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Tissue Mimicking Phantom Design and Characterization for Thermal Imaging Applications on Breast Cancer Diagnosis

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Abstract

Breast cancer is one of the mortal cancerous for women and an early diagnosis, applying an appropriate treatment and prognosis increases the survival chance of the patients. There are different screening methods and thermal imaging is one of the noninvasive promising diagnosis techniques to detect thermal profile anomalies in breasts. This work includes both simulation and experimental studies for the detection of breast tumors by using thermal images. The first step is the simulation studies based on heat transfer in biological tissues. By using the Bio-Heat transfer theory, temperature differences between the healthy and tumorous tissues are acquired. The second step consists of phantom designs and detection of breast tumor via thermographic imaging in in-vitro. Designing an appropriate phantom is tremendously crucial for the calibration of the thermal imaging system and diagnosis of breast cancer. As a result of the study, it is presented that the detection of temperatures difference especially with asymmetry factor between the tumor and healthy tissue region is feasible. Also, it is shown that the simulation based results are consistent with the experimental as well.

Keywords: breast tumor, cancer, phantom, temperature distribution, thermal imaging thermography.

1. Introduction

Breast cancer is one of the leading deathful cancer types among women. According to the latest report of the International Agency for Research on Cancer (IARC), the most commonly seen cancer is the female breast cancer which is ~11.7% of the total new cases by 2020 [1]. However, early diagnosis is crucial for increasing survival rate. Therefore, there have been employed many studies and techniques to detect and monitor the breast cancer and early diagnosis is still a hot topic. One of the important methods for early breast cancer diagnosis is infrared thermography or in another saying thermal imaging. Infrared thermography of the breast is a promising method to early diagnosis of tumor evaluation [2,3]. The major advantage of the thermography is can detect the cancer cells at least a year earlier than current screening methods such as mammography [4]. While magnetic resonance imaging (MRI), ultrasound, and mammography are looking for a lump or structural changes, the thermography screens for unusual new blood vessel formation which is called angiogenesis. Infrared thermography is a non-invasive functional monitoring technique which detects surface temperature deviations of an object [2]. Therefore, infrared thermography is totally safe for the patients and there is no ionizing radiation exposure. Another advantage is non-contact and applicable without any pain or stress. Nevertheless, it is worth to mention that thermography is an adjunct to mammography.

Essentially, the history of deployment of infrared thermography to screen breast cancer/tumor goes back 1950s. Ray N. Lawson discovered the breast tumors were relatively warmer than the surrounding healthy breast tissue for the first time in 1956 [5]. The following year in 1957, Lawson proposed to use infrared thermography to detect/monitor breast cancer in his study [6, 7]. After that, many different studies employed and were presented in breast cancer screening by using thermography [6]. One of them is Collett et al. conducted a dynamic imaging technique which is first applying cold air onto the breast, then taking sequential images or video series while the breast warms up to screen breast cancer or abnormalities. They imaged 121 female patients and used 99 of them, but the sensitivity and selectivity results were not promising [8]. However, Wu et al. in 2016 [9], Rassiwala et al. in 2014 [10], and

Delgado [11] et al. in 2010 studied with large groups of patients, 143 in Taiwan, 1,008 in India, and 911 in Mexico, respectively and their conclusions were infrared thermography was a useful and promising tool for prognosis in breast cancer patients. Besides in-vivo studies, many in-vitro based experiments were conducted as well. Levy et al. carried out an in-vitro study where they used inductive heating mechanism and thermal imaging techniques. They were able to detect up to 5 mm diameter size and 14 mm depth tumor structure [4]. Wahab et. al. employed a thermal distribution (TD) analysis into homogenous phantoms and suggested that the TD technique may be applied to detect different tissue structure [12]. Hossain and Mohammadi used temperature profiles to predict physiological, biological, and thermal properties of the tumor. They proposed that skin temperature distribution profile was correlated with tumor structure [13]. In addition, especially some of the recent research have been employed that thermographic breast images are promising non-invasive breast cancer monitoring tool by using machine learning and specifically deep learning algorithms as well [14–17]. Furthermore, infrared thermography is a Food and Drug Administration (FDA) approved supplementary technique to mammography the gold standard for screening breast cancer [6]. Therefore, early breast cancer detection via thermographic imaging is still a trend research field and needs to be investigated further.
This work is an early stage study of an in-vitro research of the thermal imaging for early diagnosis of breast cancer detection via manufactured breast phantoms. It is aimed to show the capabilities and effectiveness of the thermography such as tumor size and depth wise. This paper is divided into two main parts. The first part of the study is based on the modelling of a heat transfer simulation in breast tissues. The second part contains manufacturing process of the breast phantoms, mimicking tumors, and then screening the phantoms by a thermal camera. As it is known that the phantom manufacturing has dispensable in medical studies because of ease mimicking the organs and calibration of the device/methods under test. Also, this is the first phase out of three of a medical study which is in-vitro, animal model, and human studies, respectively. In this work, we show that the tumor-wise abnormalities can be detected up to 45 mm depth instead of shallower range. Moreover, we also show that the asymmetry factor is a promising feature to identify the difference between the healthy and cancerous breast.

