometry was - 94.4%, and inflammatory diseases of the uterus - 79-98% (depending on the nature of inflammation), in contrast to transabdominal, in which the information content was - 83.3%, and 54%, respectively.
6. Identify during laparoscopy external genital endometriosis is an indirect indication of the presence of interstitial cystitis and indication for simultaneous cystoscopy to clarify state of the bladder mucosa.

SAFETY

No side effects were mentioned.

Sinelnikov Olga Aleksandrovna, Moscow 2013 – the results of thesis was published in medical journal Clinical examination in 2013 „ULTRA-HIGH FREQUENCY RADIOTHERMAL MAMMOGRAPHY IN NEOADJUVANT BREAST CANCER THERAPY EFFECT EVALUATION“.

Ultra-high frequency radio thermal mammography permits thermal changes to be estimated both within the breast and onto its surface. Due to its simplicity, non-invasiveness and safety, decametric microwave radio-thermometry may be a promising method for diagnosing breast cancer and evaluating the effi ciency of its treatment.

Tne worh was carried out at "Blokhin Russian Cancer Research Center " of Russian Academy of Medical Sciences

Objectives and tasks of thesis.

Perpose of the study

Optimization of early diagnosis and evaluation of treatment of breast cancer using microwave radiometry.

Objectives of Research:

1. To study the effectiveness of various methods of breast cancer diagnosis.

2. To assess the sensitivity, specificity and accuracy of the microwave radiometry in the diagnosis of breast cancer.

3. Carry out a comparative analysis of the efficiency of the microwave radiometry with traditional methods of breast cancer diagnosis.

4. Identify the role of microwave radiometry to assess the effectiveness neoadjuvant therapy for breast cancer.

Scientific novelty of research

For the first time defines the place of microwave radiometry (RTM) in comprehensive diagnosis of breast cancer, to determine the accuracy, the sensitivity and specificity of the method and the evaluation of its effectiveness. For the first time on a large clinical material perfected technique radiometry of the mammary glands, the values of characteristics of temperature anomalies in tumor diseases breast. For the first time carried out a comparative analysis of microwave radiometry data ultrasound and mammography studies in different age groups, depending on the morphological structure node tumors of the mammary glands. For the first time found that the severity of the temperature anomalies, estimated by the method of microwave RTM may act as prognostic factor in breast cancer, in this case revealed that less pronounced than thermal asymmetry, and the more favorable prognosis significantly higher overall and disease-free survival in this category patients. It is shown that with the increase of efficiency of preoperative diagnosis of tumors of the mammary glands number increases detected "early" and the percentage of cancers of organ operations, This estimated effect of neoadjuvant therapy can be one of criteria prognosis in locally advanced breast cancer.

Theoretical and practical significance of the work

We describe the characteristics of breast cancer detected with using the method of microwave RTM (the value of thermal asymmetry between the same points mammary temperature spread between the individual points in the affected mammary gland, the temperature difference between the dispersion glands). A new approach to the assessment of breast tissue It allows for non-invasive dynamic control Dynamics treatment of this pathology. It is found that the dynamics of changes under the influence of temperature chemotherapy in breast cancer patients identified through RTM fixed microwave before dynamic structural changes detected by mammography (MMG) and ultrasound (US) that may be useful for evaluating the effect of the intermediate neoadjuvant therapy to its further correction. It is shown that the benefits of the proposed diagnostic method microwave RTM are accessibility, lack of radiation exposure, the opportunity quick interpretation of the results of research and non-invasive. The obtained results allow to recommend the introduction into clinical practice radiometry method for conducting surveys of women, not with clinical signs of breast diseases. It demonstrated the need for a microwave method radiometry in the framework of a comprehensive survey, along with other Modern methods of diagnostics of breast diseases.

CONCLUSIONS

1. Characteristics of the method of microwave RTM in the diagnosis of thyroid nodules comparable to US and rentgenomammografii. Sensitivity of Microwave radiometry 88.3%, 92.1% mammography and ultrasound 86.8%. Accuracy RTM is 96.5% (MMG - 98.3%, US - 94.0%), specificity microwave RTM - 94.7%, mammography and ultrasound - 100% in both cases. The sensitivity of microwave radiometry related to the identification breast malignancies is 90.1% MMG - 90.4%, US - 85.3%. The accuracy of microwave RTM 98.0%, US 97.7%, MMG - 97.9%. Specificity microwave RTM 93.5%, inferior to the respective levels index for mammography and ultrasound, respectively 98.6 and 98.0%.

2. Characteristic features of breast cancer by microwave RTM are as follows: the value of thermal asymmetry between the same points mammary temperature spread between the individual points in the affected mammary gland, the temperature difference between the dispersion glands.

3. Intensity of temperature anomalies is a predictor factor in breast cancer. The thermal asymmetry is less pronounced, the more favorable prognosis and significantly higher overall and disease-free survival. Overall survival in severe termoassimetrii (Th5) It was 5-year-old - 75%, 10-year-old - 25%. When thermoasymmetry Th1-Th3 5-year-old and 10-year overall survival rates were 85.7%.

4. In the course of neoadjuvant therapy of breast cancer in all patients observed dynamics of microwave thermometry: before the start of reatment, 100% of patients in the expert opinion of microwave systems in line with RTM level Th5, after 4-6 courses of chemotherapy Th4 level was determined at 41.7% patients, in 58.3% of women decreased performance expert Th3 system to levels (33.3% of patients) and Th2 (in 25% of cases).

5. Dynamics of temperature changes under the influence of PCTs, identified with microwave RTM fixed before structural Dynamics changes detected by MMG and US, and can be used to intermediate evaluate the effect of neoadjuvant therapy to her further correction.

6. The temperature changes that occur in the mammary glands by the impact of chemotherapy correlated with the severity of medical pathomorphism. The higher the total degree, the more pronounced pathomorphosis. Summary degrees can be used to assess the effectiveness of neoadjuvant therapy.

7. Microwave RTM can be recommended as a method for the formation of groups at risk of breast cancer, as well as additional research in differential diagnosis. At the young age of women preferred share RTM microwave and ultrasound in women older than 40 years - the use of microwave-RTM and mammography.

8. The advantages of the proposed method of diagnostics of microwave RTM it is the availability, relatively low cost studies absence of radiation exposure, the ability to quickly interpret the results research and non-invasive.

Popov Andrey Nikolaevich, Voronezh 2006 - State educational institution of higher professional education "Voronezh State Medical Academy. Burdenko Federal Agency for Health and Social Development "

The purpose and objectives of the study.

The aim is to study the use of computer radiometry method of screening for breast cancer.

Based on the goal, the following research objectives are defined:

• Based on the analysis of the dynamics of basic quality indicators for breast cancer over many years in the Voronezh region to assess the needs for screening for this disease;

• determine the diagnostic performance of the expert system apparatus RTM - 01 - RES corresponding to various breast diseases;

• Compare the results obtained with clinical, ultrasound, mammography, and morphological data;

• to establish the generalized differential - diagnostic criteria radiometry computer, allowing to use the device effectively RTM - 01 - RES in screening for breast cancer;

• The block diagram of the primary algorithms and specifying diagnostics of breast pathology.

The scientific novelty of the research results.

The following results were obtained in the dissertation, scientific novelty characterized by:

• structure of the process control systems of screening of breast pathology, based on the use of computer radiometry providing initial ranking of diseases on the advisability of specifying diagnostics;

• Integrated criteria breast pathology using a computer radiometry other than the color rendering in combination with a numeric equivalent temperature asymmetry, optimizing the implementation of screening of breast pathology;

• algorithmization process complex diagnosis of breast diseases, ensuring the rational use of mammography, ultrasound, and morphological methods of investigation after preliminary computer radioteromodiagnostiki;

• color and numerical equivalents temperature asymmetry with proliferative processes in the mammary glands, allowing identify a cohort of women with precancerous conditions, provide them with proper treatment and medical examinations with enhanced capacity and minimizing the interval between surveys;

• identification of risk areas tools for breast cancer, in determining the conditions of lack of funding prevention activities prioritize the implementation of screening programs.

The practical significance and implementation of the results.

The developed algorithms management of patients after radiometry survey, as well as practical advice on evaluating RTM-diagnostic data acquisition equipment as implemented in practical health Belgorod, Lipetsk and Voronezh regions.

Conducted oncological prophylactic examinations of women in the enterprises of Voronezh and in one area of the field. Active detection of breast cancer of 0.45%, dishormonal hyperplasia with proliferation of epithelial 3.42%.

Justified in the criteria for the identification of risk areas for breast cancer used in the formation of regional targets for oncology programs in Voronezh and Lipetsk regions with a view to sustainable financing of priority directions of medical care to patients with cancer.

The results of the thesis are introduced in the educational process of the Department of Oncology FPC and PPP VGMA.

CONCLUSION

1.It was conducted analysis for multi-year dynamics of the incidence of breast cancer, mortality from this disease, the main quality indicators of cancer care, which allows to evaluate the reasons for the lack of effectiveness of the secondary prevention methods.

2. It was formed structure of process control systems of screening of breast pathology, based on the use of computer thermometry providing initial allocation of diseases requiring specifying diagnostics.

3. It was developed the algorithms process complex diagnostics of breast pathology, optimizing the use of mammography, ultrasound, and morphological methods of examination after pre-RTM-diagnostic computer.

4. It is substantiated integrated diagnostic criteria of breast pathology using a computer radiometry, other than the color rendering in combination with a numeric equivalent temperature asymmetries that facilitate screening by doctors and nurses

5. There were proposed tools for identifying of risk areas of breast cancer, in determining the conditions of lack of funding prevention activities prioritize the implementation of screening programs (consistently high incidence rates, high average levels of its dynamics at low incidence levels, high rates of late diagnosis at low incidence levels).

6. Systematic approach to the formation of a cohort of women with precancerous conditions based on the analysis of color and numerical equivalents temperature asymmetries, promotes their full clinical examination with an expanded volume of inspections, minimizing the intervals between them, adequate treatment.

7. The results of the screening of breast pathology in 881 women show high informative method of computer radiometry, the possibility of its use in carrying out routine inspections in local hospitals, medical clinics, on obstetric points, enterprises and organizations of any form of ownership.

8.There are presented practical recommendations on the use of RTM-diagnosis during the oncological prophylactic examinations of the female population.

Daoud Hamada, Moscow 2001 – Russian Federation Ministry of Health State Research Center of Laser Medicine

Objectives and tasks of thesis.

Perpose of the study

To study the diagnostic value of deep microwave radiothermography in complex diagnostics of acute inflammatory and destructive processes of the appendix.

Objectives of research

1. Highlight features of radiothermography picture of abdominal cavity in healthy persons on topographic anatomical landmarks and projections in different age groups.

2. Determine radiothermographic features of acute appendicitis in the ordinary, pelvic and subhepatic location of the appendix.

3. Compare the results radiothermographic studies depending on the nature of inflammation in the appendix on the results of the histological study in patients with acute appendicitis.

4. Select radiothermographic diagnostic criteria for acute appendicitis, depending on the nature of morphological changes of the appendix.

5. The expediency of application and radiothemography determining the indications for surgery in the diagnosis of acute appendicitis and its complications.

Scientific novelty of research

First, based on detailed study radiothermographic data highlighted features thermographic pictures of the abdominal cavity in practically healthy people for topographic anatomical landmarks and projections in different age groups.

First settled in the role of microwave radiothermography the diagnosis of acute appendicitis. For the first time on a large clinical material compared results of the deep microwave radiothermography with clinical and laboratory performance and the results of histological examination appendix in patients with acute appendicitis.

Defined criteria for holding radiothermographic operation in hospital emergency surgery help.

For the first time described features radiothermographic acute appendicitis with normal and atypical location appendix. defined diagnostic possibilities microwave radiothermography in diagnosis appendiceal infiltrate.

The practical significance of the study

In the study of radiothermographic data from healthy subjects established that radiotermogramma of abdominal depending on the age changes and has its own characteristics.

