Combined Interstitial Laser Therapy for Cancer Using Microwave Radiometric Sensor and RODEO MRI Feedback

Part 1. Microwave Radiometry

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ABSTRACT

The concept of complex laser treatment of localized cancer is 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.

Key words: Laser, microwave, temperature control, breast cancer, diagnostic.

1. INTRODUCTION

Presently the earlier detection and treatment of breast cancer is one of the most important problems. In many countries this disease is the main course of women death. Specialists believe that early detection of breast cancer by the clinical method is later biologically. So it is expedient to use screening in conjunction with other non-invasive investigative methods.

One of the promising modality for breast treatment is Interstitial Laser Therapy (ILT) .But it is has still some problems: no real –time temperature control during ILT; high temperature gradient around fiber tip; creating a nonuniform thermal lesion; potential complications after possible overheating and charring like burning, infections, inflammations; tumor spread from water vaporization; residual disease from inadequate ILT.

Recently we developed of new approach of combined laser interstitial laser therapy with microwave radiometric sensor and RODEO MRI feedback with following features: design of a microwave thermometry-based laser temperature control system utilizing modified existing technology; comparison of the data provided by the microwave thermometry and MRI to obtain comprehensive information about temperature and changing properties of tissue during thermal treatment; design magnetic susceptibility coating for visualization of fiber on MRI; development of breast tumor treatment that combines interstitial photothermal and photodynamic therapies in order to reduce the temperature needed for thermal destruction of tumor; a study of the role of laser-induced photoacoustic and ultrasound waves in tumor cell damage; use of laser-acoustic techniques to enhance the diffusion of photosensitizing and photoabsorbing agents ;post-operative, non-invasive phototreatment of the breast by positioning Light Emitting Diode (LED) arrays around the breast to photoactivate the immune system and to complete the photodynamic destruction of residual cancer cells.

This paper focuses more on development of microwave radiomery temperature control. Microwave radiometry [1-10] is based on measuring the intensity of natural electromagnetic radiation from a patient's tissue. This intensity is proportional to the temperature of tissue. The change in temperature (thermal abnormality), that is a basis of the earlier detection of breast cancer, may be caused by increased cancer cell metabolism. It should be noted that thermal changes precede to the anatomical changes that can be detected by traditional methods such as ultrasonography, mammography and palpation. Thus microwave radiometry is a very promising method for the breast cancer detection at an earlier stage.

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The one of the first work discussing the use of microwave radiometry for the breast cancer detection was published in 1977 [1]. This subject was further also discussed in the literature [2-13]. At the same time the method has not been used widely in medicine practice. In 1997 RES, Ltd. developed the RTM-01-RES microwave computer-based radiometer which is using now for temperature control during ILT . The system includes a microwave sensor to invasively measure the temperature of internal tissue and a non-contact infrared sensor to the measure skin temperature. This paper focuses on previous clinical trials of RTM-01-RES held in 4 oncological centers on 1000 patients, and showed, that the sensitivity of RTM-01-RES in detection of breast cancer is 90%, specificity 76-81%.

2. FEATURES of MICROWAVE RADIOMETRY

Microwave radiometry allows to measure natural electromagnetic radiation from a patient's internal tissue at microwave frequencies. The intensity of the radiation is proportional to the temperature of tissue. So we can say that microwave radiometry allows to measure internal temperature of tissue and display it on the monitor of the computer. The main difference between well known infrared thermography and microwave radiometry is that the former allows to read and display skin temperature, when the latter indicates internal temperature. Microwave radiometry measures natural electromagnetic radiation from the patient's tissue, it is absolutely harmless and safe both to the patients and to the medical personnel. So the method can be used successfully for screening for the monitoring treatment.

The specific heat generation in the tumor is proportional to the grow rate of the tumor. So fast growing tumors are "hotter" and they are more contrast in thermograms [2]. 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.

The important feature of microwave radiometry is that it can distinguish proliferative mastopathy and fibroadenoma from non-proliferative mastopathy and fibroadenoma. So the method can select patients who risk to have breast cancer.

The device is a modulated null-radiometer with a slipping circuit for compensating reflection between the biological object and the antenna. The used wavelength is 26 cm. The functional scheme is illustrated in Fig. 1.

