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COB-2023-2237 NUMERICAL ANALYSIS OF INFRARED THERMOGRAPHY USING HYPOTHERMIA TREATMENT FOR EARLY SCREENING OF DEEP AND SUPERFICIAL BREAST CANCER

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Abstract. *The aim of this work is to numerically analyze the thermal contrast during hypothermia treatments using the infrared thermography technique in cases of breast cancer using the commercial software COMSOL Multiphysics. The methodology of the work consists of the solution of the Pennes equation for a three-dimensional model of the breast. Then, the 3D numerical breast was submitted during three well-defined steps: Stationary, Hypothermia and Thermal recovery. The 3D breast modeling was composed of healthy and unhealthy regions presenting similar boundary conditions to the real breast model, considering the external surface exposed to natural convection, and the internal region subjected to a constant temperature of 37 °C. During the hypothermia treatment, the external surface of the breast was exposed to constant temperatures of 5, 10 and 15 °C, simulating a gel compress for 30 minutes. In thermal recovery, after removal of cooling, the breast was subjected to natural convection on the external surface again. The thermal contrasts obtained during the analysis of superficial tumors proved to be adequate for the screening of early tumors. However, for deep tumors the results required long cooling times to reveal insufficient thermal contrasts for tracking.*

Keywords: *Breast cancer, Hypothermia, Thermal contrast, numerical simulation*

1. INTRODUCTION

The main causes of death in the world are related to cancer. The newdiagnosed cases are approximately 1,918,030, equivalent to 5,250 cases per day.Approximately 51400 new cases of ductal carcinoma in situ in women and 97920 cases of melanoma in situ diagnosed in 2022 (Siegel *et al.*, 2021).

There are several techniques available for breast cancer screening, highlighting self-examination, mammography, magnetic resonance imaging, ultrasound, among others. All the techniques used by medicine show percentages of false positives in diagnoses (Dixon and Leonard, 2012). The easiest and most available technique is manual self-examination, but with a high rate of false positives (Gonzalez-Hernandez *et al.*, 2019). Currently, mammography is generally indicated for screening breast abnormalities mainly in the age group, including older women due to lower breast density (Løberg *et al.*, 2015),(Owens *et al.*, 2019).

Cancer screening techniques have several limitations, so infrared thermography emerges as a promising technique that can use heat transfer mechanisms to detect biological changes (Lawson, 1956). Studies have revealed that high heat exchanges occur in tumor cells similar to an inflammatory process. Ng (2009) Breast thermography can be particularly useful in early stages of the tumor, which is not yet recognized by mammography, because thermography is a physiological examination, while mammography is anatomical. Physiological changes often precede anatomical changes (Etehadtavakol and Ng, 2013).

Infrared thermography is a non-invasive procedure that uses a thermographiccamera to detect patterns of heat emitted from the surface of the breast, without the need to use forms of tissue compression and radiation exposure (Abas *et al.*, 2020). Several studies have evaluated the efficiency of infrared thermography for clinical applicability by establishing a comparison with mammography technique (Gogoi *et al.*, 2019), (Khan and Arora, 2021).

The analysis of the influence of tumor size on the calculated surface temperature profile of a breast surrogate geometry has been performed in studies involving experimental infrared imaging and 3D numerical simulations. Thus, one can better understand breast abnormalities and learn more about how the use of infrared imaging can validate such calculations (Sudharsan and Ng, 2000), (Ng and Sudharsan, 2001), (Bezerra *et al.*, 2013), (Queiroz *et al.*, 2021).

The development of technology allowed new applications in engineering and medicine. In this context, concepts of passive and active thermography emerged. Passive thermography refers to when skin temperatures are analyzed under steady-state conditions. In active thermography, external thermal stimulation is introduced, such as heating or cooling, and temperatures are analyzed over time (Iljaž *et al.*, 2019), (Zeng *et al.*, 2020), (Gomboc *et al.*, 2021). Combined analyzes using the two thermographic techniques to improve breast cancer screening can also be found in the literature (Vickers, 2017).

Several methodologies to perform the reconstruction of thermal images from active thermography can be used to evaluate and detect parameters of blood vessels and tumors. Diameter and velocity of blood vessels were estimated from reconstructed thermal images during cooling and thermal recovery of human skin surface, showing that active thermography based on external cooling can be used to develop a diagnostic tool for vessel diseases (Saxena *et al.*, 2018b), (Saxena *et al.*, 2018a).