This paper is organized by following sections. In section 2, simulation and modelling procedures are given. Then, phantom manufacturing process is given in Part 3. In the 4th and last part of the study, the results are presented for thermal imaging analysis of the breast tissue phantoms with and without tumor structure cases under different scenarios such as size and depth location of the tumor.

2. Materials and Methods

2.1. Theory of the Thermal Specification of the Tissue

The prediction of the thermal distribution on biological tissues can be useful for correct evaluation or decision in some cases such as degree of burnt, irregulations, or anomalies. Bio-heat transfer in the tissue is a process contains heat production, heat transfer, heat emission, and heat radiation [18, 19]. Bio-heat transfer is actually a heat transfer procedure between blood perfusion, sweating, bio-heat metabolic heat production, skin tissue and outer surface medium. Many factors affect the bio-heat transfer procedure such as thermal features, temperature, sex, age, damage, or imperfections onto the tissue, and pressure [20, 21]. Tissue is a heterogeneous and anisotropic medium. Also, it is hard to make a theoretical solution for the heat distribution onto the real tissue structure due to the complex geometry of the tissue. Therefore, numerical simulation approach of the bio-heat transfer is more practical.

2.1.1 Bio-Heat Transfer Equation

The most common used heat transfer method on the tissue is the Pennes' bio-heat transfer equation which has been used for breast tumor temperature distribution modeling as well [2, 21]. The Pennes' bio-heat transfer equation solves the tissue temperature distribution as a function of blood perfusion and metabolic heat velocity [22, 23]. In addition, the Pennes equation gives more accurate approximation for the heat transfer process inside the tissue because of using variable metabolic heat generation and also variable blood perfusion instead of assuming constant values [24]. The equation is given by Eq. 2.1 below;

$$\rho C_p \frac{\partial T}{\partial t} - k\nabla^2 T = \rho_b C_b \omega_b (T_b - T) + Q_{met} \quad \textbf{(2.1)}$$

where ρ is tissue density in kg/m^3, C_p is heat capacity in J/kg.K, T is tissue temperature in K, k thermal conductivity in W/m.K, ρ_b blood density in kg/m^3, C_b is blood specific heat capacity in J/kg.K, ω_b blood perfusion rate in per second, T_b is blood temperature in the vessel in K, and Q_{met} volumetric metabolic heat generation velocity in W/m^3.

The Pennes' bio-heat equation is used commonly because of its mathematical simplicity and the superior ability of heat area prediction in use. Additionally, finite element method is employed to simulate the heat reaction onto the biological tissues based on Pennes' equations as well. However, the equation has some limitations due to fact that blood flow direction effect is excluded. Therefore, any convective heat transfer mechanism cannot be defined. [25].

