Assessment of Computer Regulation Thermography (CRT) as a Complemetrary Diagnostic tool for Breast Cancer Patient

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ABSTRACT

Background: Breast cancer is the most common type of cancer in women demanding accurate diagnosis to take remedial measures to treat.

Objective: Comparing the diagnostic capability of the computer regulation thermography (CRT), as a novel and safe diagnostic procedure, with common methods including sonography, mammography and clinical examinations for diagnosing breast cancer in suspicious patients against pathology as the gold standard.

Material and Methods: In this prospective clinical trial study, out of 97 referred patients, 44 meeting the inclusion criteria were selected. The selected patients were subjected to mammography, sonography, CRT and clinical examinations. Then, the patients showing suspicious symptoms of breast cancer underwent pathological examinations.

Results: CRT indicated a higher specificity compared to mammography and sonography (78.9% vs. 71.4% and 47.0%, respectively). However, CRT sensitivity was lower than those of mammography, sonography and clinical examination (52% vs. 70.6%, 82.4% and 84.0%). Furthermore, CRT accuracy was lower than mammography, sonography and clinical examination (63.6% vs. 70.9%, 64.7% and 88.6%). While CRT positive prediction value (PPV) was higher than those of mammography and sonography, it was lower than that of clinical examination (76.5% vs. 75%, 60.9% and 95.5%). The negative prediction value (NPV) of CRT was less than all other modalities (55.5% vs. 66.7%, 72.7% and 81.8% for the clinical examination, mammography and sonography, respectively).

Conclusion: Although CRT with a lower sensitivity and higher specificity, cannot be recommended to be used as a definitive diagnostic tool for breast cancer patients, it can be used as a complementary method with other methods to increase the diagnostic accuracy of suspicious patients.

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Keywords

Breast Neoplasms; Thermography; Clinical Examination; Mammography; Ultrasonography; Pathology

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Introduction

Breast cancer is the most horrifying experience for women today [1]. In 2008, more than 1.4 million people were diagnosed with breast cancer each year globally and over 458000 died of this disease [2]. In developing countries, the incident rate of this disease is growing up annually [3]. The life time risk of developing breast cancer

in Northern Europe and the USA is 1:8 and 1:10, respectively [4] and in Iran the ASR (Age Standardized Ratio) of this disease is 30/10000. Detection of breast cancer at early stages increases the effectiveness of its treatment options and patients' survivability [5]. The growth of a breast cancer tumor is proportional to its temperature [6]. In response to an ever-increasing need for nutrients, cancerous tumors produce neoangionesis. The temperature in a cancerous breast is almost always higher than that of normal breast tissues even in precancerous tissues and areas surrounding it [7]. The fundamental diagnostic measures for the detection of breast cancer still depend essentially on clinical examination and mammography [8].

Timely evidence results in early detection, thus reduction in breast cancer mortality [9]. X-ray screening mammography proves to be the most sensitive noninvasive technique for detecting early tumors [10, 11], though other non-radiation imaging methods of cancer detection such as thermography, diaphanography (light scanning), whole breast ultrasound and magnetic resonance imaging (MRI) are employed from time to time. While additional methods can refine screening mammography or clinically based impressions, they are not comparable regarding the reliability, low cost and the efficiency of conventional mammography as a mass screening test for large populations [12, 13].

Mammography, the most widely employed diagnosis method, is not effective enough for women with dense or surgically altered breasts, and those aged 40 and younger. Furthermore, some other concerns include the risk of ionizing radiation and patients' complaint of discomfort due to the high compression of their breasts required for this imaging method. In searching for developing other imaging techniques to overcome mammography limitations, thermography carries potential to improve overall detection efficiency [14].

The first recorded use of thermobiological diagnostics can be found in the writings of Hippocrates around 480 B.C. The method involved spreading mud over the patient's organ and the area that would dry first was thought to indicate core organ pathology [15]. In the 1950s, military research into infrared monitoring systems for nighttime troop movements paved the way for thermal diagnostics. Once publicized in the mid-1950s, infrared imaging technology was made available for medical purposes. The first diagnostic use of infrared imaging was performed in 1956 when Lawson discovered that the skin temperature of a cancerous area in the breast was higher than that of a normal tissue [16, 17]. Dr. Ernest Schwamm is to be honored for the introduction of radiation measurement into medicine. Together with his co-workers, he developed a thermal practical diagnosis known as thermoregulation diagnosis. Afterwards, Lawson developed the pictorial documentation of heat radiation that was considerably more convenient since the heat picture could be evaluated with a glance without having to make many individual measurements.