The application of hypothermia coupled with transient numerical simulation of surface temperatures is investigated in this work. Different hypothermia conditions were analyzed, simulating different intensities of cooling on the breast surface, with the aim of evaluating changes in thermal patterns in different cases of breast tumors. The main contribution of this study was to presentthe possibilities of thermal contrast gain in the most frequent cases of breast cancer in women worldwide, evaluating from earliest stages of the disease tolarger tumors, where the diagnosis is limited by the main existing techniques in medicine.

In this work, a three-dimensional breast model was numerically simulated in the commercial software COMSOL to analyze the thermal contrast on the skin surface at different depths and stages of cancer. The applied thermal therapy involved the steps of acclimatization, hypothermia and thermal recovery. The acclimatization step considered the body in thermal equilibrium with the external environment before the application of hypothermia. During cooling, constant temperatures of 5, 10 and 15 °C were considered on the breast skin surface. Thermal recovery was analyzed in order to find the time for maximum thermal contrast, depending on the tumor type considered. The results obtained aim to improve the detection of early stages of breast tumors using active thermography.

2. MATERIALS AND METHODS

2.1 Mathematical and physical model

The model was considered a three-dimensional structure of the breast composed of healthy and tumor tissue. The 3D model contains different tissue and thermal properties showing two types of tumors classified as Invasive Lobular Carcinoma (ILC). Figure 1 presents the three-dimensional numerical model of the breast and the boundary conditions shown in Fig. (1a) and Fig. (1b), respectively.

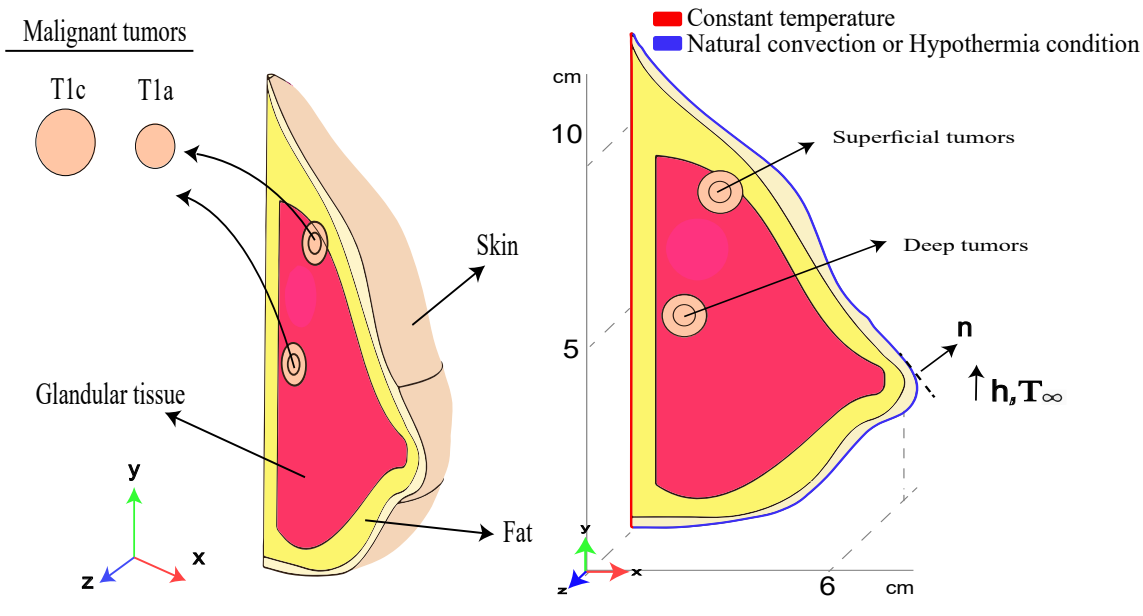


Figure 1: Numerical breast model (a) 3D breast and (b) Boundary condition (adapted from O'Regan and Society (2013))

The Pennes equation (1948) was used to model heat biotransfer, as described in Eq. (1)

$$k\nabla^2 T + \omega_b \rho_b c_b (T_b - T) + Q = \rho c \frac{\partial T}{\partial t} \tag{1}$$

where the properties k, c, ω e ρ are thermal conductivity, specific heat, blood perfusion, and tissue density, respectively. The subscript b represents the properties of blood. Metabolic heat generation and tissue temperature are Q and T, respectively. Internal and blood temperature were considered equal to T_{blood}, T_{body} = 37 °C. The external condition of the breast was characterized as natural convection, with a thermal convection coefficient of 5 W/(m² K) and an ambient temperature of T_∞ = 22 °C. Furthermore, the condition of hypothermia was defined as a constant temperature applied across the outer surface of the breast. Table 1 presents the thermal properties of the tissues considered in the breast.