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2.2 Model Based Studies

In this study, COMSOL Multiphysics simulation software package, which solves a partial differential equation by using finite element method, was used. Firstly, the breast tissue and tumor structure were modelled. Then, thermal difference between the normal and tumor tissue was calculated with bio-heat transfer module of the software. The temperature profile of the breast tissue with tumor model flowchart is given in Fig. 1. In the first step, what kind of physical problem is handling is defined. In our case, bio-heat transfer solving method is used. The second step is the geometry of the simulated structures is created. The breast model was designed as a hemispherical form with a 12 cm diameter and a tumor-like structure was placed in the hemispherical model. In the third step, physical and thermal parameters for both breast tissue and tumor structure are entered for modeling. Additionally, the features of necessary components such as fat, muscle, bone, etc. are selected and added into the model and they are defined as a function of heat source as well. The parameter selections were done according to Ref. [26]. In the final step, to solve the model, limit conditions, thermal insulation, outer borders of the breast structure, need to be declared. Then, the simulation is numerically solved the problem based on finite element methods.

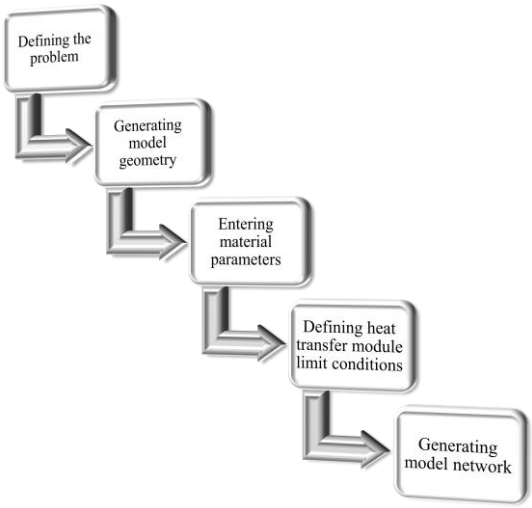

Figure 1. The flow chart of the simulation

To simulate the real cases scenarios, multi-physiology is needed. Therefore, heat transfer model was employed. Bio-heat transfer module is used to model heat transfer via transfer, convection, and radiation. The heat transfer was active in all the fields during biological tissue model. Semi-sphere geometry was designed to model the breast tissue on the simulation software. A semi-sphere geometry whose diameter was set 12 cm is shown in Fig. 2. The initial temperature value was set 36.35 °C after the beast and tumor tissue parameters entered the simulation software.

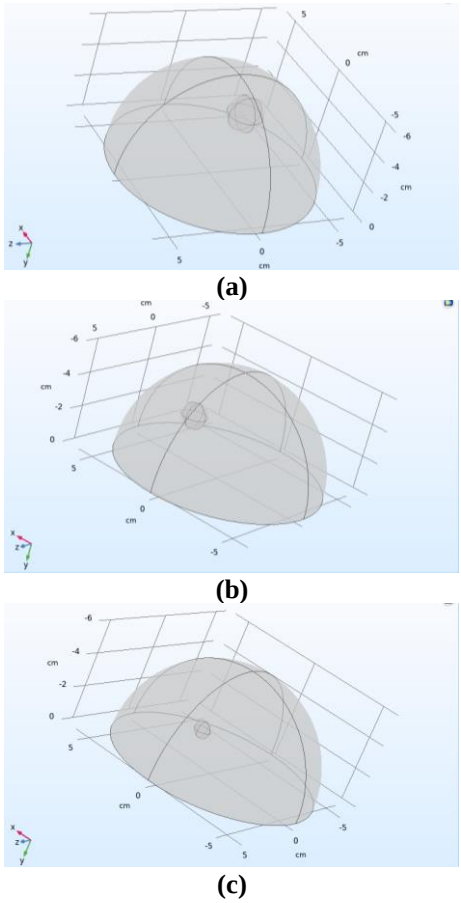

Figure 2. Simulated breast geometries with tumor for different sizes and locations. a) 1.0 cm diameter and 1.5 cm depth; b) 0.75 cm diameter and 3.0 cm depth, and; c) 0.5 cm diameter and 4.5 cm depth.

3. Phantom Design

The phantom manufacturing process is given in two parts. First part is the preparation of the medium. Dragon Skin 10 which is a high performance platinum cure silicone compounds and also are widely used prosthetics in medical fields, was used to mimic the breast tissue. The second part is placing the tumor effect into the medium. A tumor in the tissue causes high metabolic activity and higher blood flow, therefore heat increments are observed. To mimic the tumor effect, different carbon resistances were buried into the medium before pouring the Dragon Skin compounds. To simulate three different tumors, three different resistors whose resistances were 0.47, 1.00, and 1.50 kΩ respectively, were planted at different positions on the frame. The framework and resistor placement are shown in Fig. 3. A DC power supply was used to drive the resistors. The voltages were set to provide the same power to all of the resistors. The framework was fixed into the breast mold and the silicone compounds were poured.