The study of the diagnostic value of deep radiothermography in acute surgical diseases can accurately determine the value of the deep microwave radiometry in the diagnosis of acute appendicitis, as well as in different variants of its course. It was found that the RTM-specific investigational study for greater diagnostic importance is the presence of temperature asymmetry over 0.6 °C in the right and left iliac areas with localized "hot zone" in the projection of the appendix, the difference of temperature were recorded, compared with an average value of the temperature in this age group. Established supporting role deep microwave radiothermography in determining the severity and prevalence of imflammatory-destructive processes in acute appendicitis. Thus, the degree of increase of the temperature gradient can indirectly judge the nature of the inflammatory process (catarrhal and phlegmonous or gangrenous).

CONCLUSIONS

1. Deep microwave is radiothermography a highly sensitive method for early diagnosis of acute appendicitis. Possibility of comparative diagnostics, rapid registration internal temperature, non-invasive, characterized as a promising method in the complex the diagnosis of acute appendicitis.

2. According to the deep microwave radiothermography normally any of regular differences with diagnostic value in the right and left iliac areas within each age group we have not found, except for a small asymmetry in the temperature range from 0.2 °C to 0.4 °C, but no more.

3. At RTM study for a particular patient has large diagnostic importance the presence of thermal asymmetry more than 0.6 °C in the right and left iliac regions with localized "hot zone" in the projection of the apendix process.

4. According to the deep microwave radiothermography it can confirm not only the presence of an acute inflammatory process in appendix, but the degree of increase temperature gradient can judge the nature inflammation.

GULMURADOVA NARGIS TASHPULATOVNA, Moscow 2004 - State Research Center of Laser Medicine of Ministry of Health and Social Development Russian Federation

Objectives and tasks of thesis.

Perpose of the study

To improve the results of treatment of patients with skin carbuncles using modern laser technology.

Objectives of research

1. To study the possibility of a deep microwave radiometry in determining the boundaries of radical excision of skin carbuncle.

2. Carry out a comparative assessment of conventional and laser methods of excision of skin carbuncles.

3. Develop and implement into clinical practice methods of complex treatment of wounds formed after excision of skin carbuncles, using a carbon dioxide laser.

4. Carry out a comparative assessment of wound healing process in patients with wounds after excision of skin emerging carbuncles when using photodynamic therapy, bioactive wound dressings and low-intensity laser radiation.

Scientific novelty

The first time the possibility of RTM-diagnosis in the definition of necrosis and inflammatory infiltration of the area, as well as to establish the boundaries of the skin excision and carbuncle of the dynamic observation of the course of wound healing. On the basis of clinical, laboratory, morphological studies and RTM-diagnosis assessed the effectiveness of carbuncle excision of the skin using a CO2 laser.

First developed and introduced into clinical practice methods of complex treatment of wounds formed after excision of skin carbuncles, with the use of photodynamic therapy of bioactive wound dressings and low-intensity laser radiation. The possibility of imposing primary joints, optimized timing overlay early secondary sutures and autodermoplasty.

Practical significance

First developed and introduced into clinical practice RTM diagnostics carbuncle of skin, allowing to establish the boundaries of the excision of necrotic inflammatory infiltrate. Given the scientific substantiation of the use of CO2 laser radiation for the purpose of radical excision of skin carbuncle followed by the imposition of primary sutures or autodermoplasty. The developed method of complex treatment of wounds, formed after excision of skin carbuncles, with the use of photodynamic therapy, LLLT BAP and help to reduce clearance of the wounds from necrotic masses

and the appearance of granulation tissue, acceleration of reparative processes and the healing of wounds in 1,5-1,8 times in comparison with traditional treatments.

CONCLUSIONS

1. Microwave radiometry diagnosis of skin carbuncles allows to specify a zone of necrosis and prevalence of inflammatory tissue infiltration, set the boundaries of radical excision and conduct dynamic monitoring of the course of wound healing.

2. Excision of skin carbuncle CO2 laser increases the radical surgical treatment of necrotic suppurative focus, sterilize the wound, which leads to a reduction of inflammation exudative phase, early formation of granulation tissue, expanding the indications for the imposition and carrying out the primary seams autodermoplasty early, shortening the duration of treatment in 1, 6 times.

3. Photodynamic therapy of wounds after excision of skin carbuncle promotes fragmentation of coagulation necrosis, improves regional blood circulation, speeds up the process of cleansing the wounds and the formation of granulation tissue in 2.4-3.2 times, which reduces the time of complete healing of wounds.

4. Application of "Daltseks-trypsin" in combination with LLLT activates microcirculation at the wound edges, facilitates the process of granulation tissue formation and its fibrous transformation synthetic activity increases cell elements of fibroblastic and macrophage series wound healing that provides 1.5 times faster.

5. Due to the combined use of a CO2 laser, photodynamic therapy, BAP and LLLT with the imposition of primary, early secondary sutures and autodermoplasty in 70% of patients with skin carbuncles achieved good functional and aesthetic results.

Zimin Valeriy Valerievich, Nizhnii Novgorod 2004 - "Nizhny Novgorod State Medical Academy „

Objectives and tasks of thesis.

Objectives of research

The purpose of this study is to develop a technique of deep radiometry of thyroid gland, assessment of the possibilities of this technique in the diagnosis and differential diagnosis of functional states and nodular thyroid disease compared to other radiological techniques.

To achieve this goal it was necessary to solve the following problems:

1. To assess the diagnostic capabilities of radiometry of the thyroid gland in the diagnosis of her disease;

2. Develop a methodology for measuring the depth temperature of the thyroid gland;

3. Examine the results of radiometry of thyroid gland, set diagnostic criteria for various diseases of the thyroid gland to change of the deep temperature;

4. Compare the results of the clinical and radiological studies and radiometry;

5. Develop a comprehensive scheme of examination of patients with the use of radiometry in the diagnosis and differential diagnosis of thyroid diseases.

Scientific novelty.

The first time are presents data of deep radiometry of thyroid gland in normal, and the temperature of semiotics violations the functional state of the gland, with the node pathology systematization characteristic of each type of signs of pathology.

Designed a method for measuring and evaluating the temperature parameters of thyroid gland using deep radiometry. Estimated the possibility in the differential depth radiometry diagnosis of nodular thyroid gland disease and its place in the series other radiological methods of investigation of the thyroid gland.

CONCLUSION

1. The radiometry is an important additional method in radiological complex of diagnosis of thyroid gland diseases' allowing to evaluate the functional state of the body before the test of serum thyroid hormones and thyroid scanning

2. The technique developed deep radiometry thyroid gland has diagnostic value in the study of temperature characteristics (temperature index, focus and total thermal asymmetry), and it allows you to assess the functional status of each thyroid gland, nodal colloidal entities including the implementation of minimally invasive and after traditional operations on the thyroid gland.

3. In the evaluation of the functional state of the thyroid gland temperature index at euthyroid is equal or close to 0 °C (0,057 ° ± 0,013 °C), at hyperthyroidism is 0,60 ° ± 0,07 °C, at hypothyroidism is -0,41 ° ± 0,04 °C.

4. Deep radiometry is an important diagnostic method in combination with the investigation and scanning of thyroid gland hormones` in identifying sites with functional autonomy, zone of hyperfixation of the RFP have a greater temperature than the zone of reduced accumulation of the RFP.

5. The use of radiometry in patients at an early postoperatively to evaluate the state functions thyroid to changes in the level of thyroid hormones.

6. Deep radiometry can be used in general complex radiological studies in the diagnosis of diseases of thyroid gland as a screening method, as well as a control method for the postoperative course with thyroidectomy.

Kolesov S.N.

LITERATURE REVIEW

The temperature as a parameter to assess the pathology of the central and peripheral nervous system.
Thermal imaging and radiometry.
Medical aspects of thermica and radio thermometric diagnosis.
Brain Pathology.
Spinal cord Pathology.
Peripheral nervous system pathology.
Osteocondritis of the spine.
Damage of the peripheral nerves.

EXPERIMENTAL grounding for application of millimeter and centimeter radiometry in the diagnosis of intracranial pathology.
Influence of the shielding effect of the hair on the registration of intracranial pathology in the millimeter wavelength range .
Evaluation of the depth of penetration of microwave radiation on the models of various tissues.
Thermo Topography of brain temperature
Thermo Topography of the spine and limbs in the centimeter wavelength range.
DISTRIBUTION of contrasts in internal temperature and depth´s thermoprofiles in healthy volunteers
THERMOVION AND RADIO THERMOMETRIC diagnosis of tumors and brain injuries .
Methods of research .
Brain Tumors.
Traumatic brain injury .
Traumatic brain compression.
Preoperative thermovision and microwave radiometry diagnosis of tumors and spinal cord injuries
Thermovision and microwave radiometry diagnosis of lumbar osteochondrosis

Polydiapason thermo-radiometry - a new direction in the study and diagnosis of diseases of the central and peripheral nervous system

ALIBAKHSHOVA Farhangez Kayhusravovna, Moscow 2010 – Federal State Autonomous Educational Institution of Higher Education RUSSIAN PEOPLES FRIENDSHIP UNIVERSITY

Objectives and tasks of thesis.

Perpose of the study

1. To present the clinical characteristics of patients with various factors of infertility given the state of the mammary glands according to clinical examination, ultrasound and rentgenomammography.

2. To analyze the frequency and structure of various breast diseases in women with infertility.

3. Determine the dynamic state of the mammary glands by ultrasonography and radiometry during treatment with inducers of ovulation.

4. Develop a set of preventive measures to prevent possible negative dynamics of the state of the mammary glands within Assisted Reproductive Technologies ART programs.

Scientific novelty

The structure of benign breast changes in women with various factors of infertility has been analysed. Defined influance of hormone replacement therapy in cycles of ovulation induction on breast condition in women with various infertility factors, depending on age, pregnancy in assisted reproductive technologies (ART), induction schemes ovulation, the number of attempts at in vitro fertilization (IVF), the dose of gonadotropins, the number of derived oocytes, ovarian hyperstimulation syndrome (OHSS) and preovulatory estradiol levels. Spend evaluation is not only an objective condition of the breast, but the subjective assessment of women with the help of a specially developed test profiles.

The practical significance of the work

It was proved the necessity of compulsory inspection of mammary glands in women with various infertility factors in the preparation for the ART program, due to the high incidence of benign breast changes in women of this contingent.

It is substantiates the duration of the interval between the holding of ART programs at least six months.

I tis presented the necessity of carrying out preventive measures to reduce the negative effects of hormone therapy in ART programs nonhormonal drugs, in particular, homeopathic medicines.

CONCLUSION

1. At 62.6% of women with various factors of infertility observed changes benign breast; the most common diffuse fibrocystic breast disease - 51.6%. This benign breast changes found in patients with endocrine infertility factor - 75.5%; when tuboperitoneal factor - 57.5%; while men - 53.1%; infertility of unknown origin - 50% of cases.

2. After the induction of ovulation by ultrasound results in breast occurs a significant increase in the diameter of the ducts (before treatment - 1,22 ± 0,06 mm after-1,50 ± 0,07mm ($P < 0,05$)). Return to the original diameter of the ducts is not earlier than 6 months after the induction of ovulation.

3. According to the radiometry in 38.5% of women after ovulation induction was an increase in the average t° breast tissue; at 61.5% - the dynamics was observed. No correlation was found between the increase in average t° breast tissue and patients age ($R = 0,12$), ovulation induction scheme ("short» -$R = 0,07$; «long» -$R = 0,11$) and the onset of pregnancy in the program ART ($R = 0,16$).

4. A direct correlation between the increase in average tº breast tissue and the number of IVF attempts (R = 0,41), the dose of gonadotropins (R = 0,46), number of oocytes (R = 0,37), the level of preovulatory E2 (R = 0.40) and the presence of ovarian hyperstimulation syndrome (R = 0,52). Normalization average tº breast tissue does not take place earlier than 12 months after ovulation induction.

