Диагностические возможности современной радиотермометрии в онкомаммологической практике

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АННОТАЦИЯ

Обоснование. Радиотермометрия (РТМ) является актуальным методом обследования молочной железы, позволяющим помимо визуализации патологических очагов оценить качество метаболизма, что важно с позиций определения биологических подтипов рака молочной железы (РМЖ) и возможности оценки степени агрессивности опухоли до иммуногистохимического анализа.

Цель. Исследовать возможности современной РТМ в дифференциальной диагностике доброкачественной и злокачественной патологии молочной железы и при различных биологических подтипах РМЖ.

Материалы и методы. Обследовано 118 пациенток с различной патологией молочной железы с помощью компьютеризированного диагностического комплекса РТМ 01 РЭС, Замеры выполнялись в 9 точках: непосредственно на молочной железе — для визуализации опухоли, двух контрольных точках (в области эпигастрия и мечевидного отростка грудины) и одной точке в аксиллярной зоне с обеих сторон — для выявления возможных метастазов. Время проведения исследования 15–20 минут — для каждой женщины. Результаты РТМ сопоставлялись с данными гистологической верификации, ультразвуковой, маммографической и клинических картины.

Результаты. Чувствительность РТМ в дифференциальной диагностике патологии молочной железы составила 96,9%, точность — 74,5%. Специфичность РТМ для дифференциации агрессивных и неагрессивных подтипов РМЖ оказалась низкой — 6,6%. При оценке разницы температур между патологической и нормальной тканью наблюдается тенденция к увеличению значения над опухолью по сравнению с непораженной тканью, однако статистически значимых различий между средними температурами здоровой и пораженной молочной железы не получено. Корреляции между индексом пролиферативной активности РМЖ и частоты термоасимметрии, либо степенью ее выраженности не выявлено ($r < 0,3$).

Заключение. РТМ продемонстрировала эффективность в дифференциальной диагностике доброкачественных и злокачественных изменений ткани молочной железы, при этом она не является методом выбора в оценке распространённости и биологического подтипа рака молочной железы.

Ключевые слова: *радиотермометрия; рак молочной железы; фенотипы рака*

Diagnostic potentials of modern radiothermometry in oncomammological practice

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ABSTRACT

BACKGROUND: Radiothermometry (RTM) is a breast examination method that permits, besides visualization of the pathological foci, to evaluate the quality of metabolism, which is important for the determination of the biological subtypes of breast cancer (BC) and the possibility of the evaluation of the degree of tumor aggressiveness before immunohistochemical analysis.

AIM: To study the potentials of modern RTM in the differential diagnosis of benign and malignant breast pathologies and in different biological subtypes of BC.

MATERIALS AND METHODS: Overall, 118 patients with different breast pathologies were examined using PTM 01 РЭС computerized diagnostic complex. Measurements were performed in nine points: directly on the breast — for the visualization of tumor, in two control points (in the region of the epigastrium and sternal xiphoid process), and in one point in the axillary zone on both sides — for the identification of probable metastases. The examination time was 15–20 min for each woman. RTM results were compared with histological, ultrasound, mammographic, and clinical data.

RESULTS: The sensitivity and accuracy of RMT in the differential diagnosis of breast pathology were 96.9% and 74.5%, respectively. The specificity of RTM in the differentiation of aggressive and non-aggressive BC subtypes appeared to be low at 6.6%. In the evaluation of the temperature difference between the pathological and normal tissues, a tendency to a non-increase in the temperature above the tumor in comparison with the unaffected tissue was noted; however, no significant differences between the mean values for the healthy and affected breasts were obtained. No correlations were found between the proliferative index of BC and frequency of thermoasymmetry or extent of its evidence (r < 0.3).

CONCLUSION: RTM demonstrated effectiveness in the differential diagnosis of benign and malignant alterations of the breast; thus, it is not a method of choice in the evaluation of the spread and biological subtype of BC.

Keywords: *radiothermometry; breast cancer; cancer phenotype*

LIST OF ABBREVIATIONS

MG — mammary gland
BC — breast cancer
RTM — radiothermometry

BACKGROUND

Despite significant achievements of recent years in personalized and target approaches in breast cancer (BC) diagnosis and management, the problem of its early identification remains the basis of a good patient prognosis [1]. "Rejuvenation" of breast oncopathology in some cases hinders the effectiveness of routine diagnostic methods making specialists use combinations of expensive and sometimes invasive methods of tumor process visualization and verification [2–4]. Besides direct breast neoplasm localization and confirmation, determining its biological properties, which define the management algorithm of a particular patient, is necessary.