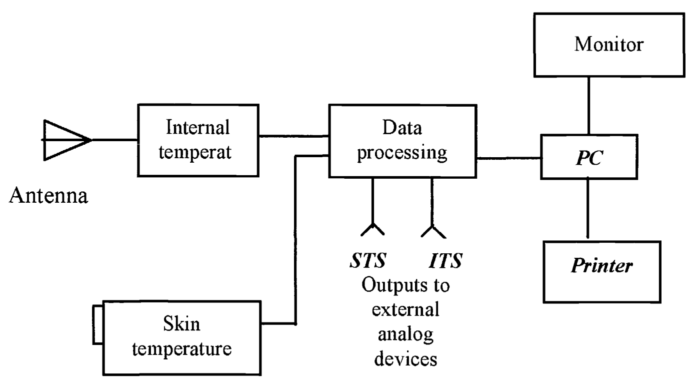

Fig.1 Functional scheme of RTM-01-RES

When the temperature is measured, the antenna contacts the patient's skin at the projection 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 (internal temperature sensor). The signal amplified in ITS is transmitted to the DPU (data processing unit), where it is processed.

The voltage from the skin temperature sensor (STS) is transmitted to the DPU too. The skin temperature sensor is non-contact infrared frequencies receiver. The modes are switched by the buttons located on the front cover of the data processing unit. The internal and skin temperature values are displayed on the 3-digit temperature indicator as degrees Celsius with discreteness of 0.1.Data processing unit produces serial digital signals for interfacing with PC.

The internal temperature is measured by contacting the antenna with a patient's skin at the point of the investigated organ or its part projection.

Noise signal power at microwave frequencies received by the antenna is

$$P = \varepsilon K T B, \qquad (1)$$

where K- the Boltzmann constant; T – averaged internal tissue temperature (Kelvins); B – microwave frequency band of the receiver (Hz); ε – emittance. When frequency band B is 100 MHz (10^8Hz) and the tissue temperature is 310K, this power is 4x 10^{-13} W. The power is proportionate to a body temperature, so it can be measured in degrees, if other conditions are constant.

There is a switch behind the antenna. It is switched from close to open position 1000 times per second. When the switch is closed the signal transfers through circulator branches (path) to the device radiometry region. When the switch is open heated resistor noise transmit to circular leg. This noise is reflected from the switch and transmitted from circulator legs *to* the radiometer input. Signals are amplified and their power (temperature) values corresponding to close and open switch positions are compared. Voltage that is proportional to the temperature differential between tissue and heated resistor heats the resistor until these temperatures are equal. Thus instead of measuring the internal temperature we measure the temperature of the heated resistor, so that the device is simplified.

The schematically described procedure compensates reflection form skin surface. Noise power of a bioobject with temperature T_p achieves the border between the bioobject surface and the antenna, then the antenna receives it reduced by 1-r (r-coefficient reflection) according to Kirchov's low*. Some noise T_p x r is reflected and absorbed in the bioobject. Noise with the temperature T_p as mentioned above achieves the border from the receiver input. Some noise with temperature T_p (1 - r) is absorbed in bioobject, and the rest of noise is reflected with the temperature T_p x r. The sum of signal temperatures in the antenna input is T_p. So the reflection at the border is compensated even if the temperature of bioobject are different.

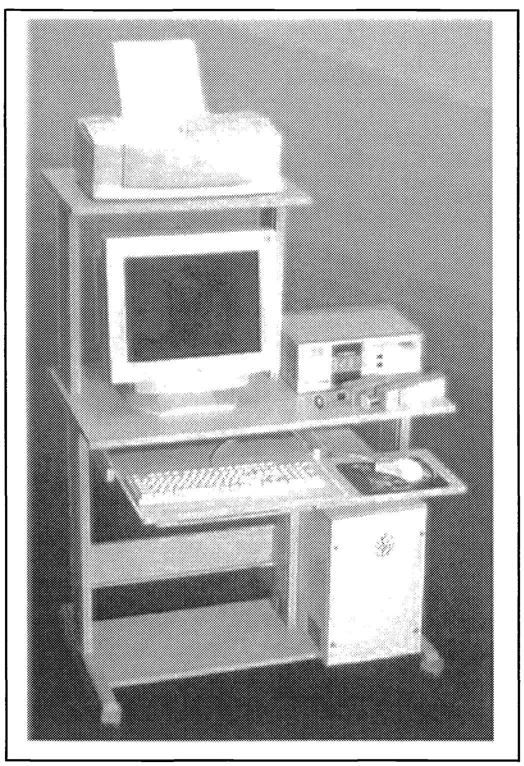

Fig. 2. RTM-01-RES computer based microwave radiometer

The skin temperature is measured by a noncontact method. The skin temperature sensor consists of an optical system that forms a surveyed surface shield, a mechanism that breaks ray flow from the compared body heated to the temperature T_1 and a radiometric part.
A spot diameter on a patient's skin under study depends on the distance between the antenna and skin.