5. As a result of the test of questioning on the background of ovulation induction marked deterioration in the subjective assessment of the state of the mammary glands: the frequency of claims, estimated at 1-2 points increased to 45% compared with 23.5% in the spontaneous cycle, complaints evaluated in 3 points - up 11% compared with 0.5% in the uninduced cycle.

6. The use of non-hormonal cycles homeopathic herbal remedies in preparation for the induction of ovulation and ovulation induction in the background can reduce the pain and breast engorgement during ART programs in women with diffuse fibrocystic mastopathy.

Nikitin Victor Sergeevich, Kirov 2007 - State establishment of the Republic of Mariy El "The Republican Clinical Hospital for war veterans" and St. Petersburg Institute of Bio-regulation and Gerontology

Objectives and tasks of thesis.

Objectives of research

1. To study by indicators of biological age rates of age` physiological changes in men aged 40-59 years who had undergone radiative forcing in the liquidation of the Chernobyl accident.

2. Identify the features of the functional state of the autonomic nervous system according to the heart rate variability (HRV) in patients with signs of premature aging.

3. Identify the characteristics of cerebral blood flow in patients with natural and premature aging, depending on the functional state of autonomic nervous system.

4. To study the characteristics of natural electromagnetic radiation tissues of the brain in patients with signs of premature aging.

The scientific novelty of the work:

Biological age of participants of liquidation of the Chernobyl NPP accident above the calendar age of 13 years.

Premature aging of the liquidation of the accident at the Chernobyl NPP is characterized by involutive changes in the blood supply system of brain and in control of autonomic functions of circulation. The parameters of the functional state of these systems close according to the values of the same indicators of elderly and senile age.

Premature aging of the liquidators of the Chernobyl accident characterized similar to people under the age of 60-74 years, functional relationships between parameters of blood flow in the arteries base of the brain and the performance of spectral analysis of variability heart rhythm.

According to the parameters of endogenous electromagnetic radiation brain tissue showed improvement of brain hydration in patients with signs of premature aging.

Theoretical and practical significance of the research

Completed work represents basic research in the field of physiology of cerebral circulation, and gerontology. Results of the study expand ideas about the pace of aging of participants of liquidation of failure on Chernobyl nuclear power plant, the role of the autonomic regulation of cerebral hemodynamics and features natural electromagnetic radiation from brain tissue in premature aging.

The results of the study allow to justify the need for identify signs of premature aging of the liquidators of the accident at the Chernobyl nuclear power plant, as well as that of other categories of people undergoing stress effects of functional diagnostics methods for timely geroprotective purpose of adequate measures in clinical practice.

The proposed methodical complex non-invasive survey (Transcranial Doppler in conjunction with the methods of the deep radiometry and spectral analysis of HRV) is recommended for introduction in medical institutions that will facilitate early detection of premature aging of the human body, had undergone extreme physical and / or psychological impact.

CONCLUSION

1. The biological age of the liquidation of the accident at the Chernobyl nuclear power plant by more than 13 conditional years higher than men of the same calendar age (40-59 years), but not involved in the emergency it.

It can be attributed to a group of liquidators to the category of persons with high rates aging and justifies the need to identify their physiological signs of involution processes with the aim of early prevention of "disease old age. "

2. Indicators of BPC (TP, LF, HF) in patients with signs of premature aging quantitatively reduced and VLF share in total power range of neuro-humoral regulation of heart rate is increased compared to control group (healthy men aged 40 - 59 years), indicating that reducing the effectiveness of autonomic control of the heart rhythm in premature aging.

3. Indicators of BPC in liquidators of the Chernobyl accident at the age of 40-59 years have similarities with those of people who have reached the age 60-74 and 75-87 years, indicating that early (premature) development involutive processes caused by radiation exposure.

4. Indicator time-averaged maximum velocity cerebral blood flow (TAMH) in the arteries of the base of the brain in people with symptoms premature aging (liquidators of the Chernobyl), is reduced, as well as in patients elderly. This should be seen as saline sign involutive changes and decrease the efficiency of the cerebral hemodynamics, even at a relatively young age.

5. Indicators of peripheral resistance to blood flow in the PCA (Pi, and S / D) in persons with signs of premature aging (the Chernobyl clean-up workers) increased by than those of the control group of the same age and approaching the values of elderly persons it. It shows an advantageous development of the involutive processes vertebro-basilar section cerebrovascular system in premature aging.

6. Premature aging of liquidators of the Chernobyl accident It demonstrated a correlation of blood flow in the arteries of the base indicators brain and spectral analysis of HRV parameters characteristic those aged 60-74 years. Which indicates a high degree of heterotopic and heterochronic manifestation of age changes of functional relationships in cerebrovascular system in premature aging.

7. Premature aging is characterized by a reduction in capacity endogenous brain electromagnetic radiation. Power endogenous electromagnetic brain of microwave radiation in Group II (control) it amounts to 53,70 ± 2,74 mK°, the radiation intensity in group I (patients with physiological signs of premature aging) 42,62 ± 1,46 mK that 26% less than those with natural aging rate.

8. Hypercapnia test in patients with signs of premature aging It leads to unreliability increase the radiation power in the "vascular sector "(oscillation period 0-10 c) 2%, and a significant increase in power radiation in brain tissue "extravascular sector" by 13%, which it helps to normalize the level of hydration of the intercellular spaces, total radiation power of the brain tissue.

Naumkin Natalia Genadyevna, Moscow 1999 - RUSSIAN ACADEMY OF MEDICAL SCIENCES Scientific Center for Obstetrics, Gynecology and Perinatology.

Objectives and tasks of thesis.

Perpose of the study

The development of new, effective ways to diagnose, dynamic control and treatment of fibrocystic breast disease.

Objectives of research

1. Study of the immune, hormone and interferon status in various forms of fibrocystic breast disease.

2. Identify and develop methods for diagnosis and objectification of dynamic breast changes as a result of treatment.

3. Evaluation of the effectiveness of treatment of mastitis by Wobenzym, cycloferon and traditional methods.

4. Comparative evaluation of various methods of treatment of fibrocystic breast disease.

a - and g- IFN-producing ability of white blood cells that may be indicative of disorders of the immune response in this disease.

Scientific novelty.

For the first time evaluated the possibility of therapeutic use of the enzyme preparation Wobenzym, and interferon inducer cycloferon having immunomodulatory, anti-inflammatory, antiproliferative, secondary analgesic effect in various forms of mastitis. Established that wobenzim has the highest efficacy compared to conventional methods and cycloferon therapy. The proposed methods of therapeutic intervention can significantly expand the arsenal of therapeutic agents for the treatment of breast cancer.

A method for objective evaluation of the quality of the therapeutic effects of various drugs - radiometry. The method detects the intensity of the thermal radiation of the internal tissues of the patient in the range of microwave frequencies at a depth of 3-7 centimeters, which distinguishes it from the previous method of infrared radiation by means of which the temperature of the surface being measured, but actually in the layer of the epidermis. Radiometry allows a differential diagnosis of breast disease, and evaluation of the treatment. The information may be presented in the form of graphs, the internal temperature of the image field and numerically. The proposed method for treatment of dynamic control quality change indirectly indicates the metabolic processes in the prostate tissue proliferation activity, the level of vascularization body and allows to adjust at any time during the treatment regimen, depending on the individual sensitivity of patients to therapy.

The data on the changes in the immune and interferon status in patients with mastopathy. It was revealed that when fibrocystic disease of the breast decreased performance subpopulations of T-cell immunity, observed high titers of interferon in serum amid falling a - and g- IFN-producing ability of white blood cells, which may indicate violations of the immune response in this disease .

Practical significance

The necessity of inclusion in a complex of survey and assessment of the immune status of interferon in patients with fibrocystic breast disease.

Studies have shown that mastitis is characterized by hyperprolactinemia, hyperestrogenia and progesterone deficiency states.

It proved the feasibility of the treatment of mastitis drugs with anti-inflammatory, antiproliferative, immunomodulatory effects - Wobenzym and cycloferon.

The necessity and methodology of dynamic monitoring of the effectiveness of therapeutic interventions by radiometry.

CONCLUSION

1. When the diffuse and nodular forms of fibrocystic disease of the breast, a change in immune parameters, expressed in relative statistically significant reduction in the content of T-lymphocytes and T-helpers, while more

severe form of the disease (nodal) is characterized by a large inhibition of T-cell immunity. For both forms of mastitis is characterized by a statistically significant increase in the number of natural killer cells, indicating that the antitumor resistance of the organism in this group of patients. When mastitis occurs a tendency to increase the levels of immunoglobulin class IgG, IgA, IgM, compared to the control group of healthy women.

When fibrocystic mastopathy marked imbalance in the interferon system, manifested by increased levels of serum interferon and inhibition of a - and g- IFN-producing ability of white blood cells, which indicates the interferondeficite state in these patients.

2. Fibrocystic breast disease without accompanying neuroendocrine pathology is characterized by a statistically significant increase in the concentration of prolactin, estradiol and a significant reduction in levels of progesterone relative to the group of healthy women.

3.Radiothermometry can be used as a new, effective, harmless method for the diagnosis of breast disease, and assessing the quality of the therapy at all stages of treatment.

4. Wobenzym and cycloferon are useful as alternative therapeutic agents for various forms of fibrocystic disease of the breast. Efficiency of application is: Wobenzym, 65.1%, cycloferon -52.2%, -43.6% conventional therapy. The most promising use Wobenzym with fibrocystic mastopathy with prevalence of fine-cystic and glandular components, cycloferon better display their action in mastopathy with prevalence of glandular and fibrous components. Traditional therapy has the greatest influence on a mastopathy with prevalence of fine-cystic component.

The effectiveness of treatment is significantly reduced in the long-term period (1 year after the end of treatment) in all observed groups and amounts: Wobenzym - 19,0%, cycloferon - 23.2% -16.7% of traditional therapy.

5. Wobenzym and cycloferon have a more pronounced stimulating effect on the relative abundance of T-lymphocyte and T-helper cells, compared with conventional therapy.

The state of interferon status greater impact (decrease in serum and increase production capacity and a-g-interferon) have cycloferon and Wobenzym.

Makieva Kiyal Bolotbekovna, Bishkek, 2010 - work has been performed at the Department of Oncology, radiation diagnosis and treatment of Kyrgyz - Russian Slavic University

Objectives and tasks of thesis.

Perpose of the study

The aim of this study is improving diagnostic measures in pathological breast formations.

Objectives of Research

1. To study the prevalence rate of breast tumors glands

2. To analyze the diagnostic procedures at pathological lesions of breast.

3. The block diagram of the primary algorithms and specifying diagnostics of breast pathology.

4. To study the possibility of using radiometry at breast health and to compare the obtained the results of clinical, ultrasonic, mammographical and morphological data.

5. Set the generalized differential – diagnostic criteria of computer radiometry, allowing efficient use of the device RTM - 01 - RES in screening of breast cancer.

Scientific novelty

1. The first time in the country was lerned the diagnostic criteria, aimed at the early detection of breast cancer.

2. For the first time was studied the comparative analysis of clinical outcomes, ultrasound, mammography and morphological methods of women examination with breast pathology.

3. For the first time in the country developed an algorithm for events the use of modern methods of research, in particular, microwave radiometry.

Scientific and practical significance

1. This work has created a risk for development of breast cancer and to determine the diagnostic criteria in patients with tumors that have great scientific and practical significance.

2. Radiometry method is absolutely safe, non-invasive, highly effective method of examination for the early detection of cancer pathology of the breast.

3. The color and the numeric equivalents of the temperature asymmetry by proliferative processes in the mammary glands allow select a cohort of women with precancerous states, to provide them with proper treatment and medical examinations with expanded capacity and minimizing the spacing between surveys.

CONCLUSION

1. The bulk of the patients (76.1%) with benign tumors of mammary gland entered to the National Oncology Center initially without any treatment. About 18% of patients treated by different specialists within 6 months. Only 2.0% of the 197 patients had a tumor the size of 1 cm at the first pass. Approximately 50% had primary tumor size from 2.0 to 5.0 cm.