One of the visualization methods of breast pathology is radiothermometry (RTM), which is firmly included in the routine algorithm of complex breast examination in many clinics [5–7]. Numerous studies revealed that this non-invasive method is a highly sensitive method, which is capable of differentiation between malignant and benign breast tissue alterations at the preclinical stage in different age groups [8–12], based on the measurement of the difference between electromagnetic radiation of healthy and neoplastic tissue cells in the microwave range at the depth up to 5 cm [13]. The study of thermoasymmetry of healthy and altered breast structures that was conducted by M. Gauthiere in 1965 on 85,000 patients revealed that a malignant tumor has a higher temperature than normal tissues due to enhanced metabolism [14,15]. Concurrently, the breast that is affected by a malignant process, as a rule, possesses higher parameters relative to the healthy side, which, in turn, can be attributed to the active angiogenesis [16]. Additionally, in a group of females (n = 1245) with questionable thermograms without any clinical or radiological breast alterations, further observation within 8 years revealed BC in 40.2% of cases [17–19]. This method has also been proven effective in evaluating benign processes with high and low proliferative activity [20]. Therefore, RTM is an actual method of breast examination since it permits metabolism quality evaluation, besides direct pathological foci visualization [21–23]. This is important from the point of view of biological BC subtypes determination since the reliable differences of thermograms of different histological forms of cancer were proven as early as the 60s. Additionally, of importance is also a question about the possibility of evaluation of the extent of tumor aggressiveness before the immunohistochemical analysis [10].

Aim — to determine the potentials of the modern RTM in the differential diagnosis of benign and malignant breast pathology and different biological BC subtypes.

MATERIALS AND METHODS

The study was conducted based on Ryazan Regional Oncological Dispensary and included 118 females with different breast pathology. All procedures were performed as part of the dispensary/routine examination. No additional interventions were performed. The females signed Informed consent within the frames of standard procedures of Ryazan Regional Oncological Dispensary.

The studied parameters were assessed on RTM 01 РЭС computerized diagnostic complex consisting of internal temperature meter, IR skin temperature meter, a means for visualization, processing, and analysis of the obtained information by the expert system [24].

Following the RTM recommendations, measurements were taken in nine points: directly on the breast to visualize the tumor, in two control points in the epigastrium and xiphoid process region of the sternum, and one axillary point on both sides for identification of probable metastases [5,13]. The examination duration was 15–20 min for each participant.

Further on, participants were divided into two groups:

The **control group** (n = 32) with benign breast alterations (mastopathy, fibroadenoma, intraductal papilloma, mastitis, and lipoma) (age 18–79 years);

The **main group** (n = 86) with malignant breast neoplasms [25] (age 24–73 years).

The main group (n = 84) was predominated with BC of different stages (I and II: 28.7% in each, III: 42.8%) of different phenotypes, as well as one case of melanoma metastasis and one sarcoma breast metastasis. Here more aggressive phenotypes of BC were more common in young patients (Figure 1).

Additionally, RTM data were compared with the results of histological verification, ultrasound, mammographic, and clinical picture.

In statistical analysis, methods of descriptive (%) and comparative (T-Student test, Mann-Whitney test) statistics were used, sensitivity and specificity of the diagnostic method (RTM) were determined. Differences were considered statistically significant at $p < 0.05$.
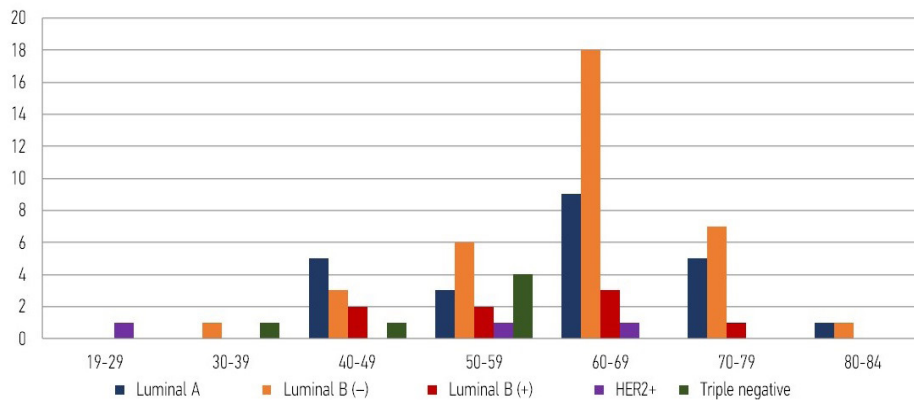
Fig. 1. Relationship of BC phenotype (n) with age (years).