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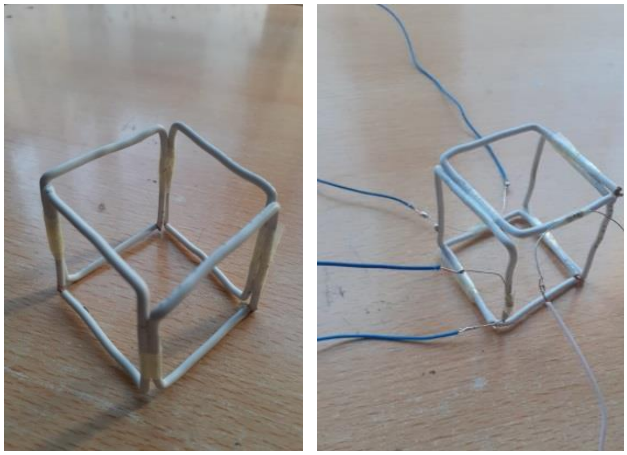

(a) **(b)**

Figure 3. The frameworks for the breast phantoms. a) the framework itself; b) after the resistors planted and wires connected.

The silicone based Dragon Skin 10 poured into semi-hemisphere mold and when it was cured, taken out carefully. An actual view of a final product solid phantom pair is shown in Fig. 4. The electrical wires are for the connection to drive the resistors.

Figure 4. The prepared breast phantoms with buried different resistors as a tumor structure.

4. Results

4.1 Simulation Results

The simulations were modelled based on three different sizes and depths of the tumor. The depth, metabolic speed, and diameter of the simulated tumors were 1.50, 3.00, 4.50 cm, 29,000, 45,000, 80,000 W/m^3, and 2.00, 1.50, 1.00 cm respectively. Breast models were created to search the relation between the tumor structure and surface temperature distribution.

The comparison of different metabolic speeds for the tumor had 1.50 cm depth and 2.00 cm diameter is given is Fig. 5. Approximately, 1.0 °C temperature difference from 36.8 to 37.8 °C observed at 29,000 W/m^3 metabolic speed (Fig 5(a)). Similarly, 1.40 °C temperature difference from 36.8 to 38.2 °C occurred while the metabolic speed was 45,000 W/m^3 and shown in Fig 5(b). Then, 2.4 °C difference from 36.8 to 39.2 °C measured at 80,000 W/m^3 given in Fig. 5(c). The results showed that the surface temperature profile linearly correlated with the metabolic speed of the tumor.

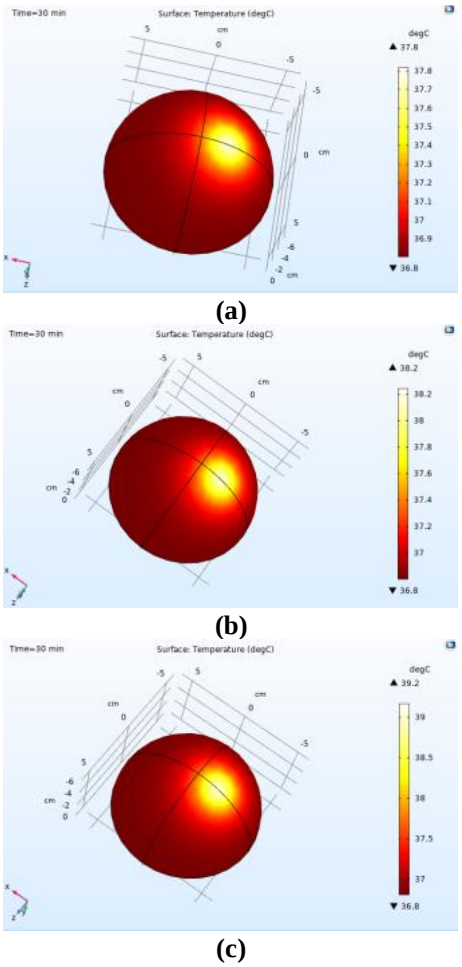

Figure 5. Thermal distribution of 1.5 cm depth and 2.0 cm diameter tumor for (a) 29,000 W/m^3; (b) 45,000 W/m^3 and; (c) 80,000 W/m^3 metabolic speeds.