2. Most often patients with benign tumors of the breast occurred (35.5%) in the group of 40-49 years, and breast cancer - 50-59 years (25.0%). The stage I of breast cancer was diagnosed only by 3%, despite the relatively good tumor visualization. At the same time, cancer cytological verification was confirmed only a third of patients. Histologically, the most often tumor it was introduced like infiltrative forms of cancer (85%).

3. In algorithm of breast tumor and non-neoplastic lesions diagnostic must be enabled method of microwave radiometry, since the sensitivity of the RTM method was 86.0%. When used together, the RTM and mammography the sensitivity comes to 98.0%.

4. The sensitivity of ultrasound in breast cancer was 81.9%, while mammography - 84.3%. When tumor size is less 2.0 cm the sensitivity of RTM - diagnosis was 84.8%, while indices of ultrasonic and X-ray methods were 75.9% and 66.8% respectively.

Kanevtsov Valery Viktorovich, Moscow 2004 - Study guide is intended for oncologists, surgeons, gynecologists and general practitioners.

The guide presents new sights in application of diagnostic methods like ultrasonography, mammography and microwave radiometry.

Cheboksarov Dmitry Vasilyevich, Moscow 2015 - Federal State Autonomous Educational Institution of Higher Education of RUSSIAN PEOPLES FRIENDSHIP UNIVERSITY

Objectives and tasks of thesis.

Perpose of the study

In order to improve the results of treatment and reduce the number of deaths to identify features of the temperature of the brain balance disorders in patients with acute ischemic stroke and to determine the possibility of their correction by cranio-cerebral hypothermia (CCH).

Objectives of research

1. In experimental model of acute brain ischemia and general hypothermia in animals to compare the results obtained with microwave radiometry of the brain and with using invasive thermometry.

2. Investigate the temperature balance of the brain by microwave termoregistratsii in healthy subjects at rest and during the session cranio-cerebral hypothermia.

3. To study the temperature balance of the brain by microwave thermo-recording in patients with acute ischemic stroke.

4. Identify the effects of the correction of the disorders of temperature balance of the brain by cranio-cerebral hypothermia in patients during the acute phase of ischemic stroke.

5. Develop a methodology and protocol of cranio-cerebral hypothermia with cerebral cortex controlled temperature in patients with acute ischemic stroke.

Scientific novelty

1. In condition of acute experiments on animals for the first time shown that the method of microwave radiometry in the range 3.2-4.5 GHz allows non-invasively assess the dynamics changes in brain temperature during ischemia and hypothermia.

2. Firstly, it was shown that in healthy individuals is not marked heterogeneity of the temperature of brain at rest, and the use of cranio-cerebral cooling allows quickly and safely lower the temperature of the cerebral cortex at 1-3 °C without changes in basal body temperature.

3. It was developed the method of cranio-cerebral hypothermia in patients with acute ischemic stroke.

4. For the first time, it was studied characteristics of the temperature heterogeneity of the cortex of the cerebral hemispheres in patients with acute ischemic stroke and in conditions of use cranio-cerebral hypothermia.

5. The efficiency of the use of cranio-cerebral hypothermia in correction of disorders of the thermal balance in patients with ischemic stroke.

The practical significance of the work

We prove the prospects of using microwave radiometry as a safe non-invasive method for assessing violations of the temperature balance in the brain focal ischemia and correction of cerebral hyperthermia using the CCH.

The use of non-invasive brain termomonitoring in patients with ischemic stroke to determine the indications for the use of terapeutic hyperthermia and predict the flow pattern of the acute period of the disease.

The developed technique and protocol of the CCH are aimed at correcting pirogenic states in acute ischemic stroke.

CONCLUSION

1. In acute experiments on animals have shown that the possibility of non-invasive method - microwave radiometry - can adequately assess the changes in temperature at different points of the cerebral cortex, resulting in cerebral ischemia, as well as during intravenous hypothermia and comparable with the dynamics of the thermometer.

2. The temperature of the cerebral cortex, determined by microwave thermometry, in healthy subjects at rest is 36,8 ± 0,8 ° C, demonstrating the absence of severe thermal heterogeneity. Cranio-cerebral hypothermia significantly lowers the temperature of the brain without causing hypothermia and general changes in the physiological parameters.

3. In patients with ischemic stroke in the first or second day of onset form local centers of hyperthermia (by microwave thermometry), in 82% of cases coinciding with the localization zones of the cerebral cortex lesions detected during imaging (CT / MRI), which is not displayed tympanic and axillary temperature.

4. Cranio-cerebral hypothermia provided stabilize the scalp temperature in the range 2-5 °C can be induced by local hypothermia cerebral cortex (32-36 °C) without any changes in body temperature and changes in the physiological parameters in patients with stroke.

5. One of the leading causes hypothermia cranio-cerebral positive action is to prevent the development of cerebral edema due to low temperature preservation of the cerebral cortex 24 hours after the session of cranio-cerebral hypothermia.

6. It was developed a method and protocol of cranio-cerebral hypothermia in ischemic stroke. It was presented the efficiency of the developed method for the correction of cranio-cerebral hypothermia in correction of local hyperthermia, which will greatly reduce mortality in patients with cerebral ischemia without complications from the basic functions of the body.

Avramenko Galina Vilyamovna, Moscow 2009 - Federal State Institution "National Medical and Surgical Center. Pirogov Medical University "

Objectives and tasks of thesis.

Perpose of the study

Improving the results of surgical treatment of breast non-palpable tumors by the use of radiometry at the stage of diagnostic search.

Research objectives.

1. Examine the possibility of microwave radiometry by screening to detect palpable breast tumors.

2. Evaluate the accuracy, sensitivity and specificity of radiometry method in detecting non-palpable breast tumors.

3. Evaluate the effectiveness of radiometry in comparison with ultrasonic and radiographic diagnosis of non-palpable breast tumors.

4. Assess the possibility of using microwave radiometry for the topical diagnosis of breast tumors when preoperative marking of tumors.

5. Determine the place radiometry in the algorithm of surgical treatment of women with palpable breast tumors.

Scientific novelty of research.

For the first time evaluated the possibility of using radiometry by screening for the early detection of non-palpable breast tumors. The accuracy, sensitivity and specificity of the method to the cytological differential diagnosis of benign and malignant tumors.

A comparative analysis of radiometry results with ultrasound and mammography studies in different age groups, depending on the presence of concomitant diffuse changes in the mammary glands, as well as depending on the size of nodular tumors.

The evaluation of radiometry capabilities in topical diagnosis of non-palpable breast tumors.

The place of radiometry in the algorithm of preoperative diagnosis and surgical treatment of women with palpable breast tumors.

With an increase in the efficiency of preoperative diagnosis of non-palpable breast tumors revealed an increasing number of "small" percentage of cancers and organ operations.

The practical significance of the study.

The results allow us to recommend the introduction into clinical practice of radiometry method for skrinningovyh without facing women surveys of specific complaints, and no clinical signs of breast diseases. Due to the high sensitivity of radiometry and ability to detect tumors in the "preclinical" stage, the use of this method for regular surveys of women will allow to form a risk with a shorter interval of observation, and thus a higher frequency identification "interval cancers" Formation of groups of patients with an increased occurrence of risk malignant tumors also make it possible to carry out preventive measures aimed at preventing and / or slowing down the development of tumors.

It developed and introduced into clinical practice examination of women algorithm to eliminate tumors in the mammary glands. Using microwave radiometry in the regular survey of women makes it possible to identify previously unsuspected, including malignant tumors and, therefore, more effective and less traumatic treatment of cancer patients. However, it should be noted that microwave radiometry can not be an independent method of definitive diagnosis of breast disease and to determine the exact diagnosis should only be used as part of a comprehensive survey of the mammary glands.

Conclusions.

1. The radiometry is an effective method of screening for the detection of non-palpable breast tumors.

2. The radiometer is characterized by high sensitivity, accuracy and specificity of the detection of non-palpable breast tumors. The sensitivity, specificity and accuracy of radiometry increases with age, as in benign and malignant tumors, regardless of the size of the tumors and the presence of concomitant diffuse breast changes fibrocystic breast. Sensitivity radiometry higher in breast cancer than in benign entities - in all age groups.

3. Performance indicators of radiometry are differ from the parameters of mammography and ultrasonography:

A. Sensitivity of radiometry exceeds the sensitivity of mammography in all age groups, as well as the sensitivity of ultrasonography among women older than 40 years, regardless of concomitant fibrocystic breast tumors and character.

B. Accuracy of radiometry is almost equal, and in some cases (in women older than 40 years) exceeds the accuracy of other methods of research in identifying both malignant and benign tumors, reaching maximum values in the older age group.

C. Specificity radiometry in most cases inferior specificity of mammography and ultrasonography, reaching equal values only in women older age group, regardless of the nature of the tumors.

D. When the size of tumors are less than 1 cm, radiometry has the highest sensitivity and accuracy in comparison with other diagnostic methods, however, the lower specificity. As the size of formations growing, sensitivity and accuracy as the radiometry and mammography and ultrasonography increases too.

4. Conducting radiometry not accurately determine the localization of non-palpable breast tumors, so topical diagnosis and minimize the extent of surgical intervention is necessary to conduct a comprehensive survey of the mammary glands.

5. The use of radiometry in the algorithm of surgical treatment as a patient selection step allows you to create high risk of having undiagnosed non-palpable breast tumors, which in turn leads to better surgical results.

CONCLUSION FROM ALL THESISES

Today it is possible to find in internet sites 14 thesis work. The physicians of different specialisation presents the results of the application of microwave radiometer RTM-01-RES in proces of screening, diagnosis or control of therapy. In many thesis the results of microwave thermometry was verified with basic method of diagnosis (US, X-ray, CT, NMR) and it was stated that results are comparable.
Radiothermometry can be used as a new, effective, harmless method for the diagnosis of different organs pathology

(breast disease, brain, thyroid gland, spinal cord ets.) and assessing the quality of the therapy at all stages of treatment. Side effects was not mentioned.

On the basis of conclusions of fourteen thesis, the producer RES Ltd., Moscow can stated that MD RTM-01-RES fulfiling all requirements regarding the safety and performance mentioned in Directive 93/42/EEC.

THESIS	Period	# patient	Pathology or control of therapy	Sensitivity %	Specificity %	Side effects
TSOMAEVA Elena Aleksandrovna, Moscow	2012	220	diagnosis	diagnosis and differential diagnosis of the pelvic organs diseases		No side effects were mentioned
Sinelnikov Olga Aleksandrovna, Moscow	2013	7	Diagnosis of CaMa and control of therapy	diagnosis and evaluation of effectiveness of neoadjuvant treatment of breast cancer 88.3%	94.7%	No side effects were mentioned
Popov Andrey Nikolaevich, Voronezh	2006	881	breast diagnosis	breast pathology screening		No side effects were mentioned
Daoud Hamada, Moscow	2001	207	diagnosis	diagnostics of acute inflammatory and destructive processes of the appendix		No side effects were mentioned
GULMURADOVA NARGIS TASHPULATOVNA, Moscow	2004	140	control of therapy	determining the boundaries of radical excision of skin carbuncle		No side effects were mentioned
Zimin Valeriy Valerievich, Nizhnii Novgorod, Russia	2004	271	diagnosis	diagnosis and differential diagnosis of functional states and nodular thyroid disease compared to other radiological techniques		No side effects were mentioned
ALIBAHSHOVA Farhangez Kayhusravovna, Moscow	2010	215	control of therapy	control of treatment by hormone replacement therapy in cycles of ovulation		No side effects were mentioned
Nikitin Victor Sergeevich, Kirov, Russia	2007	200	diagnosis	control of "disease old age"		No side effects were mentioned
Naumkin Natalia Genadyevna, Moscow, Russia	1999	210	diagnosis and control of therapy	control of therapy of benign pathology of breast		No side effects were mentioned
Makieva Kiyal Bolotbekovna, Bishkek, Kyrgyz rep.	2010	197	screening of breast	screening of breast pathology 86.0%		No side effects were mentioned
Kanevtsov Valery Viktorovich, Moscow, Russia	2004	223	diagnosis and screening	breast examination in a complex algorithm study of mammary glands as a prophylactic and diagnostic purposes		No side effects were mentioned
Cheboksarov Dmitry Vasilyevich, Moscow, Russia	2015	275	diagnosis and screening of therapy	study of acute phase of ischemic stroke and control of cranio-cerebral hypothermial therapy		No side effects were mentioned
Avramenko Galina Vilyamovna,	2009	700	diagnosis and therapy	improving the results of surgical treatment of breast non-palpable		No side effects were mentioned

Moscow, Russia				tumors by the use of radiometry at the stage of diagnostic search	

ARTICLE

Microwaves have been used over the 20 years in various applications in order to support clinical practice in Russia. Microwave radiometry was proposed approximately 40 years ago to be used as a diagnostic imaging method to noninvasively measure temperature distributions inside the human body. Since then numerous research results have been reported all the world regarding the clinical practical value of this passive imaging methodology which exhibits unique capabilities. The applications of microwave radiometry RTM-01 in clinical medicine aim mainly at obtaining information about internal in-depth body temperature patterns by the
non-traumatic measurement of natural thermal radiation from body tissues at low microwave and infrared frequencies. Knowledge of such internal body thermal patterns can assist clinical disease detection and diagnosis, e.g., as a noninvasive complement to the current computed tomography (CT) and magnetic resonance imaging (MRI) [1], X-ray mammography [2,3,4,5] and ultrasonography [2,3,5,11] technologies , and may have a role in the monitoring of therapeutic processes , e.g., during hyperthermia, PDT[1] or radio-chemo therapy, laser[1] and surgical treatment[2].