Table 1: Properties of biological tissues (Hossain and Mohammadi, 2016).

Properties	Tissue		
	Skin, Fat	Lymphatic Nodes, Duct and Lobule	Tumor
Thermal conductivity, k [W/m K]	0,21	0,52	0,62
Blood perfusion, ω [1/s]	0,00022	0,00052	0,01600
Specific mass, ρ [kg/m³]	1000	1000	1000
Specific heat, c [J/kg K]	4186	4186	4186
Heat source, Qm [W/m³]	420	420	70000

Amin *et al.* (2017) presents the TNM system as a tool for classifying tumors, where T represents the size of the tumor, N the occurrence of infected lymph nodes, and M the evidence of metastasis. Tumors present stages of development in the breast, with stage 0 characterized as non-invasive tumors known as Carcinoma in situ (DCIS); and stages 1 to 4 for invasive tumors. According to Brierley *et al.* (2017), Tis tumors are Carcinomas in situ, located within the ducts or lobules of the breast tissue and do not spread to the surrounding tissues. the T1 classification refers to tumors up to 2.0 cm in size, which can be subdivided into the other cases T1mi, T1a, T1b and T1c. Thus, the results are combined to determine the cancer stage for each individual. In this simulation, breast tumors were classified as (T1,N0,M0), representing diameters of up to 2 cm, with no occurrence of cancer in the lymph nodes and no evidence of metastasis, respectively. The classification of tumors used during the simulations were T1a and T1c with diameters equal to 0.5 and 1.0 cm, respectively.

2.2 Numerical Simulation

The heat transfer model and boundary conditions in breast tissue were solved using commercial software COMSOL multiphysics by finite element method. Figure 2 shows the mesh used in the simulation composed of 67,415 tetrahedral elements.

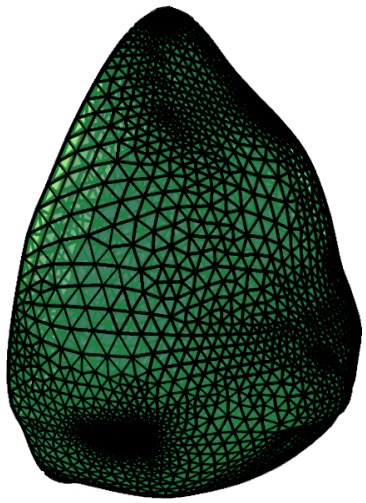


Figure 2: COMSOL 3D Numeric Mesh

Figure 3 shows the steps performed during the application of the thermal procedure and analysis of the results in the steps: stationary, hypothermia and thermal recovery. Initially, the passive thermography technique was simulated to obtain the temperature distribution, where the breast was subjected to the acclimatization period, in a steady state, where the thermal balance of the body and the external environment was established, that is, the external surface of the breast

was exposed to natural convection of the external environment equal to 5 W/(m² K) and external temperature of the room equal to T_∞ = 22 °C. Then, the hypothermia procedure step was applied, in which the external surface of the breast was conditioned to three constant cooling temperatures equal to 5, 10 and 15 °C, simulating a gel compress at exposure times equal to 60, 300, 600 and 1200 s using the active thermography technique. The last step consists of the thermal recovery stage, in a transient regime, where the hypothermia condition of the external surface was removed and again conditioning the breast to the natural convection of the environment for 60 min. Thermal contrast was obtained by subtracting the temperatures of the breast with and without tumor at the end of the thermal procedure. During the simulations, the thermal therapy steps were applied to each tumor stage separately.