Moreover, the simulations were conducted while the metabolic speed (80,000 W/m^3) and tumor diameter (1.50 cm) kept constant and the depth was variable.

It was reported that the metabolic speeds of a tumor were faster than healthy tissues between the ranges 20 to 200 times [14]. In this study, simulation results showed that 29,000, 45,000, and 80,000 W/m3 metabolic speeds were faster than healthy tissues about 65, 100, and 178 times respectively. In addition, when the ratio of tumor tissue metabolic speeds changes, the temperature gradient between tumor and neighborhood tissue varies as well.

Fig. 6 shows thermal distributions for different positioned tumors with the constant metabolic speed

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(80,000 W/m^3) and tumor diameter (1.0 cm). When the tumor depth was 4.5 cm, the temperature difference 0.9 °C and the tumor depth was 1.5 cm (Fig. 6(a)), temperature difference increased to 1.1 °C shown in Fig.6(b). Therefore, if tumor is located closer to the breast surface, the temperature difference goes up.

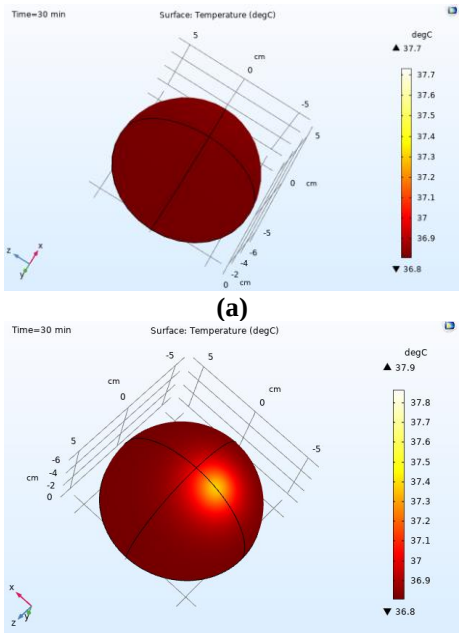

Figure 6. Thermal distribution for 80,000 W/m^3 metabolic speed and 1.0 cm diameter tumor placed in (a) 4.5 cm and; (b) 1.5 cm depth.

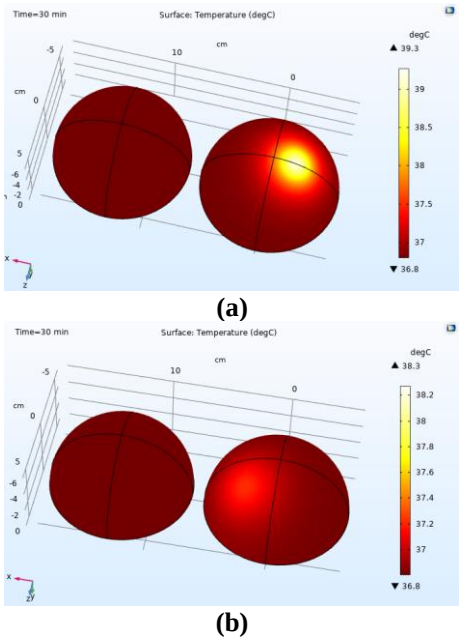

Figure 7. Asymmetry analysis simulation results for thermal distributions of healthy and a) 2.0 cm; b) 1.5 cm diameter tumor.

Moreover, asymmetry is another useful parameter to detect any differences into the breast. To analyze the asymmetry, another breast with the same features was added and is shown in Fig 7. The left hand side breast was healthy and the right one had a tumor. It has been observed that when the temperature difference ≥0.5 °C between the breasts, this difference can be used as an indicator parameter for an existence a tumor. In Fig. 7(a) includes a 2.0 cm diameter tumor and the temperature difference with the health one is 2.5 °C. Similarly, 1.5 cm diameter tumor and the temperature difference measured 1.5 °C in Fig. 7(b). Therefore, this is an indicator for thermal features through asymmetric studies can be used to detect tumor existence.