The ability to observe temperature variations inside the human body may help in detecting the presence of medical anomalies. Abnormal changes in physiological parameters (such as metabolic and blood perfusion rates) cause localized tissue temperature change.

In the article [1] **Zharov et al.** presents the concept of complex laser treatment of localized cancer which was recently suggested with the focus on optimization, increasing efficiency and selectivity of Interstitial Laser Therapy (ILT) with interactive imaging and temperature feedback. This treatment is based upon a combination of ILT, photoacoustic (PA) and photodynamic therapy (PDT) with microwave radiometric remote control of the temperature in the treated zone. The features of this concept for primary breast and head and neck cancer are: 1) the application of microwave thermometry for non-invasive real-time overheating control during ILP; 2) direct intralesional injection of a photosensitizer and dye enhancer through a tiny needle, followed by PA and ultrasonic impregnation and partly cancer cells damage; 3) combination ILT and PDT therapies; 4) post-operative PDT of the tumor by positioning LED arrays around breast; 5) using RODEO MRI for control of location of the tumor, needle and fiber and to monitor tissue changes during complex laser treatment. This paper focuses more on development of microwave radiometry temperature control. The previous experiments are presented concerning the study of remote microwave radiometric sensor for diagnostic purpose including the results of the clinical trials that have been conducted among over 1000 patients.

In the paper [2] **Burdina L.M. et al.** presents the results of application microwave radiometer RTM-01 in diagnosis of breast pathology. In Branch-1 of the Mammology Health Centre, Moscow the RTM-01-RES microwave imaging system has been used from December of 1997. For 5 years 2233 examinations have been performed and 1506 patients have been examined. For evaluating the reliability of RTM-diagnosis, its results were compared with cytological and histological results, if a patient had surgery. The use of RTM-diagnosis in conjunction with Mammography provides an extremely high sensitivity for breast cancer diagnosis. Each method had a sensitivity of about 90%. In the same time, when they were used together the sensitivity increased up to 98%. Mammography detects anatomical changes, while RTM-Diagnosis detects functional changes, so the share of the joint omissions is less than 2%. It should be noted that in 14 cases (7%) RTM-diagnosis detected breast cancer earlier than other methods could detect the disease, as thermal changes precede anatomical changes detected by Mammography and Ultrasound. Thus RTM-diagnosis allows an examiner to select patents, who are at a risk of breast cancer for further complex diagnosis and treatment. The method is absolutely harmless, so it can be repeated many times.

Sdvigkov A.M. et al. in paper [3] presents data of clinical trials of the RTM-01-RES, where the aim of trial was to estimate its diagnostic abilities and to determine its role as a method for diagnosis of breast cancer

in medicine practice. Today, the diagnostic techniques may be divided into two groups. The first one includes X-ray examination (mammography), ultrasonography. These methods and some others such as tomography investigate anatomical structure of the breast and detect abnormalities, e.g. tumors. The second group includes thermal methods, namely infrared thermometry and radiometry. These methods detect physiologic pathologies represented by thermal abnormalities and thermal differentials. Each method included in these groups is independent and has its own benefits and imperfections. In 1997 RES, Ltd. developed the RTM-01-RES computer-based radiometer. The device includes internal and skin temperature sensors. The method provided by the RTM-01-RES radiometer has some advantages in comparison with the methods used in mammology. It allows to detect non-invasively pathological conditions in the internal organs, e.g. malignant tumors, at their earlier stages, as changes in temperature caused by inflammation or increased cell metabolism precede the anatomical changes that can be detected by mammography or ultrasonography. Radiometry can select patients with the most dangerous tumors, as, according to current data, the tumor doubling time is higher, the tumor is hotter. Therefore radiometry selects patients with fast growing tumors first of all. Also the method is absolutely harmless for patients of all ages and with any disease as well as for medical personnel. Thus the procedure can be performed repeatedly to detect pathological conditions and monitor treatment without extra radiation.

Burdina L.M. et al., in paper [4] presents that physicians and developers of diagnostic equipment permanently look for new methods for early detection of the breast disease. Present cancer detection methods other than radiometry (i.e., palpation physical examination, mammography, ultrasonography) require that the tumour have mass and contrast with respect to the surrounding tissue (i.e., they detect formed structure changes in tissues). The microwave radiometry method (RTM-diagnosis) represents a passive, non-invasive procedure determining thermal activity of tissues. As the changes in temperature precedes the structure changes in tissues there is a fundamental possibility of early detection of breast cancer. In comparison with infrared thermography, reading the infra-red heat radiating from the surface of the body, RTM-diagnosis measures the heat of tissue at depth of several centimetres and so it is more informative. The another important advantage is that RTM-diagnosis is harmless absolutely, that allows to test a patient repeatedly, analyse dynamics of disease and choose a proper treatment.

Mustata L. and Baltag O. from Romania in article [5] shows the results obtained after an analysis upon a specific group, from which selected for discussion only the cases in which the results obtained by classical methods (X-ray, US) are contradictory to the results obtained by microwave radiometry (RTM-01) and IR thermography.

Ojica S. et al., in paper [6] presents some recent advances concerning a non-invasive microwave method used to investigate living structures. An overview of the main investigation methods in breast cancer are presented, as well as their classification. Microwaves thermography, like infrared thermography, is a noninvasive and passive technique. It does not subject the patient to radiation, discomfort, stress and physical stress. The cancer detection is based on the contrast between the thermal images of the mammary normal and malign tissues
respectively, obtained through radiometry, the last one having a higher temperature. Microwave medical imaging is a completely noninvasive technique. The microwave technique also permits to show the difference between malign and a benign tumours, thus reducing the number of invasive and expensive biopsies.
Mapping the spatial microwave emitting loci of the normal and malignant tissue we may early detect the areas
with an increased biological activity.

In 2001 at the International Conference "Laser and Informative Technologies in Medicine of XXI Century", St.-Petersburg, **Geinitz A.V. et al.** presented report [7] about application of microwave in the surgical unit. The present radiometric method is a universal diagnostic method allowing detection of various internal organ diseases. Dynamic detection of changes in tissue temperature promotes early detection of pathologic changes caused by such processes as inflammation, sclerotic changes or malignant degeneration. The system allows a doctor to noninvasively detect pathologies in tissues including acute pathologic processes at earlier stages, as changes in temperature caused by increased cell metabolism or inflammation

precede to anatomical changes detected by ultrasound and x-ray. Totally 70 patients came into the clinic, 15 of them with acute appendicitis and 10 patients with acute cholecystitis. According to RTM-Diagnosis all patients with acute appendicitis had thermal asymmetry in the right and left iliac regions; the diagnosis was confirmed by histology.

In 2013 at The 4th IEEE International Conference on E-Health and Bioengineering – EHB, Romania, **Ojica Silvana** presented in paper [8] study regarding the evolution of the mammary gland during the woman pregnancy
using the only non-invasive investigation methods: infrared thermography and microwave radiometry. The cell
thermogenesis is explored using a thermography method under the conditions of thickness or health, and permits to reveal some affections or the early detection of the risk to pathology status.
During pregnancy any exposure to ionizing radiation is forbidden. If a mammary pathology is developed during the pregnancy period, only the thermography and radiometry techniques can be used in order to monitor the mammary glands. Using these methods possible physiological or pathological modifications can be detected. On this study, we found that if the pregnancy is closer to the final delivery date, the breasts temperatures gets higher and the galactofore channels are more pronounced in the IR imaging.

In 2007 at 7th WSEAS International Conference on APPLIED COMPUTER SCIENCE, Venice, Italy, **Costin M. et al.,** presented in paper [9] about the most osteophyl cancer diagnosed amongst women is breast cancer. It's incidence depends on antecedents, on race, on environment, medication and life quality, but it is arising to all ages and it is not forgiving patient ignorance. Easy, non-harmful ways of cancer detection implemented nowadays, became more accessible for all the possible subjects. The main non-invasive methods of breast abnormal area detection are conceived using the optical reflection, and respectively infrared and (our approach) microwave body emission. Noninvasive methods have the advantage of the possibility to be repeated as often as necessary for grow rate or remission survey, essential in diagnosis. Microwave radiometry has been implemented in a complex installation in the Bioengineering Faculty scientific research laboratory, by a multi-disciplinary team.

In March 2006 at The Second International Meeting on Physiology and Pharmacology of Temperature Regulation, in Phenix, State of Arizona, USA, **Vesnin G.S. and Gorbach M.A.**, presented in paper [10] results of experiments for radiometric temperature measurement of layer structure. At the workshop on biological objects control the temperature, discussed prospects for the development of non-invasive temperature measurement methods: infrared, optical, microwave, ultrasound, and magnetic resonance. Representatives of Russian scientific schools showed the meeting a method of passive microwave RTM based on the measurement and analysis of natural electromagnetic radiation from internal tissues, which is proportional to the temperature of the deep power. The results of experiments confirmed that only the microwave antenna is sensitive to body temperature changes due to application of a distant heating/cooling patch or exercise.

Khashukoeva A.Z. et al., in article [11] presented the results of deep microwave radiometry in the diagnosis of inflammatory diseases of the uterus. Diagnosis of inflammation of the pelvic organs is the actual problem in gynecology because of their prevalence among patients of reproductive age, the low efficiency of traditional diagnostic methods, and as a consequence of the late begining of etiopathogenic therapy. Radiometry - is one of the new methods of diagnosis, which is based on the measurement of electromagnetic radiation the patient's own tissue at microwave frequencies. The basis of this method is the analysis of the temperature values recorded in the projection of the internal organs in order to evaluate pathological processes. The change in temperature (thermal abnormality) can be, in particular, caused by increased blood flow and metabolism of cancer cells, and this is the early diagnosis of cancer. Since biological tissues are relatively transparent to radiofrequency electromagnetic waves, it is possible to measure the temperature at a depth of several centimeters. The use of clinical and laboratory (blood count, bacteriological and direct microscopic study, the definition of acute phase proteins) and other techniques (ultrasound, radiometry) allows to make a differential diagnosis of inflammatory diseases of the uterus, to select the optimal method of conducting the patients and the control over a course of treatment.