The regulation diagnosis initiated by Schwamm and the picture-producing method according to Lawson, are both termed radiation measurements. Fergenson (1963) introduced cholesterol crystals into heat diagnosis. These crystals change their color according to their temperature. When applied to the skin, a colorful picture is developed depending on the local temperature. Whenever encapsulated in foils, it is known as Liquid Crystal Thermography. This is a picture-producing method in contact with the skin. Skin temperature measurements with contact sensors, as used today in regular thermography, did not exist and the reaction time of the existing thermometer was still too lengthy to use for this procedure. Thermal contact sensors with a reaction time of one second have come into existence over the past ten years. Arno Rost took up this method and improved it so that it could be used in office. A diagnosis of the whole

body can be obtained by means of two other methods producing a graphic picture by means of individual measurements: the non-contact infra-red thermography and the contact thermography. These two methods measure totally different parameters: infra-red radiation in the former and temperature in the latter. Therefore, they produce diverse results which have to be evaluated differently [18].

Recent advances in sensor technology and awareness of using non-invasive and non-ionizing medical imaging techniques have made breast thermography a choice for breast cancer diagnosis [19].

Thermography is very useful for the detection of non-palpable breast cancer; that is, those that cannot be detected by other tests. This also applies to non-palpable but histological advanced ones or those with fast and aggressive growth [20].

It has been reported that this modality can detect breast cancer 10 years earlier than the traditional method-mammography [21]. In this study, the diagnostic value of the computer regulation thermography (CRT) has been compared with clinical examination, as well as common imaging methods of sonography and mammography in patients with suspecious breast cancer even the pathology results have also been taken into consideration.

Material and Methods

This prospective clinical trial study, was made to assess the computer regulation thermography diagnostic modalities along with other common modalities for diagnosing patients having breast neoplasms.

Participants

Among 97 patients referred to Cancer Research Center in Shohadaye Tajrish Hospital, 44 were selected meeting our inclusion criteria. The selected patients were then examined by mammography and sonography tests if necessary, and all of them underwent clinical examination by specialist Breast Surgeons confirming them as suspicous of clinical diagnosis of breast cancer. Afterwards, tissue diagnosis with pathological comfirmation for breast cancer were performed. Then, all of the patients diagnosed with breast cancer were referred to have CRT test.

Procedure

CRT 2000® (Eidam Diagnostics Corporation) Thermographic System includes CRT Core Unit, CRT Sensor, CRT Display, CRT Measurement and Analysis Software and CRT server-based analysis service. CRT 2000® device analyzes the input data and provides both a graphic representation of the thermal measurements and an interpretation based on the combined data. The computer program also analyzes and points out a variety of interpretive indices. The procedure was done in a temperature controlled room maintained between 20 and 23 ˚C. The 30-minute procedure begins with 119 measurements of predefined points on the head and torso. After the first measurement, the patient disrobes and waits for the cooling stimulus to apply stress to the patient's organs, after which, a second reading of the same points is taken.

Patients' Preparation for CRT Imaging

Room temperature was kept stable wherein the patient first sits fully clothed in a slightly cool room, 20˚C to 23˚C, for 10 to 15 minutes while her body temperature acclimates. The technician begins the measurements by gently touching a temperature probe on specific points of the patient on her face, neck, arms, chest, upper and lower abdomen, back and breasts. Thereafter, the patient was asked to disrobe from the waist down and stands unclothed in her underwear, with arms by her sides, exposed to the cool room air for 10 minutes. This exposure provides a challenge to the body's temperature regulation processes. While still undressed, the same points are measured again to conclude the test.

Imaging and Interpretation

After having the two sets of measurements taken from 119 described points, the data are sent to a Canadian Server supporting CRT imaging equipment for the analysis.

Statistical Analysis

Collected data were analyzed with SPSS software (Version 20) and described by calculating the TP (True-Positive), TN (True-Negative), FP (False-Positive) and FN (False-Negative) values and also the sensitivity and specificity of Computer Regulation Thermography (CRT) tests, as well as the mammography and sonography exams of the patients against the pathology result as the gold standard examination. Variables were described with Mean+SD, frequency (percent) and compared with each other by using independent t-test and chi square test. A p-value less than 0.05 was assumed significant. The sensitivity, specificity and total accuracy of breast CRT were derived from the comparison of the breast CRT results against the gold standard (biopsy) and compared with those of the mammography, sonography and clinical examination) in selected patients.

Results

From 44 selected patients, 19 were benign including fibrocystic, fibroadenomas, ductal huperplasia, granulomatous mastitis and 25 were malignant including invasive ductal carcinoma and in situ carcinoma.