4.2 Experimental Study Results

Breast tumor is related with the temperature difference or deviation of the surrounding tissue. Therefore, by applying an electrical current to the resistors buried into the phantoms, a heat is generated according to the physical size of the resistors. Thermographic images were captured by a thermal camera (Med200 Iris, Meditherm, USA) whose resolution and spectral range was 320 x 240 and 7 – 14 µm respectively.

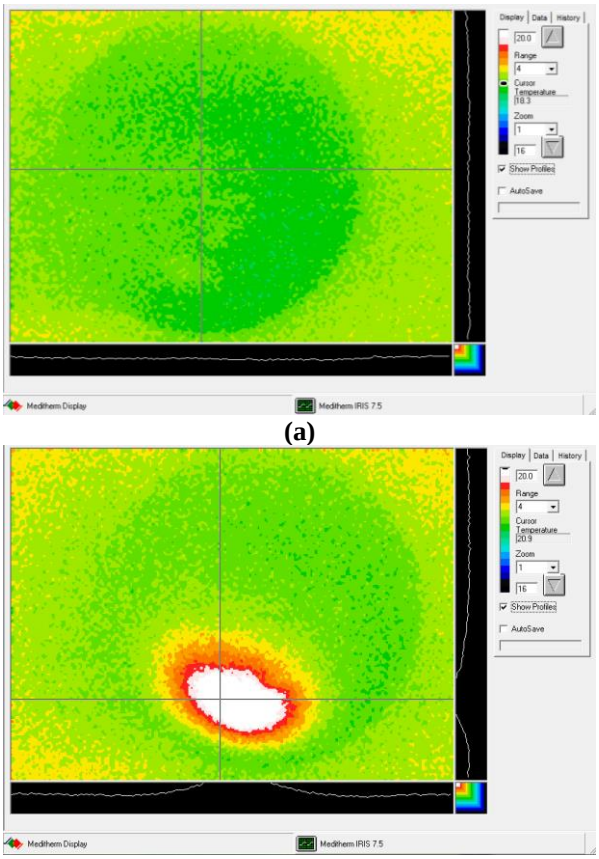

Figure 8. Thermographic image for the tumor structure (a) without tumor; (b) with the tumor in 1.5 cm depth.

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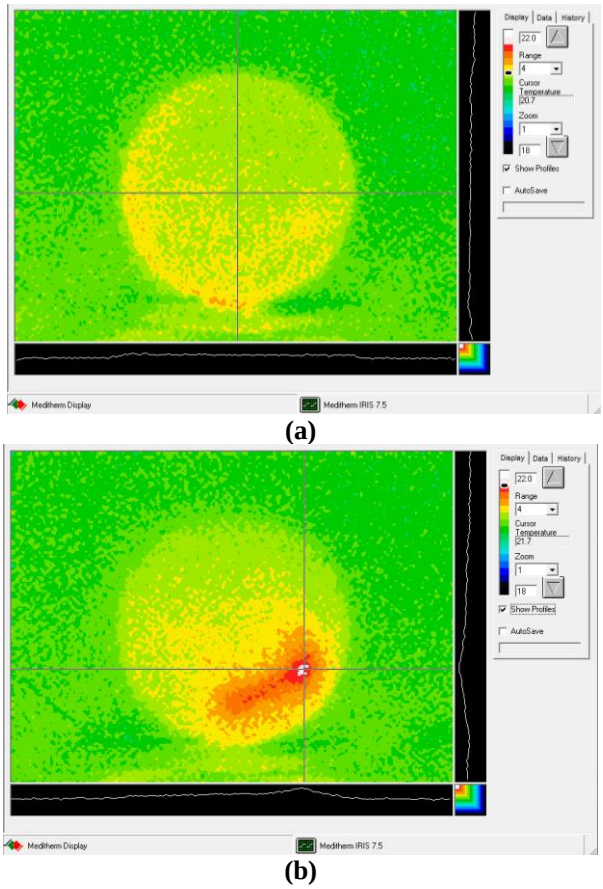
The largest size and closest to the surface tumor in the breast phantom where is in 1.5 cm depth was imaged in Fig. 8. The initial condition thermographic image is in Fig 8(a) and the temperature was ~18.3 °C. After the resistor was driven, the temperature difference between the tumor region and surrounding tissue reached 20.9 °C and the difference was ~2.6 °C which is shown in Fig. 8(b).