RESULTS

The result analysis revealed the following patterns: RTM is effective in the differential diagnosis of benign and malignant breast processes (for the Student t-test, p = 0.00053), the sensitivity of RTM in breast pathology diagnosis compared with histological verification, ultrasound, mammographic, and clinical picture results were 96.9%, specificity for aggressive and non-aggressive BC subtypes differentiation was low (6.6%).

The temperature difference evaluation between pathological and normal tissue, a tendency to increase measured values above the tumor compared to the unaffected tissue was found; however, no statistically significant differences were obtained either between the average temperatures of healthy and affected breast or between different phenotypes (Table 1). The

Mann-Whitney test showed no temperature differences between luminal A and B groups (U = 342), nor did it confirm more aggressive properties of luminal human epidermal growth factor receptor 2 (HER-2)-positive phenotype relative to luminal HER-2-negative type (U = 114.5), which does not speak in favor of the hypothesis about the effectiveness of RTM in aggressive and non-aggressive BC diagnosis. Ambiguous is the fact of a complete absence of thermoasymmetry in sarcoma and melanoma metastasis to the breast, since a high degree of aggressiveness of both tumors is evident a priori.

Evaluation of the extent of spread of the process by temperature measurement of axillary regions revealed no reliably significant deviations (U = 182). Additionally, hypothermia relative to even healthy tissues in cases with confirmed axillary lymph nodes metastases (Table 1).

Table 1. Distribution of Average Temperatures in Groups with Different Breast Cancer Phenotypes

Average Temperature, °C	Breast Cancer Phenotypes				
	Luminal A	Luminal B (-)	Luminal B HER2+	Non-Luminal HER2+	Triple-Negative
Above tumor	34.4	34.1	34.1	34.5	35.4
Pathological breast	33.6	33.3	33.1	33.6	34.7
Healthy breast	33.2	32.5	32.4	32.8	34.8
Altered lymph nodes	33.9	33.4	33.9	33.1	34.3
Non-altered lymph nodes	33.9	33.3	33.0	32.9	34.0

A statistically significant result was obtained compared to the frequency and difference of thermoasymmetry in groups with aggressive phenotypes (p < 0.05). Here, the group of non-luminal HER2-positive phenotype had a greater difference of the average temperature between affected and healthy tissue was greater (by 1.8 °C) than in triple-negative variant (by 0.9 °C, Table 2). This fact does not confirm the hypothesis that more aggressive phenotypes, particularly, triple-negative subtype, should give a more resonant picture of thermometry.

Of special interest is Ki67, tumor biological potential index (RTM is based on metabolism in tumor tissue). Our study revealed that the highest average value of Ki67 was observed in triple-negative cancer (63.3%), somewhat lower in groups with HER2-positivity (50.6%), in truly luminal subtypes this parameter was reliably lower, that is 42.2% in luminal B and 10.6% in luminal A. However, no correlation was found between tumor proliferative activity index and frequency of thermoasymmetry or the extent of its evidence (r < 0.3).

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Table 2. Distribution of Average Temperatures in Groups of Aggressive Breast Cancer Phenotype