Vaisblat A.V. et al., presented in paper [12] the results of the expert system of RTM-01 apparatus for the differential diagnosis of breast cancer. The studies were conducted in cancer centers in Moscow from December 1997 to September 1999. In total 1599 patients were examined. Some patients underwent repeated examination, so all was conducted in 2154 surveys. Conducted research, clinical trials and experience with RTM-01-RES in leading cancer institutions have shown that microwave radiometry is very effective for early detection of breast cancer. With absolutely harmless, it allows at early stage to identify patients with abnormal thermograms, which is necessary to conduct a comprehensive examination of mammary glands. According to sensitivity, this method is comparable with the data of mammography and ultrasound. The method is of particular interest in the diagnosis of young women who have X-ray studies are ineffective. Note also the ability of the method to detect proliferative processes in the mammary gland. Unconditional interest is the use of microwave radiometry to monitor the treatment of benign tumors.

In 2002, Burdina L.M. et al., at the 3rd Russian Scientific Forum, Aviaizdat, presented in paper [13] results of using microwave radiometer RTM-01-RES for diadnosis of breast diseases. Radiometer RTM-01-RES was used in complex of diagnosis in branch №1 of Moscow Breast Clinic, since December 1997. Within five years of measurements were conducted 2233 examination, by 1506 patients with different diseases of the mammary glands. Many years of experience in the use of diagnostic complex RTM-01-RES has shown its high efficiency and the desirability of placing on the RTM-diagnostic algorithm in the comprehensive diagnosis of breast diseases.

In 1997 Burdina L.M. et al., published in medical journal Mammalogy №2 [15] the results of clinical trials of medical RTM-01 for the diagnosis of breast cancer obtained using 116 women with different breast diseases, and one year latter published in medical journal Mammalogy №2 [14] the results of the application of microwave radiometry RTM-01 for the diagnosis of breast cancer obtained using 500 women with different breast diseases. Undertaken work in the course of which was surveyed a large group of women with various forms of breast pathology showed that RTM - diagnostics using computer processing methods gives a high detection rate of breast cancer (90%). In some cases, RTM - method gives an earlier diagnosis of breast cancer than traditional methods. Given the high detection rate of breast cancer, the absolute harmlessness of RTM-diagnosis and the relatively low cost of diagnostic equipment in comparison with the devices for the US and mammography, it is advisable to use the RTM diagnostics in clinics, in order to identify risk patients for further integrated additional examination and treatment of patients in specialized centers. Besides the fundamental possibility of early diagnosis of breast cancer and monitoring of the treatment process are of interest for use RTM-diagnosis in complex examination of patients in mammologycal dispensaries.

Rozhkova N.I. et al., published in 2007 in medical journal [16] „Factors influencing the efficiency of radiothermometric breast measurements by a RTM-01-RES diagnostic unit". The authors give the results of radiothermometric studies in 79 patients with various breast diseases (6 with cancer in situ, 24 with invasive carcinoma, 15 with proliferation with atypia, 34 with other benign diseases). The radiometric study involved the measurement of internal breast temperatures and skin temperatures with a RTM-01-RES radiometer. Thermal changes were rated by a 6-score scale from Th0 to Th5. A relationship of the level of thermal changes to the grade of tumor malignancy and a corelation between the temperature values and the findings of color Doppler study were defined. The magnitude of thermal changes was shown to be primarily determined by the grade of malignancy. The maximum thermal changes (Th5) occured in 85% of the patients having a high malignancy grade. Pronounced thermal changes were observed in 83, 96.6, 80, and 44.4% of the patients with cancer in situ, invasive carcinoma, atypia, and ductal hyperplasia, respectively, at the same time, color Doppler study revealed no blood flow changes in any patients with cancer in situ. It is concluded that the method is recomended for screening and differential diagnosis in borderline breast conditions.

Kozlov S. V., and Neretin E. Y., in article [17] discusses one of the problems of oncology — skin melanoma. *The research objective* was to study and to compare diagnostic methods of preinvasive melanoma including fluorescence diagnosis, dermatoscopy and microwave radiometry. *Materials and Methods:* The survey has used dermatoscope of Heine Delta 20 Company, the unit RTM-01‑RES and the instrument of

fluorescent diagnostics «Spectrum-Cluster.» The *results* suggest the possibility of early detection of melanoma with the use of dermatoscopy. The method may be applied to radiometry screening study. Fluorescence diagnostics is effective for the differential diagnosis of melanoma and melanocytic nevi. *In conclusion* it has been proved the need for an integrated approach to the diagnostics of melanoma of skin, depending on the different clinical situations.

Voloshin V.N. et al., presented the results in paper [18] of the use of radiothermometry in determining the level and the way of lower limbs amputation in patients with critical ischemia. **The aim of the investigation was** to assess the possibility of using radiothermometry when choosing an optimal level of lower limb amputation in patients with critical ischemia and the way of its performance. **Materials and Methods.** Radiothermometrical investigations were carried out in 60 apparently healthy people and in 130 patients with arteriosclerosis
obliterans with III and IV degrees of chronic arterial failure. **Results.** There was suggested and developed the method of determining amputation level and the way of its performance based on the measurements of low limbs deep temperatures.
Conclusion. Radiothermometric technique is very informative when determining the level of low limbs amputation and the ways of its performance.

Clinical cases of hyper- and hypodiagnostics of acute venous thrombosis of the lower extremities and a possibility of combined radiothermometry for the purpose of specifying the diagnosis are considered in the article [19] presented by **Larin S.I. et al.**,.

Cheboksarov D.V. et al.,presented the results of the effect of acute focal ischenia on the thermal balance on the brain in paper [20]. Heat balance of homoiothermic animals allows significant physiological deviation from the preset settings "set point" centers of hypothalamic regulation despite of the difficult-organised system of its
maintenance. In other words, the warm-blooded organism normally has thermal heterogeneity. With the development of pathological states, accompanied by fever and increasing of body temperature, temperature heterogeneity is changing. The origin of these changes is rarely the subject of special studies, because the algorithm of the diagnosis is usually considered as an assessment of basal temperature in one department thermal "center" only. However, the increase of the temperature of the brain in patients with cerebral accidents does not always correspond to the changes in basal body temperature, which can lead to the underestimation of local hyperthermia of the brain in traditional thermomonitoring.
Anatomical, functional and metabolic features create the special conditions of maintenance of the cerebral temperature balance in comparison with the conditions of regulation of temperature of the heat "center". Firstly, using microwave radiometry managed data confirm known to raise the temperature of the brain in ischemic defeat. This is important not only for diagnostic and prognostic points view, but also due to the fact that one can speak about affirmative neuromonitoring temperature capability significantly extends the amount of information about the state of the lesion in the central nervous system.
Secondly, the growth of the organism functional heterogeneity in systems it reflects the processes violations relationships between elements of the system and makes the whole system unstable, whereas a decrease in functional heterogeneity indicates a growing rigidity of the system and loss of functional adaptation reserve. Metabolic provision of functional activity of the system elements is reflected in the changes in temperature.

Konstantinos T. et al., presented in paper [21] the application of microwave radiometry in the clinical setting in order to prevent ischemic strokes due to carotid atheromatosis has certain advantages and disadvantages. The technological improvement of the current device is mandatory in order to proceed with large prospective studies

Zampeli E. et al., presented the results of study Microwave Radiometry as a non-invasive method which determines within seconds the in vivo temperature of internal tissues at a depth of 3–7 cm with an accuracy of ±0.2 °C in paper [22]. In this proof-of-concept study, they tested the hypothesis that, in absence of relevant clinical signs, increased local temperature detected by microwave radiometry reflects subclinical synovial inflammation, using ultrasound as reference method. Knees of healthy controls, subjects with recent knee trauma and symptom-free patients with rheumatoid arthritis (RA) or osteoarthritis were

examined by placing the microwave radiometry sensor, a) at the upper one third of the anteriorsurface of the thigh (control-point), and b) over the suprapatellar recess. Ultrasound was performed immediately after and the possible presence of fluid and/or synovitis was correlated with microwave radiometry findings. In 30 healthy and 10 injured knees the temperature was always lower than thigh (32.3±1.1 and 31.8±1.4 versus 34.1±0.9 and 33.6±1.2°C with a difference (DT) of 21.8±0.2 and 21.9±0.4°C respectively). Of 40 RA and 20 osteoarthritis knees examined, ultrasound findings indicative of subclinical inflammation (fluid effusion and/or Doppler signal) were found
in 24 and 12, respectively, in which the temperature was higher than healthy knees and DT was lower (20.9±0.7 in RA and 21.0±0.5 in osteoarthritis versus 21.8±0.2°C, p,0.001). The 5 RA knees with power Doppler findings indicative of grade 2 inflammation had a DT 3 times lower compared to healthy (20.6±0.6, p = 0.007), whereas the 9 RA and the 7 osteoarthritis knees with additionally fluid effusion, had even lower DT (20.4±0.7, p,0.001). Using a safe, rapid and easy-to-perform method, such as microwave radiometry, thermal changes within the
knee joint may reflect non-clinically apparent joint inflammation. Refinement of this method, including production of sensors for small joints, could result to the development of the ideal objective tool to detect subclinical synovitis in clinical practice.

Samokish A.C. and Marchenko N.A. in article [22] which is dedicated to methods of diagnostics of oncological diseases, reviewed the main methods of diagnosis. An attempt was made to increase the sensitivity of cancer detection using a neural network. In article are presented information, that in the study, the developers of RTM-01-RES, has analyzed the majority thermal images of patients already established diagnosis of breast cancer and identified the following signs of the disease.
1. Increased maximum nipple temperature in comparison with an average temperature of the breast,
2. Increased temperature difference between the right and left nipple breast,
3. Increased the maximum temperature difference between the symmetrical points left and right breast,
4. Increased rms temperature differences between symmetrical points left and right breast,
5. Increased rms temperature differences between symmetrical points left and the right breast and the middle
the temperatures of all survey points,
6. Increased rms in one of the breast and an average temperature of all survey points thus selected
the larger of two values.

Konstantinos T. et al., in article [24] presented the results of first In Vivo Application of Microwave Radiometry in Human Carotids. This study investigated whether temperature differences: 1) can be measured in vivo noninvasively by microwave radiometry (MR); and 2) are associated with ultrasound and histological findings. Studies of human carotid artery samples showed increased heat production. MR allows in vivo noninvasive measurement of internal temperature of tissues.

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PROTOTYPE OF MICROWAVE RADIOMETERS INTEDED FOR CLINICAL USE

Live objects are literally immersed in an invisible ocean of various physical fields, both external and produced by the body. You can jokingly say that we are in the "electromagnetic soup", and the continuous and normal functioning of living systems of the body is reflected in the complex picture of the physical fields and radiations emanating from it, as well as parametric changes in natural background fields and radiation, which usually surrounds a person .
Therefore, the picture of physical fields can be judged on the physiological systems of the body. Any biological object throughout his life generates different nature of the radiation that interacts with the physical fields of the environment, providing a living organism he needs the exchange of information. Visualization of fields and radiation from the body (now in medicine have used X-ray, ultrasound and tomographic methods, electrocardiography, electroencephalography, and others.) allows you to "see" the dynamics of the various physiological processes and identify irregularities in their work. Physiological information is contained in the spatial and temporal distribution of signals in their dynamic images. Therefore, we can figuratively say that physical fields in the human body - is "working knock" of physiological processes. Any functioning organ sends information through many channels, some reflect the rapid processes (neutron bioelectrical activity of muscles), others - slow (blood microcirculation, metabolism, etc.). The study and measurement of the characteristics of these "knock" - signals for diagnosis of the condition of the body - can provide a wealth of information.
If you put the question more broadly, it is, in essence, the application of physical methods of biofield examination. In a general sense under the biofield means the totality of physical fields specific to the objects animate and inanimate nature, by which they are carried out cooperation and exchange of energy and information. Accurate measurements and dynamic spatio-temporal mapping of these fields, radiation and change the background enable the development and application of new methods for early non-invasive diagnosis as a basis for preventive medicine, including the development of appropriate equipment.