When the distance is ten centimeters the diameter is 1.5 cm. When the distance is one centimeter the spot diameter is about 0.5 cm. These distances are set with help of special facilities.
The skin temperature and compared body temperature are compared with help of the mechanical breaker that operates 24 times in a second. The results of measurement are transmitted as direct voltage to the switch and then to analog-digital converter (ADC).

External view of RTM-01-RES is showed in fig 2. The system includes a microwave sensor to 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. RTM-01–RES has no organs of regulation and control. The device does not require calibration. Instrument tests on long and continuous operation have shown that RTM-01-RES radiometer keep not only differential but also an absolute accuracy measurement of the internal tissues temperature.

The main device specifications are the following:

Table 1

Items	Specifications
Thermal abnormality (i.e. a lower or higher temperature) is detected at a depth of, cm	3 -7 (depending on water content tissue type)
Accuracy of measuring the averaged internal temperature, when a temperature is 32 - 38 °C, °C	± 0,2
Time required for measuring internal temperature at a point, seconds	10
Antenna diameter, mm	39
Accuracy of measuring the skin temperature, °C	± 0,2
Time required for measuring skin temperature at a point, when the temperature is 32 - 38 °C, seconds	1
Device mass, kg	4
Power consumption, Watt	20

In some works [9-10] discussing microwave radiometry temperature data are displayed as a diagram, when the names of the measured points go along the horizontal axis and the internal temperature values are along the vertical axis. This method allows to analyze temperature differentials between corresponding points on the left and right breasts. However it is difficult to analyze the temperature at various locations on one entire breast by this method. Therefore temperature data are also displayed as a temperature field, which is used in infrared thermography In the temperature field each temperature value is displayed by its own color on the monitor (Fig.3).
In the temperature field cold areas of the breast are displayed by "cold" colors (i.e. blue) and hot ones are reflected by "warm" colors (red and pink).Imaging thermal data as a internal temperature field show temperature abnormalities, that, in particularly, correspond to location of cancer. The presented on Fig. 3A data just s example image for healthy person without significant asymmetry between left and right breast. The Fig.3B shows a significant asymmetry due with local cancer when nipple heat of right and left are compared. The thermal differential is about 1 C. Analysis of great number of such termograms has showed that different cancer types have different temperature image features.
Note that for medical personnel it is easier to analyze temperature data displayed as a thermogram or a temperature field than numerical values of the measured temperature.
The feature of RTM-01-RES is an expert computer system for the breast cancer detection. The expert system analyzes several parameters, including thermal asymmetry, dispersion of the temperature within the breast, etc.

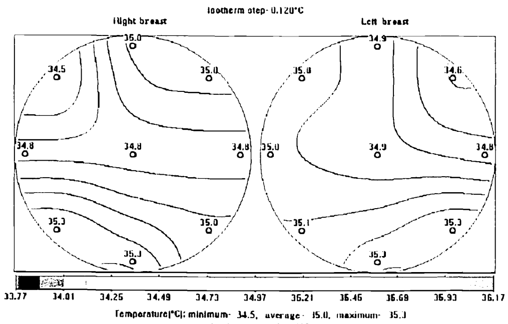

Fig. 3A Thermogram of a normal healthy patient.

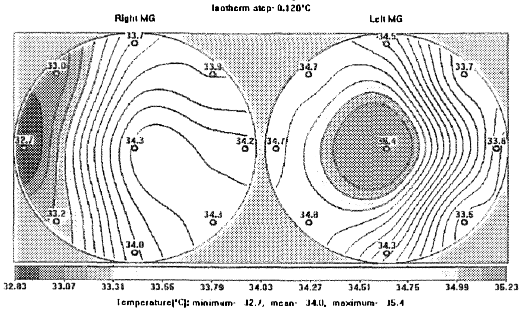

Fig. 3B Thermogram with breast bnormalatiesa.

3. CLINICAL TRIALS OF MICROWAVE THERMOMETRY

The clinical trials were held under the direction of leader Russian specialists at four Moscow medical centers. They are the following: The Branch #1 of the Mammology Health Center; The Municipal Hospital #40;The Russian Oncological Institute under the Science Center of the Russian Academy of Medicine Sciences; The Oncology Health Center of the Moscow Committee of Health.

The purpose of the clinical trials was to estimate the ability of the RTM-01-RES system to detect breast cancer and monitor the treatment of benign tumors. At the Oncology Health Center of the Moscow Committee of Health specialists estimated ability of RTM-01-RES to select risk patients. The risk patients are patient that should be undergo complex diagnosis. RTM-diagnosis was carried out independently from clinical, X-ray and other examinations. The results of RTM-diagnosis were compared with results reported by histology. They were blind clinical trials (a doctor did not know results reported by other methods). The results of the clinical trials are displayed in Fig. 4.