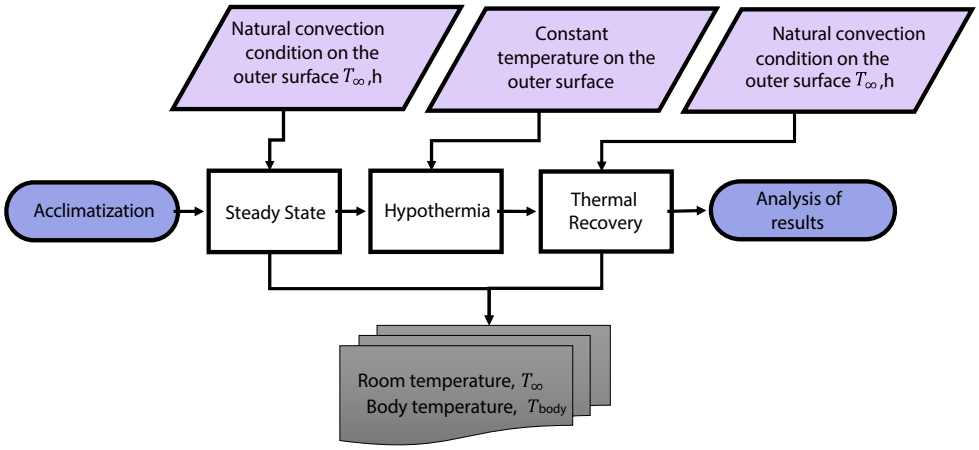
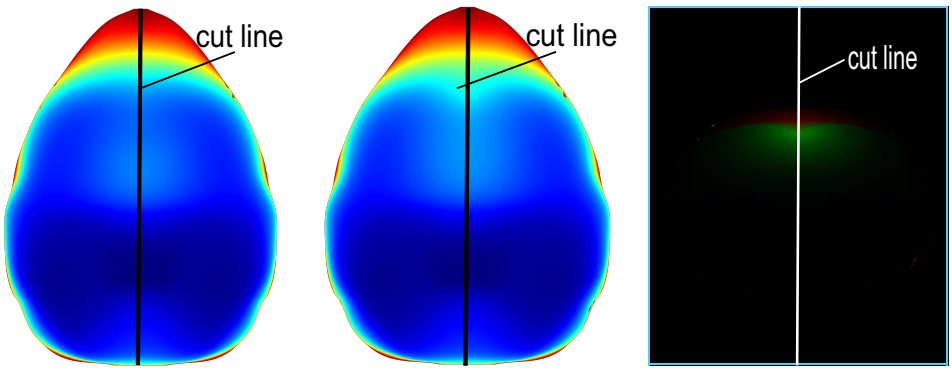


Figure 3: Thermal procedure steps

3. RESULTS AND DISCUSSION

The tumors were positioned in the upper quadrant of the breast, located on the cut line of the model. Depths were defined as superficial and deep from the breast surface for each tumor classification, T1a and T1c. Figure 4 shows the temperature distribution in thermography of breasts with and without tumor.The cut line intercepts the maximum temperature values. The temperature values were taken from a point of highest temperature on the cut line of the breast and subtracted to obtain the thermal contrast.

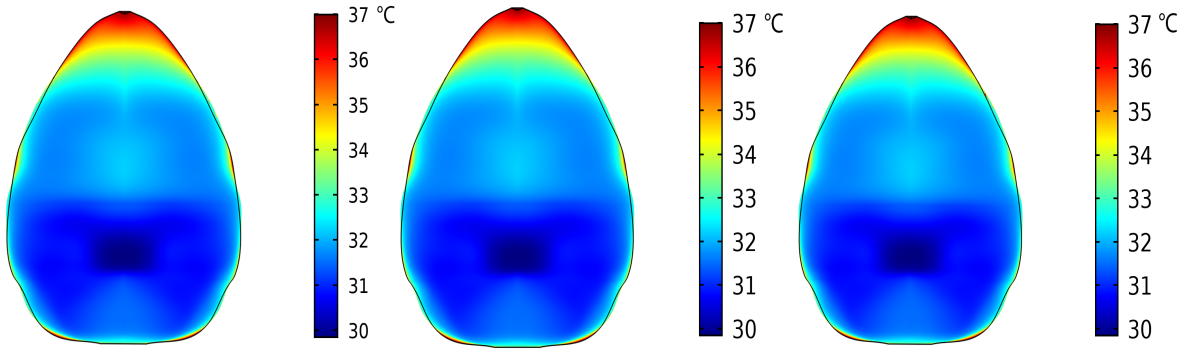


(a) (b) (c)

Figure 4: Breast thermography (a) Without tumor, (b) With tumor and (c) Thermal contrast