Microwave method noninvasively measure of temperature distributions inside the human body have been used over the years in various applications in order to support clinical practice [1,2,3,4]. Theoretical and experimental results conclude that with the appropriate combination of conformal patch antennas and microwave receiver it is possible to monitor areas of interest inside human breast [5,6,7,14], head [8,16], skin [9], carotid artery [10] thyroid gland [13] and other models with a variety of temperature resolutions and detection depths. The applications of microwave radiometry in clinical medicine aim mainly at obtaining information about internal in-depth body temperature patterns by the non-traumatic measurement of natural thermal radiation from body tissues at low microwave frequencies. Knowledge of such internal body thermal patterns can assist clinical disease detection and diagnosis, e.g., as a non-invasive complement to the current computed tomography (CT) and magnetic resonance imaging (MRI) technologies [11], and may have a role in the monitoring of therapeutic processes [12,13,14], e.g., during hyperthermia [15,16].

Taking into account the above considerations and findings, a prototype microwave radiometric system was designed, simulated, constructed and tested.

Asimakis N.P. et al., presented in paper [8]the results of the theoretical analysis of application conformal and hemispheric head model antenna intended for the near-field electromagnetic (EM) energy detection from biological head tissue and constructed prototype of passive microwave radiometry system which consists of a microwave receiver which comprises a sensitive radiometer and one or two (array) contact antennas (conformal microstrip patch antennas) that are used to receive the radiometric signals. It is a Dicke switch radiometer with operating ability in any frequency of the range 1 - 3.5 GHz, using a local oscillator.

Cheboksary D. V. presented in Master`s thesis in Master`s of MD [16] the results of i) experimental model of acute brain ischemia and general hypothermia in animals to compare the results obtained with microwave radiometry of the brain and with using invasive thermometry; ii) investigation of the temperature balance of the brain by microwave thermoregistration in healthy subjects at rest and during the session of cranio-cerebral hypothermia; iii) study of the temperature balance of brain by microwave thermo-recording in patients with acute ischemic stroke; iiii) identifying the effects of the correction of the disorders of temperature balance of the brain by cranio-cerebral hypothermia in patients during the acute phase of ischemic stroke.

In 2000s, Meany et al. developed a clinical prototype for 2D microwave imaging system [18]. The configuration of this system comprised 16 monopole antennas, which all operate as transmitters and receivers in a circular pattern. The reason for applying monopole antennas in this study, was that the monopole antennas can be modelled and operated as a line source and have acceptable radiation in lossy mediums, such as breast. The principle concept of this work is based on their earlier research [19], [20]. The measurement system is mounted on a transportable bed, which includes a hollow part for placing the circular measurement system. The patient's breast is suspended in the circular shaped antenna system to be imaged. The experiment was performed on five patients and 2D images with satisfying accuracy were acquired from real breast tissues.

Naseri M. from Chalmers University of Technology, Sweden in Master`s thesis of Biomedical Engineering [17] presented the results of experimental „Microwave Tomography for Breast Cancer Detection"model. The algorithm and system, both have a great potential to be utilized as a complementary method to mammography modality in order to provide desired sensitivity and specificity to detect malignant tissues in breast during early stages.

Thomas A. R. from University of South Florida in his dissertation work [21] presented the results of application the active and passive microwave radiometry for transcutaneous measurements of temperature and oxygen saturation. He investigated several potential new applications of microwave radiometry for the biomedical field.

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EQUIVALENT DEVICE

RADIOMETER RT-17

According to existing hypothesis, changing tissue temperature is usually preceded by structural changes that are detected by traditional methods of research of breast - ultrasound, mammography and palpation. Therefore, RTM is of interest for the early diagnosis of diseases. For the first time in 1975 by the American scientist A. Barrett the method of studying breast was used, called microwave RTM based on the assessment of the intensity of the electromagnetic radiation of internal tissues.

In radiofrequency the wave processes are described by Planck's law, which determines the emission power as a function of the absolute temperature and frequency "for microwave frequencies transparency (attenuation value) of biological objects depends upon their moisture content ... ".

Theoretical basics of using the RTM technique in breast care are based on research of M. Gautherie et al., which were carried out for 16 years. Based on the clinical data of 85,000 patients, he spent a year studying the relationship between thermal anomalies, physiological processes, X-ray data and histological studies. Furthermore, using thermocouples located on the end of the needle, the temperature measured by the malignant tumor and surrounding breast tissue. It should be noted that all the work on thermal methods for diagnosis of breast cancer are based on this law, the experimentally established by Gautherie, and unknown works refuting the findings of a linear relationship between tumor heat and rate of its growth.

Later, in the Soviet Union, Germany, Japan, France and the United States appeared scientific schools in the development of this method. In Russia the greatest progress has been made by the scientific school headed by a member of the Academy of Sciences of the USSR V.S. Troitsky and scientists of the Academy of Sciences of the USSR under the leadership of the Academy of Sciences of the USSR Y.V. Gulyaev. In 1996 he published a monograph - "Radiometry in complex diagnostics and evaluation of treatment of breast cancer," the authors: Terentiev I.G., Komov D.V., Necklaces A.S., Orinovsky M.B., in which has been described technology of non-invasive detection of breast cancer using microwave radiometer RT-17, established in Nizhny Novgorod.

Over the years there have been published more than a hundred works by using RTM in mammalogy and other areas of medicine. But despite the obvious advantages of the method, it has not received due application in medical practice.

In 1997, a new generation of computerized diagnostic systems appeared on the Russian market, combined with the computer (RTM-01-RES). Unlike the first generation of radiometry, representing an internal temperature measuring devices, computerized diagnostic systems include measuring the internal temperature, skin temperature meter, visualization, processing the information received and evaluation (expert system).

In 1999, more than forty members of the US Congress during his visit in Moscow to get acquainted with the possibilities of application of the RTM method in medicine. Now the largest medical center of the USA - The National Institute of Health conducts research in this direction.

The high level of Russian development was marked in 2005 at a workshop held in the framework of an international conference on thermoregulation in Arizona.

Multinational corporations such as "Samsung" and "Aloka" conduct research in this area, using the Russian equipment, clinical trials of RTM in several university hospitals in Japan. US medical equipment certification National Authority in 2005 issued a certificate FDA 510K on a simplified version of the device RTM-02-RES.

The main difference of the RTM method from widely known in 70-80s thermography is that the radiometry measures not only temperature of the skin but measures the tissue temperature of the depth of several centimeters. It is known that efficiency decreases thermography for tumors less than 1 cm in diameter.

A distinctive feature of the microwave RTM is and its ability to distinguish proliferative mastopathy and fibroadenoma from mastitis and fibroadenoma without proliferation and thus allocate risk patients who have breast cancer can occur under certain conditions.

PRIORITY OF MICROWAVE RADIOMETRY DEPENDING PERFORMANCE AND SAFETY

- *Non-hazardous*

Microwave radiometry is non-hazardous both to the patients and to the personnel taking the thermograms, as during the examination the intensity of natural electromagnetic radiation from the patient's tissue is measured only.

- *Non-invasive*

Temperature is measured non-invasively.

- *Earlier detection of diseases*

It should be noted that thermal changes precede to the anatomical changes that can be detected by traditional methods such as ultrasound, mammography and palpation. Thus microwave radiometry is a very promising method for breast cancer detection at an earlier stage.

- *Detection of fast growing tumors*

The specific heat generation in the tumor is proportional to grow rate of the tumor. So fast growing tumors are "hotter" and they are more contrast in thermograms. Thus microwave radiometry is an unique method that allows to detect first of all fast growing tumors. Using microwave radiometry (RTM-Diagnosis) in conjunction with other tradition methods allows to select patients with fast growing tumors.

- *Ability to detect patient with increased proliferative activity of cells*

The important feature of the microwave radiometry is that it can distinguish mastopathy and fibroadenoma with proliferation from mastopathy and fibroadenoma without proliferation. So the method allows to select patients who are at the greatest risk of having breast cancer.

- *Ability to monitor treatment*

Microwave radiometry is non-hazardous both to the patients and to the personnel taking the thermal measurements, so it can be effectively used for the monitoring of treatment.

PRODUCT LITERATURE AND INSTRUCTION FOR USE

Manufacturer of Microwave radiometer RTM-01-RES of the RES Company Ltd., states, that proposed product literature and Istruction for Use are consistent with the clinical data and cover all the hazards and other clinically relevant information that may inpact on the use of the device.

CONCLUSION

A malignant tumor has higher temperature than normal tissue and the temperature of the tumor is dependent on the tumor growth rate. Thus tumor temperature is the universal indicator of tumor activity.

The temperature changes begin in the stage of atypical hyperplasia and increased proliferation and this opens up the possibilities for detection of patients with high risk lesions.

Microwave radiometer (RTM-01-RES) allows measurement of temperature changes of internal tissue at the depth of several centimetre and allows visualization of the temperature on the thermogram and temperature field.

It is noninvasive and the measurement of internal temperature is based on receiving natural electromagnetic radiation from the tissue in the gigahertz (GHz) frequency range. The device is absolutely harmless and has no risk because it does not emit any radiation. It can be used repeatedly as a method of monitoring.

Microwave radiometry has successfully completed seven clinical trials of more than 1000 patients in different countries. Microwave device (RTM-01-RES) is used in more than 300 medical centers in 30 countries.

Medical technology of microwave radiometry is included in the nomenclature of medical services in the Russian Federation, the Ministry of Health and is part of the standard of care for patients with malignant tumors of the breast.

This method of microwave radiometry is recommended by leading Russian mammalogists in the National guidelines of breast care.

The clinical results obtained by microwave radiometer RTM-01-RES were compared with the results given by another paralel method (X-ray mammography, ultrasonography, histology, mammoscintigraphy, IR) the two methods reinforcing each other, and influencing the expert's opinion in order to take a decision.

For each proposed clinical indication producer states that:

- the clinical evidence demonstrates conformity with relevant Essential Requirements;
- the performance and safety of the device as claimed have been established; and
- the risks associated with the use of the device are acceptable when weighed against the benefits to the patient

Detailed Justification

The temperature of a malignant tumour is a universal indicator of the growth rate of the tumor.

Tumor temperature can be used as a prediction of the benefit of individual therapies and in monitoring the efficacy of breast cancer treatment.

The temperature of tissue around a malignant tumour is correlated with micro vessel density (MVD) - the main indicator of angiogenesis.

A traditional infrared camera allows measurement of the temperature of the skin and the breast tumor at a depth of several centimetres.

It is well known that it is possible to detect thermal abnormality of internal tissues with the help of measuring the natural electromagnetic radiation in microwave frequency range. Microwave radiometer (RTM-01-RES) allows one to measure noninvasively any temperature changes of internal tissue at the depth of several centimetres and visualize the internal temperature on the thermogram and temperature field.

It was shown that the device can be used for detection of carotid temperature abnormalities and the temperature of the carotid is a good correlation to the risk of stroke in the patient.

Today it is technically possible to obtain non-invasively the information concerning thermal activity of the tumor and use this information for the prediction of individual therapies and monitoring the efficacy of breast cancer treatment.

The clinical trials in Russia show that tumors with a low degree of malignancy have low temperature changes and the tumor with high degree of malignancy have high temperature changes.

Seven clinical trials of (RTM-01-RES) with 1000 patients have shown that 90% of breast malignant tumours have substantial temperature changes (the sensitivity is 85%-95%, specificity 56%-75%).

The standard of care for patients with malignant tumors of the breast is to use microwave radiometry and this is recommended by leading Russian mammalogists in the National guidelines of breast care.

Given that the temperature of a malignant tumor is higher than a benign lesion and that the temperature of more proliferative and thus poorer outlook cancers is greater than less proliferative cancers, the aim is whether with the most up to date technology these temperatures can be measured accurately on the skin.

The benefits of such a device are

1. Diagnostic - to help differentiate benign from malignant lesions.
2. Prognostic - to provide insight into the proliferation rate using a non-invasive test.
3. Predictive of benefit - to show that changes in temperature predate changes in tumors volume in patients treated with drug therapy initially.

The investigation is non-invasive. According the conclusions of clinical trials made in Russia, Greece, Turkey and United Kingdom it were demonstrate the benefit, that this simple non-invasive test play a useful role in assessing patients with breast lumps and in particularly breast cancer.