Table 1 shows that the demographic factors of the two samples (the malignant and benign patients) in terms of overall criteria (including: Vitality Index, Waist Hip Ratio, Entropathy Index, Therapy Index, and Lymphatic Index) indicating no significant differences between any of the variables (having p-values <0.05).

The 44 selected patients had CRT, clinical examination, mammography and sonography imaging modalities done on them. The CRT had 15 true-negative, 4 false-positive, 13 true-positive and 12 false-negative results. The calculated CRT sensitivity was 52%, specificity: 78.9%, total accuracy: 63.6%, positive predictive value (PPV): 76.5% and negative predictive value (NPV): 55.5%. For a sub-group of 31 patients, mammography indicated a sensitivity of 70.6%, specificity: 71.4%, total accuracy: 70.9%, PPV: 75% and NPV: 66.7%. For a sub-group of 34 patients, sonography showed a sensitivity of 82.4%, specificity: 47%, total accuracy: 64.7%, PPV: 60.9% and NPV: 72.7%. These values are shown in Table 2. For the whole selected group of 44 patients, the clinical examination had a sensitivity of 84%, specificity: 94.7%, total accu-

Table 1: Demographic data of the malignant and benign patients

Criteria	Malignant			Benign		
	Range	Mean	SD	Range	Mean	SD
Age (year)	29 to 62	49	11	24 to 58	45	10
Blood Pressure (mmHg)	90/60 to 140/90	115/75	15	100/70 to 150/10	117/70	13
BMI	21.4 to 38.3	27.96	4.52	21 to 37.3	27.71	3.96
VI*	1.3 to 4.2	2.46	0.76	1.7 to 3.6	2.41	0.62
WHR**	0.8 to 1	0.69	0.36	0.7 to 1	0.66	0.35
ENI***	1.6 to 5.8	3.6	1.2	1.9 to 5.8	3.8	1.1
THI****	12 to 21	14.5	4.9	12 to 19	12.9	6
LI*****	1 to 6	4.3	1.6	1 to 6	4.5	1.7

*Vitality Index, **Waist Hip Ratio, ***Entropathy Index, ****Therapy Index, *****Lymphatic Index

Table 2: Statistical parameters calculated from the patients for various diagnostic methods

Statistical parameters	CRT	Mammography	Sonography	Clinical Examination
Sensitivity (%)	52.0	70.6	82.4	84.0
Specificity (%)	78.9	71.4	47.0	94.7
Total Accuracy (%)	63.6	70.9	64.7	88.6
PPV* (%)	76.5	75.0	60.9	95.5
NPV (%)**	55.5	66.7	72.7	81.7

*Positive Prediction Value, **Negative Prediction Value

racy: 88.6%, PPV: 95.5% and NPV: 81.8%. In this study, the CRT and the clinical examination were performed on the same number of patients in each group. Some of the patients did not have sonography and mammography imaging done.

Figure 1 shows the sensitivity, specificity, total accuracy, PPV and NPV of the four diagnostic methods of breast cancer detection (CRT, Mammography, Sonography and Clinical Examination) in comparison with the biopsy as the gold standard.

Discussion

Early diagnosis of breast cancer with common imaging/clinical modalities is the optimal goal of health delivery system. The computer regulation thermography is more or less an emerging technique recommended to be used for the early detection of breast cancer.

Our study showed that although CRT indicates a lower sensitivity (52%) in detecting breast cancer, it favors a higher specificity (78.9%) in detecting benign breasts.

Our results in an intermediate acceptable condition demonstrate that CRT is effective in diagnosing the benign lesion and breast cancer comparing with mammography (sensitivity: 70.6%, specificity:71.4%), sonography (sensitivity: 82.4%, specificity: 47%), clinical exam-