The resistor placed in 4.5 cm depth and is given in Fig. 9. While Fig 9(a) shows the initial condition with 20.7 °C initial temperature, Fig. 9(b) shows 1.0 °C difference between the tumor and breast tissue region.



(a)

(b)

Figure 9. Thermographic images for the tumor structure (a) without tumor; (b) with the tumor in 4.5 cm depth.

As it is known that a healthy body temperature distribution is symmetrical. Thermal asymmetry is a distinctive feature abnormality in the thermography. Therefore, infrared thermography has a potential to detect breast cancers by using asymmetrical temperature distribution regions. A pair of breast is given in Fig. 10. While the left hand side one simulates the healthy breast, the right one stands for tumor mimicking. The temperature difference between the breasts was 2.3 °C. When the tumor size bigger or the location is closer to surface, the temperature difference is higher.

5. Conclusions

In this study, breast tumor detection by thermal heat distribution was demonstrated both model based simulation and also experimental in in-vitro. Tumors placed in with different sizes and depths. While the tumor metabolic speed was faster, the temperature difference was higher. In addition, when the tumor location was closer to the surface, the temperature difference was higher as well. For instance, when the tumor was of a depth ~1.5 cm, the temperature difference found 2.6 °C experimentally and 2.4 °C in modeled study. Similarly, when the tumor depth was placed at a 4.5 cm depth, it was observed 1.0 °C and 0.9 °C temperature difference experimentally and modeled, respectively. As can be seen, the results are highly correlated with both the simulation and experimental results. Another finding was if the tumor size was bigger, temperature difference can be distinguished better. Furthermore, it is proved that the asymmetry parameter is another promising indicator for anomalies during breast cancer. The asymmetry parameter makes the comparison easier and thermal detection reveals the anomaly detection and makes it more obvious. Therefore, it can be said that thermographic imaging is an encouraging noninvasive breast cancer imaging candidate and a useful tool for screening.

In this study, tumor detection depth was extended to 45 mm with different tumor sizes. Also, the asymmetry factor performance was shown to reveal the tumor structure with ease. In addition for the further studies, in-vitro conditions may extend to mimic more complex breast structure such as vein and capillary networks and fat, muscle, ducts, and lymph nodes, etc. Moreover, it needs to be done to measure sensitivity, specificity, and selectivity performances. Therefore, it can help to differentiate normal, benign, and malignant cases in breast cancer.

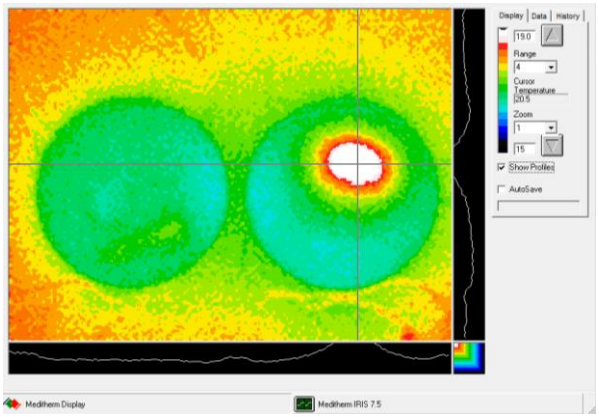


Figure 10. Asymmetric case demonstration for the healthy and tumor breasts. Left had side is healthy, right hand side is cancer case.

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Authors' contributions

Zeynep Ayyildiz: planned, and conducted all the experiments,
Ibrahim Akkaya: involved in writing original draft, creating, and editing some figures and manuscript,
Mehmet Engin: Obtained support, had conceptualization, and investigation.
All authors read and approved the final manuscript.

Competing interests

The authors declare that they have no competing interests.

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