3.1 Superficial tumors

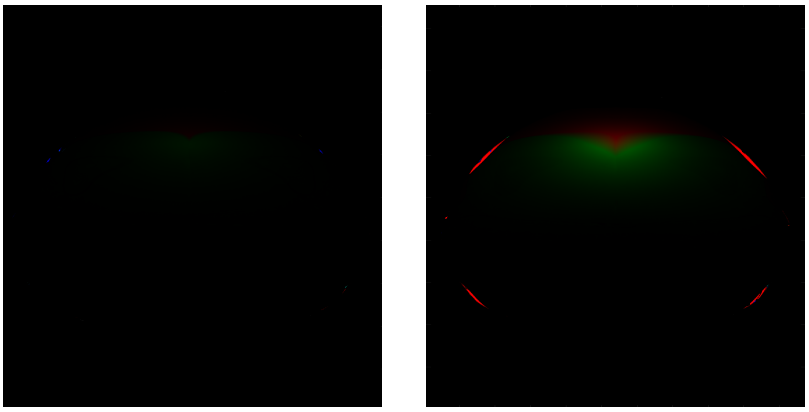
The breast was analyzed during steady state by thermography of the outer surface of the breast, as shown in Fig. 5. The temperature distributions were very similar for healthy tissue, Tumor T1a and Tumor T1c for a sensitive analysis of the thermal images, as shown in Fig (5a), Fig. (5b) and Fig. (5c), respectively. Thus, it was necessary to use the subtraction of stationary images of breasts with and without tumor to obtain thermal contrast.



(a) (b) (c)

Figure 5: Breast Temperature Distribution (a) Healthy, (b) T1a and (c) T1c

Figure 6 shows the thermal contrasts of thermal images of breast tumors T1a and T1c, as shown in Fig. (6b) and Fig. (6b), respectively. The analysis of the thermal contrasts allowed us to verify that there are significant differences in the thermal images of the breast that previously went unnoticed in the static thermograms.



(a) (b)

Figure 6: Thermal contrast of tumors (a) T1a and (b) T1c

After the acclimatization period, the breast with and without tumor was submitted to hypothermia conditions with times of 60, 300, 600 and 1200 s and temperatures equal to 5, 10 and 15 °C. Tumors were analyzed in superficial and deep regions of the breast tissue, offering different answers to the scientific community. Figure 7 shows the thermal contrast during thermal recovery for the 15 °C temperature of the superficial tumors T1a and T1c. During exposure times to cooling equal to 1200 s, it was possible to obtain the highest values of thermal contrast for all tumor cases. In stationary analyses, the T1a tumor presented thermal contrast equal to 0.12 °C, that is, hypothermia applications were necessary to improve thermal contrast. Thus, performing the hypothermia procedure with exposure times of 1200 s, a maximum thermal contrast of 0.2 °C was achieved. For the T1c tumor, during the acclimatization period, it was possible to obtain a value equal to 0.82 °C, representing a significant increase in relation to the T1a tumor. Applying the thermal cooling procedure, the maximum thermal contrast achieved was equal to 1.39 °C. Thus, the T1a tumor obtained lower temperature values, requiring cameras with high thermal sensitivity and resolution to capture small temperature variations.