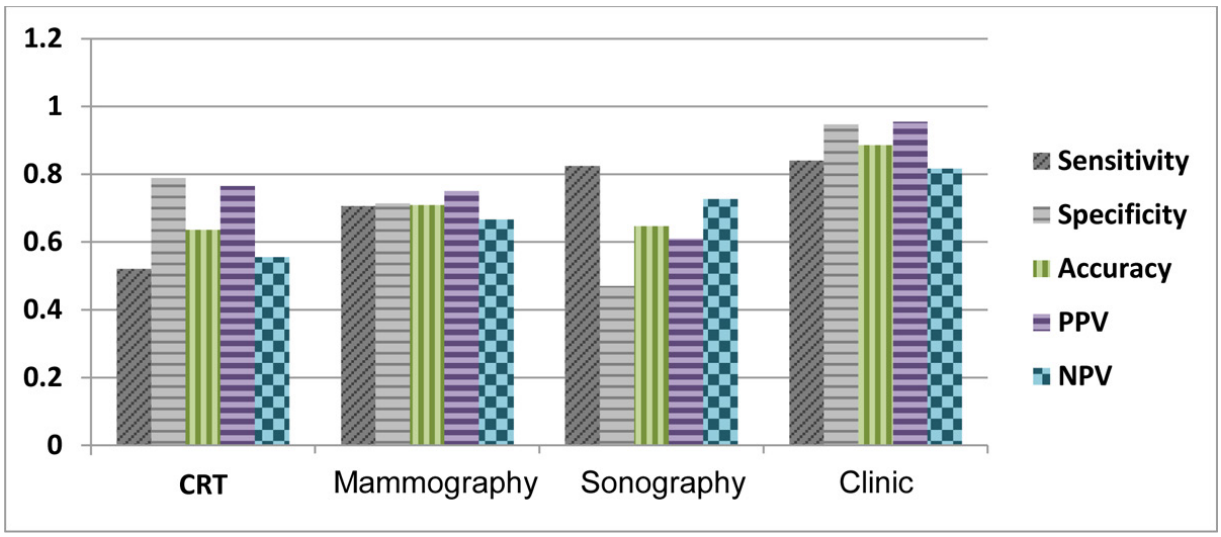

Figure 1: Statistical results of various diagnostic methods compared with the biopsy as the gold standard (PPV: Positive Prediction Value, NNP: Negative Prediction Value)

ination (sensitivity: 84%, specificity: 94.7%). Despite the findings of this study proving the CRT as an effective early diagnosis method, medical practitioners are not fully aware of this imaging method. Thus, it is recommended to pair this modality up with other common existing methods.

Based on the manufacturer's recommendations and based on other studies in which the CRT is used for the areas other than chest, we also examined several other areas of the patients' body through CRT test. The upcoming results can then be interpreted as an indication for investigating the lack of influencing the cancer on uninvolved areas over a long term-period to prove the absence of metastasis in such patients. This claim can be confirmed via a long-term follow-up of the patients participated in this study and the biopsy of suspicious areas may be necessary to ascertain such a conclusion.

The results obtained in this study were reasonably acceptable considering some limitations we were faced with. All of the patients did not meet all the necessary prerequisites of CRT tests. These limitations lead to lower levels of sensitivity, specificity, total accuracy, PPN and NPV of the CRT than what we expected. For instance, some of the patients were wearing tight clothes and makeup or/and experiencing tiredness due to a long distance trip or some other discomfort of any kind, despite instructing them to avoid such circumstances.

The specific conditions required to be met for CRT 2000® test by patients are as follows: sustained room temperature (20-23˚C), stress-free status, no manipulation on the organ, not wearing tight clothes and not using cosmetics. Implementing such ideal conditions is far from being realistic. For example, in our study, some patients had traveled from far distances and others had applied make-up having significant impact on their test results. Future studies on a larger sample of this population are advised to take such factors into considerations.

Based on the promising potential of CRT 2000®, other investigators can be hereby recommended to focus on the diseases affecting other parts of the body than breast. However, based on this introductory investigation, CRT can also be recommended to be used as a complementary imaging tool along with other well known imaging methods for earlier detection of breast cancer.

Conclusion

In this prospective clinical trial, 44 women with suspicious breast lesions underwent CRT test to identify the breast cancer prior to clinical examinations, mammography and sonography imaging modalities. The findings showed that CRT can detect breast cancer pathology with a sensitivity of 52%, specificity of 78.9%, total accuracy of 63.6%, PPV of 76.5% and NPV of 55.5%.

CRT does not entail the use of ionizing radiation, venous access, radioactive dyes or any other invasive procedures, has no ionizing radiation risk for the patient, provides immediate results and is relatively inexpensive.

In conclusion, we have shown that a modernized CRT 2000® can be a useful adjunctive test in detecting benign breast with a high specificity of 78.9% based on this prospective clinical trial on the patients leading to an increase in the total accuracy of their diagnosis. In addition, if this technique is implemented in a way that all of its confounders can be controlled, the sensitivity of this technique and consequently its total accuracy might also increase.

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Conflict of Interest

The CRT device was provided on no condition by Ganjineh Salamat Pasargad Company (Tehran, Iran), free of any charge/cost. However, the authors declare no conflict of interest regarding this research.