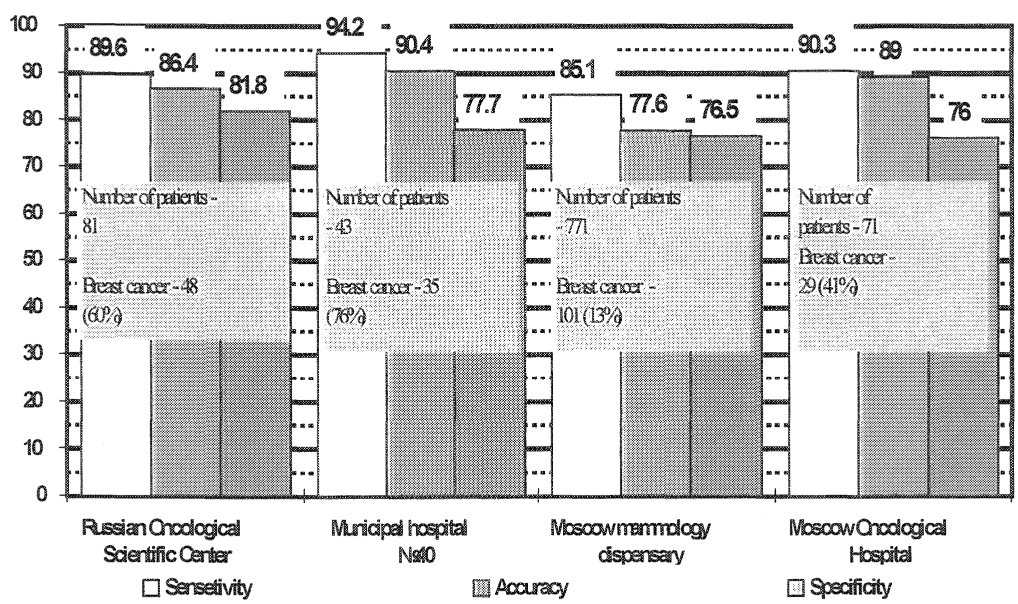

Fig. 4 The result of clinical trials of microwave radiometer (diagnostic of breast cancer).

The Fig. 4 shows that all data are coordinated. The sensitivity of the method is 85-94%, the specificity is 76-81%, and the accuracy is 77-90%. These results are comparable with results of mammography.

The investigation has also shown that RTM-Diagnosis can distinguish mastopathy and fibroadenoma with proliferation from mastopathy and fibroadenoma without proliferation. Therefore it can select patients who may get cancer under unfavorable conditions. These patients should have an complex examination in specialised health centers. The results are represented in Table 2.

Table 2

Disease	Number of examined patients	Ultrasound	Mammography	RTM-Diagnosis
Mastopathy and fibroadenoma with proliferation	11	2 – cancer 4- mastopathy 5- fibroadenoma	4 – cancer 6 – mastopathy 1- fibroadenoma	9- Thermogram shows RTM-features of risk group 2-There are no RTM-features of risk group
Mastopathy and fibroadenoma without proliferation	18	12- mastopathy 4- fibroadenoma 2 – not performed	14 – mastopathy 2 – fibroadenoma 1 – cancer 1 – not performed	3 – Thermogram shows RTM-features of risk group 15–There are no RTM-features of risk group

The table 2 shows that RTM-Diagnosis distinguish mastopathy and fibroadenoma with proliferation from mastopathy and fibroadenoma without proliferation enough well. Thus one of the advantages of RTM-Diagnosis is to select patients with fibroadenoma and mastopathy with proliferation. Other diagnostic techniques can not do this as they detect anatomical changes in the breast. RTM-Diagnosis provides a doctor with information on active processes in the breast.

4. RESUME

The clinical trials and experience of using RTM-01-RES at the leader oncological centers have shown that microwave radiometry is an effective method for the earlier breast cancer detection. As it is harmless, it allows to select patients with abnormal thermograms at an earlier stage. These patients should undergo the complex breast examination. The sensitivity for the method is comparable with the sensitivity for mammography and ultrasound. The method is very promising to be used for diagnosing young women, as mammography is not effective for this group. Also microwave radiometry is useful for monitoring the treatment of benign diseases. . It will be important to compare data obtaining by microwave and MRI technique.

Mammology is not a single area where microwave radiometry can be used. The system can be also used in urology for diagnostics prostate cancer , gynecology, for diagnosis of thyroid diseases and very promising for temperature control during different therapies including ILT. Right now spatial resolution is not so high to measure spatial temperature distribution and system allow just to control average temperature at functional diagnostics. The possible improvements are concluded in development of multi-frequency and multi-channel schemes to provide possibility to measure of spatial temperature distribution with good spatial resolution.

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