Average Temperature, °C	Aggressive Phenotypes of Breast Cancer	
	Non-luminal HER2+	Triple-negative
Pathological breast	34.7	35.4
Healthy breast	32.9	34.5
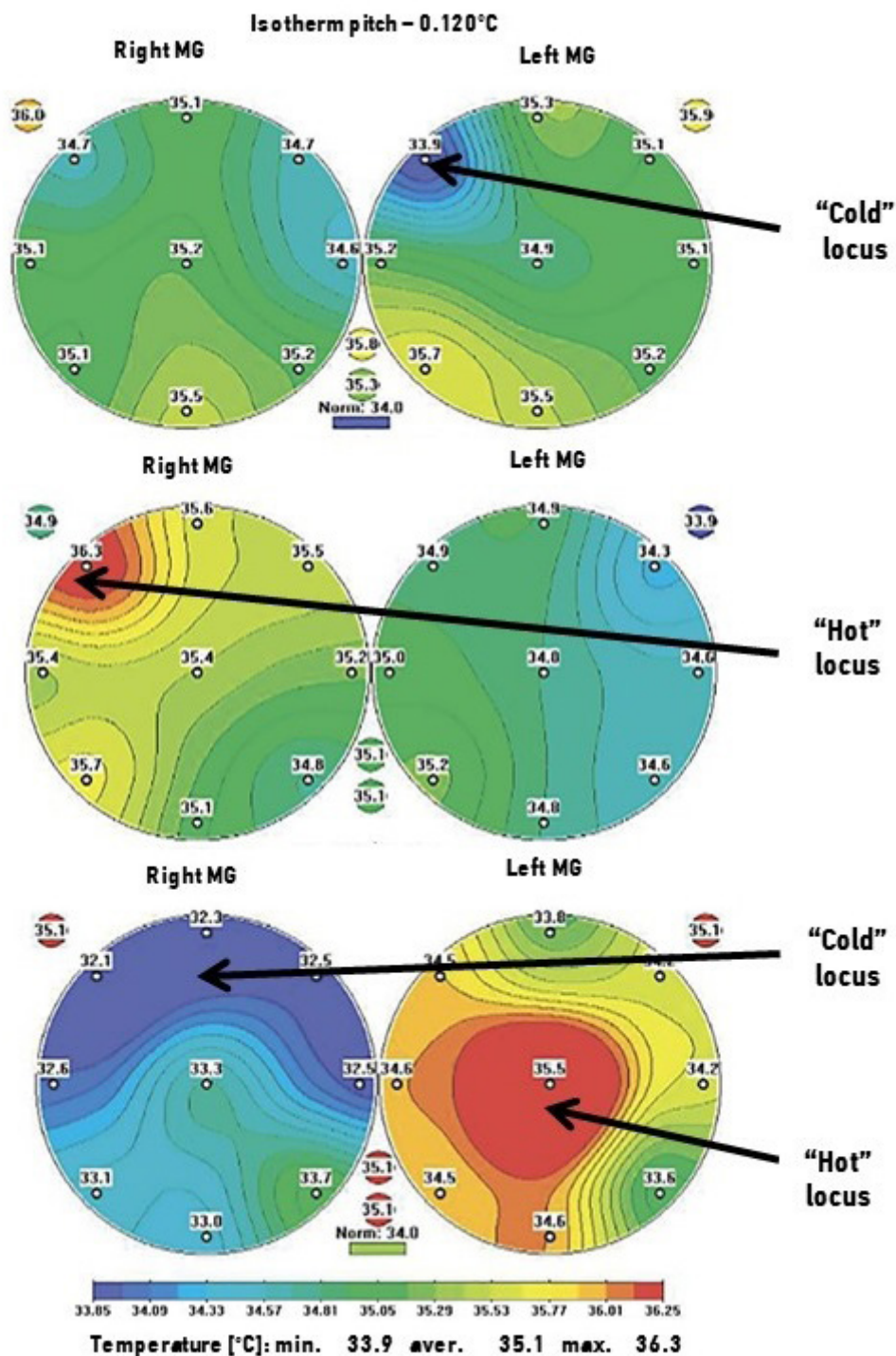
Fig. 2. Examples of radiothermometry results: A — benign breast tumor; B — breast cancer, triple-negative, localized form; C — breast cancer, luminal B, diffused form.

DISCUSSION

Thus, diffused (locally spread) forms of BC are presented in the forms of thermograms with the most significant spread and large areas of maximal and minimal temperatures.

Below, several demonstrative results of RTM of benign process, localized, and diffused BC are presented (Figure 2).

CONCLUSIONS

1. Radiothermometry demonstrated effectiveness in the differential diagnosis of benign and malignant breast tissue alterations.

2. Radiothermometry is not a method of choice in diagnosing the extent of spread and evaluating the biological subtype of breast cancer , since no correlation was found between the frequency and extent of thermoasymmetry and phenotype, nor the connection between temperature difference with Ki67, as well as with metastatic regional lymph node lesions.

ADDITIONAL INFORMATION

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