References

1. Gautherie M. Temperature and blood flow patterns in breast cancer during natural evolution and following radiotherapy. *Prog Clin Biol Res*. 1982;**107**:21-64. PubMed PMID: 7167480.
2. Ferlay J, Shin H-R, Bray F, Forman D, Mathers C, Parkin DM. *GLOBOCAN 2008, cancer incidence and mortality worldwide: IARC CancerBase No. 10*. Lyon, France: International Agency for Research on Cancer. 2010;**2010**:29.
3. Akbari ME. Iranian Female Cancer Report. Tehran: Entesharat Mohsen; 2014.
4. Ng EY, Fok SC, Peh YC, Ng FC, Sim LS. Computerized detection of breast cancer with artificial intelligence and thermograms. *J Med Eng Technol*. 2002;**26**:152-7. doi.org/10.1080/03091900210146941. PubMed PMID: 12396330.
5. Lee CH. Screening mammography: proven benefit, continued controversy. *Radiol Clin North Am*. 2002;**40**:395-407. doi.org/10.1016/S0033-8389(01)00015-X. PubMed PMID: 12117183.
6. Usuki H, Onoda Y, Kawasaki S, Misumi T, Murakami M, Komatsubara S, et al. Relationship between thermographic observations of breast tumors and the DNA indices obtained by flow cytometry. *Biomedical Thermololgy*. 1990;**10**:282-5.
7. Gautherie M, Gros CM. Breast thermography and cancer risk prediction. *Cancer.* 1980;**45**(1):51-6. doi.org/10.1002/cncr.2820450110. PubMed PMID: 7351006.
8. Thomas DB, Gao DL, Self SG, Allison CJ, Tao Y, Mahloch J, et al. Randomized trial of breast self-examination in Shanghai: methodology and preliminary results. *J Natl Cancer Inst*. 1997;**89**:355-65. doi.org/10.1093/jnci/89.5.355. PubMed PMID: 9060957.
9. Carter CL, Allen C, Henson DE. Relation of tumor size, lymph node status, and survival in 24,740 breast cancer cases. *Cancer*. 1989;**63**:181-7. doi.org/10.1002/1097-0142(19890101)63:1<181::AID-CNCR2820630129>3.0.CO;2-H. PubMed PMID: 2910416.
10. Kopans D. Breast cancer screening: women 40 to 49 years of age. *Principles and Practice of Oncology*. 1994;**8**:1-11.
11. Feig SA. Decreased breast cancer mortality through mammographic screening: results of clinical trials. *Radiology*. 1988;**167**:659-65. doi.org/10.1148/radiology.167.3.3283836. PubMed PMID: 3283836.
12. Smart CR, Byrne C, Smith RA, Garfinkel L, Letton AH, Dodd GD, et al. Twenty-year follow-up of the breast cancers diagnosed during the Breast Cancer Detection Demonstration Project. *CA Cancer J Clin*. 1997;**47**:134-49. doi.org/10.3322/canjclin.47.3.134. PubMed PMID: 9152171.
13. Tabar L, Dean PB. The control of breast cancer through mammography screening. What is the evidence? *Radiol Clin North Am*. 1987;**25**:993-1005. PubMed PMID: 3306777.
14. Kapoor P, Prasad S, Bhayana E. Real time intelligent thermal analysis approach for early diagnosis of breast cancer. *International Journal of computer applications*. 2010;**1**:22-4. doi.org/10.5120/129-246.
15. James Odell O. *Introduction to contact regulation thermography*. Richmond, BC, Canada: Eidam Diagnostics Corporation; 2010.
16. Lawson R. Implications of surface temperatures in the diagnosis of breast cancer. *Can Med Assoc J*. 1956;**75**:309-11. PubMed PMID: 13343098. PubMed PMCID: 1824571.
17. Lawson RN. A new infrared imaging device. *Can Med Assoc J*. 1958;**79**(5):402-3. PubMed PMID: 13573292. PubMed PMCID: 1830404.
18. Rost A, Rost J. Introduction to Regulation Thermography. Stuttgart. Hippokrates; 1987.
19. Umadevi V, Raghavan SV, Jaipurkar S. Framework for estimating tumour parameters using thermal imaging. *Indian J Med Res*. 2011;**134**:725-31. doi.org/10.4103/0971-5916.91012. PubMed PMID: 22199114. PubMed PMCID: 3249973.

20. Usuki H, Ikeda T, Igarashi Y, Takahashi I, Fukami A, Yokoe T, et al. What kinds of non-palpable breast cancer can be detected by thermography? *Biomedical Thermology: the journal of the Japanese Society of Thermorogy*. 1998;**18**:8-12.
21. In: Natural Doctor. Eccles N. Thermography: Its role in early breast cancer detection. [August 7, 2013]. Available from: www.chironclinic.com.