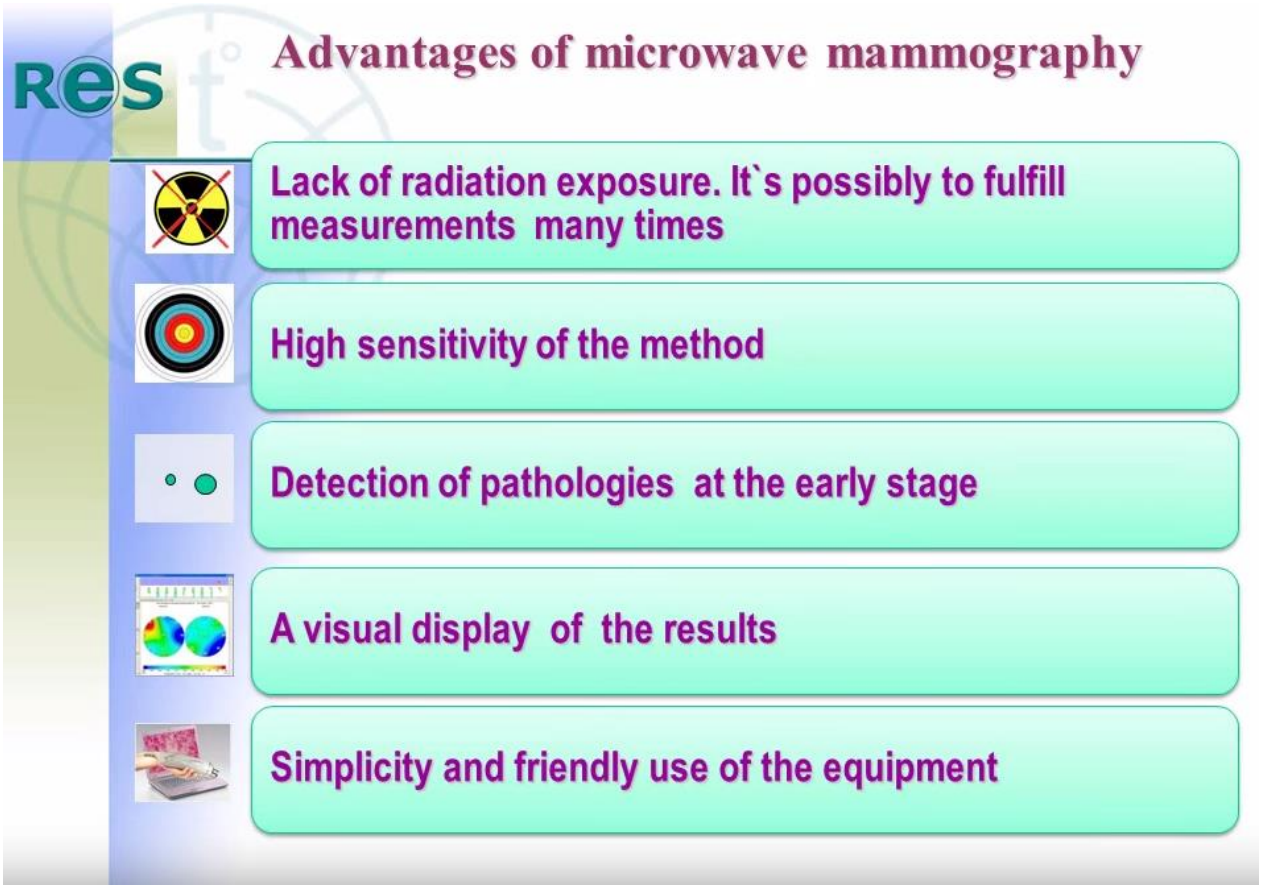
No side effects were mentioned at any clinical trial.

Advantages of microwave radiometry especialy applicated in breast detection are presented in slide.

TOTAL CONCLUSION

On the basis of physician´s conclusions who organized the clinical trials or has examined the microwave radiometry in clinical-hospital practice in process of fulfillment of dissertation works or presented the results of using device in practice in medical journals or in reviews, it all gave producer of MD RTM-01-RES to made the statement as follow:

- Microwave radiometer RTM-01-RES allows measurement of temperature changes of internal tissue at the depth of several centimetre and allows visualization of the temperature on the thermogram and temperature field.
- The proces is noninvasive and the measurement of internal temperature is based on receiving natural electromagnetic radiation from the tissue in the gigahertz (GHz) frequency range.
- The radiometer RTM-01-RES is characterized by high sensitivity, accuracy and specificity of the detection of non-palpable breast tumors. The sensitivity, specificity and accuracy of radiometry increases with age, as in benign and malignant tumors, regardless of the size of the tumors and the presence of concomitant diffuse breast changes fibrocystic breast. Sensitivity of radiometry is higher in breast cancer than in benign entities - in all age groups. The mutual use of classical methods of diagnosis and RTM method increases diagnostic efficiency of surveys. The number of false-negative conclusions for complex survey decreases.
- RTM method allows to determine the response of breast tissue to carry out treatment and can be used for dynamic monitoring of the treatment.
- RTM procedure is absolutely harmless to the patient and the physician, and may repeatedly performed at any age group.
- It should be noted high information and method of its versatility, ease of use and compact of equipment.
- Results of the visualization of RTM results in the form of heat fields are rather evident. Automated expert system allows you to focus medical attention to patients at risk.
- The advantages of the microwave method of diagnosis is the availability, relatively low cost studies absence of radiation exposure, the ability to quickly interpret the results of research and non-invasive.
- No side effects were mentioned at any clinical trials (15), thesis (14), reviews (21) or articles (100).



LITERATURE SEARCH REPORT

1.) DEVICE NAME: Microwave Radiometer-Internal Temperature Diagnostic Computerized Imaging System RTM-01-RES (shortly Microwave Radiometer RTM-01-RES)

2.) SCOPE OF THE LITERATURE SEARCH

Clinical trials of Microwave Radiometer RTM-01-RES

3.) METHODS

(i) Date of search: 2000 08 01 – 2015 09 01

(ii) Vesnin Sergey, RES Company, Moscow, Russia
Jusko Peter, ONKOCET Ltd., Bratislava, Slovakia

(iii) Literature sources used to identify data:

- scientific databases – bibliographic (e.g. MEDLINE, EMBASE),
- specialised databases (e.g. MEDION)
- systematic review databases (e.g. Cochrane Collaboration)
- clinical trial registers (e.g. CENTRAL),
- adverse event report databases (e.g. MAUDE, IRIS)
- reference texts

Table 1

#	RESOURCE	# of id. cl.trials	NAME OF TRIAL
1	MEDLINE (PubMed – NCBI)	0	No items found
2	EMBASE (Elsevier)	0	No items found
3	MEDION	0	No items found
4	CENTRAL	4	Early Detection of Breast Disease Using Medical Radiometer - RTM - 01 – RES https://clinicaltrials.gov/ct2/show/NCT02286583 Microwave Radiometry for the Diagnosis and Monitoring of Breast Cancer https://clinicaltrials.gov/ct2/show/NCT02514837 Comparative Study of Microwave Radiometry and Ultrasonography for the Diagnosis of Acute Appendicitis https://clinicaltrials.gov/ct2/show/NCT02108340 Natural History of Carotid Atherosclerosis https://clinicaltrials.gov/ct2/show/NCT01521351
5	CENTRAL	0	No items found
6	Cochrane Collaboration	0	No items found
7	IRIS	0	No items found
8	reference texts	6	A Microwave Radiometer for Close Proximity Core Body Temperature Monitoring: Design, Development, and Experimentation (Graduate Theses and Dissertation, University of South Florida) Report on the scientific research work conducted on the assessment of the factors influencing upon the efficiency of radio-thermometric measurements with the use of the diagnostics complex RTM-01-RES (company RES, Russia) 4x Clinical Trial Protocol of the RTM-01 Microwave Radiometer Developed by RES Ltd.
9	Europe PubMed Central	1	Efficacy and safety of breast radiothermometry in the differential diagnosis of breast lesions.

Setting of included studies

The majority of the clinical studies were performed in the Russia (6), with a further one from the USA, one from the Malaysia, one from United Kingdom (University of Edingburgh – in proces). Full details of the 9 included studies are shown in Table 1.

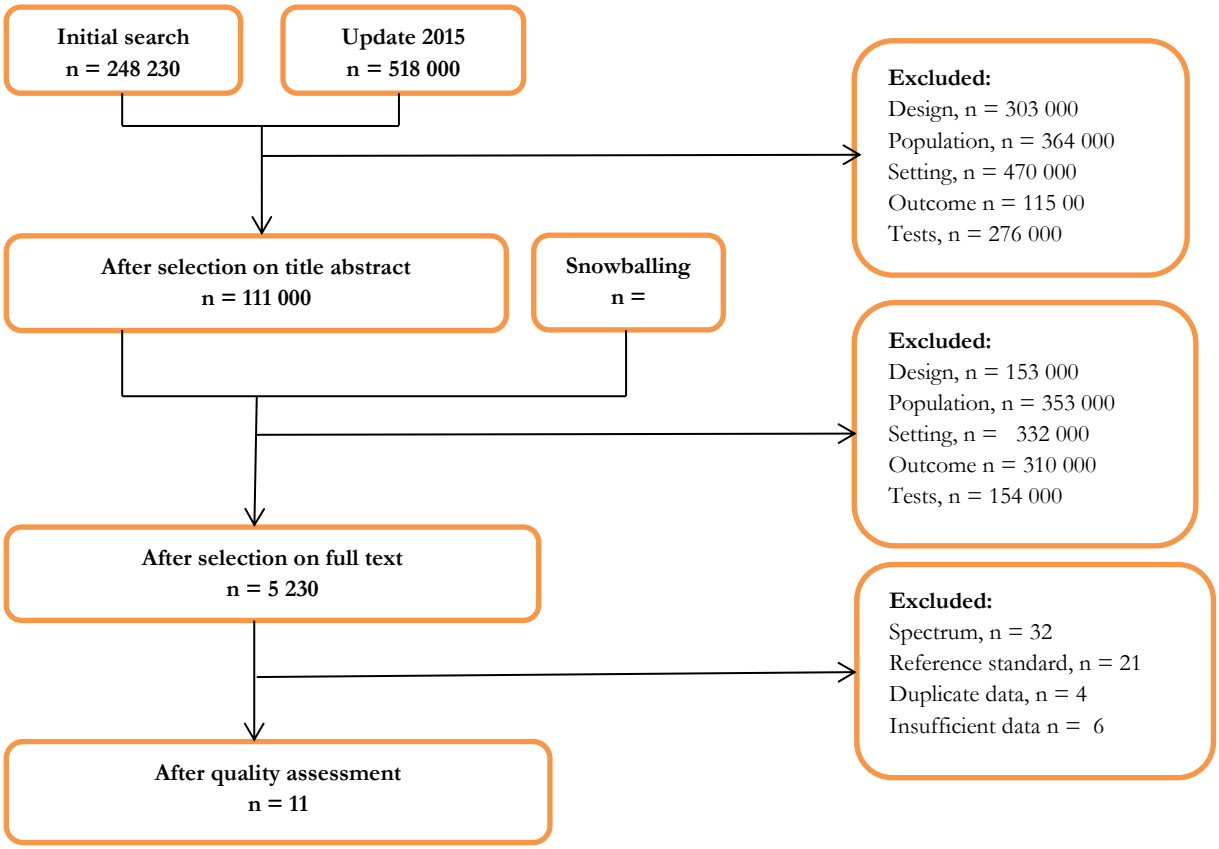


FIGURE 1 Flow of literature seach

Notes:

EMBASE Excerpta Medica published by Elsevier

CENTRAL The Cochrane Central Register of Controlled Trials

IRIS The TGA's Medical Device Incident Report Investigation Scheme

MAUDE US FDA's Manufacturer And User Facility Medical Device Experience database

MEDION Database that indexes literature on diagnostic tests

MEDLINE Published by US National Library of Medicine