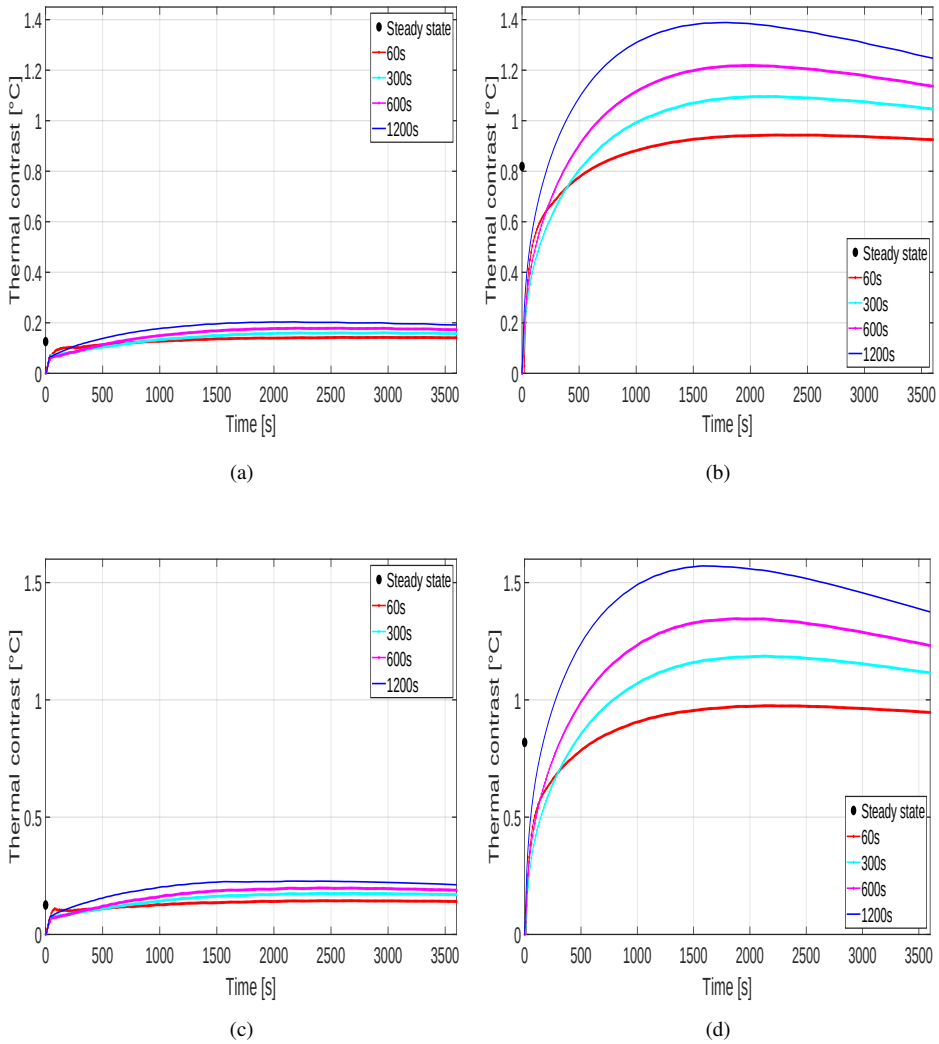


Figure 7: Superficial thermal contrast at 15 °C, (a) T1a, (b) T1c and 10 °C, (c) T1a and (d)T1c

During the applications of the thermal procedure at a temperature of 15 °C, it was possible to perform analyzes similar to cooling at 10 and 5 °C. However, the difference is in the values of thermal contrasts obtained that were higher for the temperature of 10 °C. This phenomenon occurs because the healthy breast has a slower thermal recovery than the tumor breast, and therefore, a greater thermal contrast occurs when lower temperatures are applied.

3.2 Deep tumors

Deep tumors were positioned in regions greater than 3 cm from the skin surface, to analyze the behavior of thermal contrast in complex regions for cases of T1a and T1c tumors. Temperatures of 10 and 15 °C were not shown in this work, as a more aggressive temperature of 5 °C was used. Figure 8 shows the thermal contrast of T1a and T1c tumors in deep regions at a temperature of 5 °C. Stationary analyzes showed non-significant values for tracking anomalies for both T1a and T1c cases, therefore, tumors should be subjected to hypothermic conditions to improve thermal contrast. During the cooling applications, the maximum thermal contrasts of the T1a and T1c tumors obtained for the application of hypothermia equal to 1200 s of exposure were equal to 0 and 0.12 °C, respectively. Thus, for tumors located in deep regions of the breast, it was not possible to obtain significant thermal contrast values.

Table 2 shows the thermal contrasts obtained in numerical simulations of T1a and T1c tumors, for three cooling temperatures and two depths during stationary analysis and thermal recovery. The highest thermal contrasts were obtained at an application temperature of 5 °C during 1200 s of exposure to cooling in superficial cases. For deep tumors, thermal contrasts did not show significant values.

Cheng and Herman (2014) evaluated the thermal contrast of the tumor in human tissue using a two-dimensional geometry applying the active thermography technique. After short cooling applications of 5 and 10 s, the maximum thermal contrasts obtained were close to 0.4 °C. During longer cooling, the maximum thermal contrasts achieved were close to 0.3 °C for the tumor close to the skin surface with a diameter equal to 0.1 cm. Subsequently, Zhou and Herman

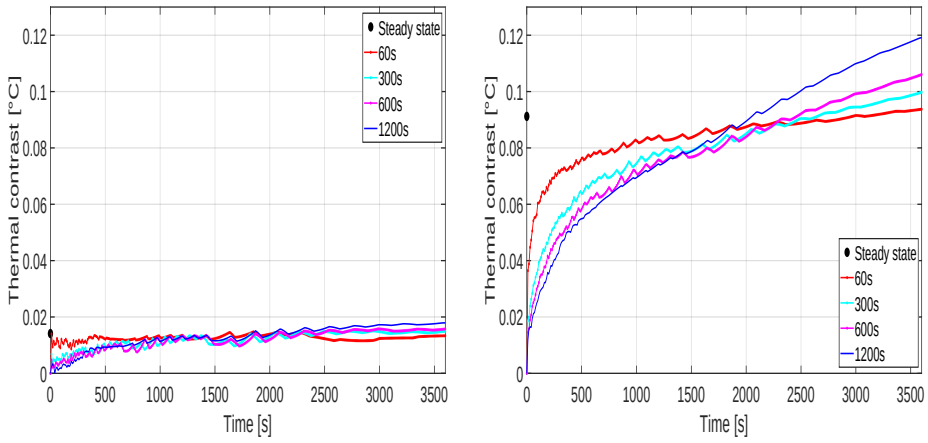


Figure 8: Deep thermal contrast at 5 °C, (a) T1a and (b) T1c

Table 2: Maximum thermal contrasts for case T1a and T1c

Depths	Steady state	Hypothermia (15 °C)	Hypothermia (10 °C)	Hypothermia (5 °C)
Superficial tumors				
T1a	0.12	0.2	0.23	0.26
T1c	0.82	1.39	1.57	1.76
Deep Tumors				
T1a	0.01	0.02	0.02	0.02
T1c	0.09	0.10	0.11	0.12

(2018) optimized the detection of breast cancer using the infrared thermography technique for cooling applications on the external surface of the breast. For large and superficial tumors, the passive infrared thermography technique was capable of detection, revealing values close to 0.6 °C. For small tumors located in intermediate and deep regions, it was necessary to use active thermography. The thermal contrast values obtained for these tumors were close to 0.1 °C.

Furthermore, some studies used experimental approaches to validate numerical models of the breast using temperature profiles obtained from the passive thermography technique. Tumors were simulated at different depths ranging from 5 to 25 mm from the breast surface, revealing maximum differences in thermal contrasts equal to 0.34 and 1.37 °C (Igali *et al.*, 2018), (Mukhmetov *et al.*, 2021).

Our work, unlike others, presents more aggressive applications of hypothermia, considering 20 min of exposure in order to analyze thermal responses for superficial and deep tumors. During thermal therapy applications, thermal contrast was more evident for the large tumor located close to the breast surface, reaching thermal contrast equal to 0.82 °C for stage T1c in the steady state. Applying cooling to stage T1a it was possible to observe a gain of 0.14 °C in relation to passive thermography. For tumors located in deep regions, thermal contrast values were not significant for the passive and active technique, due to the distance from the external surface, reaching maximum thermal contrasts equal to 0.02 and 0.12 °C for stages T1a and T1c in active therapy, respectively. Thus, assuming more severe cooling conditions in thermal therapy, it was possible to obtain gains in thermal contrast, although small in deep cases, but it is valid as an adjuvant technique to improve thermal contrast and the traceability of breast tumors.

4. CONCLUSION

In this work, three-dimensional models of the breast composed of healthy and tumor tissue were simulated in the commercial software COMSOL multiphysics for different cooling temperatures and depths. The thermal procedure consisted of three stages: acclimatization, hypothermia and thermal recovery. During cooling applications, three temperatures of 5, 10 and 15 °C were considered in times of 60, 300, 600 and 1200 s of exposure. In thermal recovery, the breast was exposed to the external environment for 60 min. Thermal contrast was obtained by subtracting the temperatures obtained from the cut line of the breast with and without tumor.

Thermal contrasts for superficial tumors during stationary analyzes were equal to 0.12 and 0.82 °C, respectively. The T1a tumor showed a contrast increase equal to 0.14 °C for aggressive temperatures. Case T1c showed a significant

result for tracking using passive thermography, and reached 1.76 °C during cooling applications to a temperature of 5 °C. Therefore, for superficial tumors with small diameters, thermographic cameras with high sensitivity are needed to capture small temperature differences. For tumors located in deep regions of the breast, it was not possible to obtain significant values for cancer traceability.

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