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NUMERICAL ANALYSIS OF THERMAL CONTRAST AND THERMAL DAMAGE DURING HYPERTHERMIA IN BREAST CANCER CASES.

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Abstract. *Breast cancer is the most common type of malignant tumor among women, excluding non-melanoma skin cancers. Mammography is the main test for diagnosing the disease. However, there are still several limitations for mammographic exam, marking it unable to diagnose tumors for a large part of the population. Infrared thermography has been studied as an auxiliary technique for the early detection of diseases. The purpose of this work is to present thermal contrasts on the breast surface from numerical simulations of several cases of breast tumors during hyperthermia treatment using dynamic thermographic images by commercial software COMSOL. The proposed methodology is based on the solution of the bioheat equation for geometric models similar to the breast anatomy. The problem is analogous to the actual performance of dynamic thermography for early detection of breast cancer. This study consists of three stages: stationary, hyperthermia, and thermal recovery, developed according to steady-state and transient bioheat modules. The models will consist of regions of healthy tissue and tumors. The boundary conditions will be preserved from the real breast model, where the skin external surface was exposed to thermal convection, and internal surface was subjected to a constant temperature equal to the body temperature. During hyperthermia treatment, external surface boundary condition had the partial addition of constant heat flux for different times according to the analyzed tumor case. The control of heat input from the use of thermal laser in hyperthermia was determined by thermal damage degree to ensure tissue integrity. Considering that the applied heat flux was constant, the maximum thermal contrast occurs after the end of the hyperthermia. During thermal recovery, no greater thermal contrasts were obtained due to the thermal laser application method. However, it is observed that the analysis of thermal damage during hyperthermia is essential for optimizing the heat flux application and maintaining the integrity of living tissue.*

Keywords: *breast cancer, hyperthermia, thermal damage, thermal contrast, numerical simulation.*

1. INTRODUCTION

Cancer is a major public health problem and one of the leading causes of death worldwide. In total, there will be about 1,898,160 cancer cases diagnosed and 608,570 deaths in 2021. The most common cancers diagnosed in women are breast, lung and colorectal cancers, accounting for 50% of all new diagnoses. Breast cancer accounts for 30% of these new cases and 22% of deaths among women in the United States (Siegel *et al*., 2021).

Hyperthermia refers to the condition of body temperature above normal, considered approximately from 42ºC. Some illnesses such as fever or thermal shocks can present elevated body temperatures, however, the controlled use of thermal therapies on tissue can treat several diseases (Shirkavand and Nazif, 2013).

Some techniques to detect biological changes have been developed using heat transfer analysis, such as through the use of infrared thermography (Lawson, 1956). Several studies claim that high heat exchange occurs in tumor cells similar to an inflammatory process. The blood flow dissipates thermal energy from the tumor and ambient conditions accentuate temperature changes on the breast surface, which can be observed by thermographic patterns (Lawson and Chughtai, 1963).

Shivand and Nazif (2019) studied a three-dimensional model of the human forearm to obtain the temperature distribution considering the characteristics of blood perfusion and metabolic heat during hyperthermia treatment. The 3D model was solved using the Pennes's equation based on experimental works from the literature and biological tissue properties for boundary conditions and external heat sources. The results for the superficial tissue layers using a uniform external heat source showed the temperature variation directly proportional to the applied heat flux. However, there were no temperature changes in the deeper tissue layers.

Medeiros *et al.,* (2019) analyzed alternatives for increasing the effectiveness of the thermographic imaging technique for the early diagnosis of breast cancer. A two-dimensional hemispherical breast model was considered to solve the bioheat problem using COMSOL commercial software. First, the stationary temperatures on the breast skin surface were evaluated for tissue with and without tumor. Then, a square waveform heat rate was inserted over the skin. For the different tumors studied, the results obtained showed that heating the breast skin increases the thermal contrast caused by tumors when they are in deeper regions of the breast tissue.

Singh *et al*., (2021) performed a numerical analysis of the breast tissue considering variable blood perfusion to evaluating temperature distribution and thermal damage. The breast was developed using MRI images. The Pennes and Arrhenius equations were solved using COMSOL commercial software. The results show that the heat-dosage is 22% higher for highly perfused tumor compared to moderately perfused tumor with an approximately double time to ablation of the entire tumor volume.

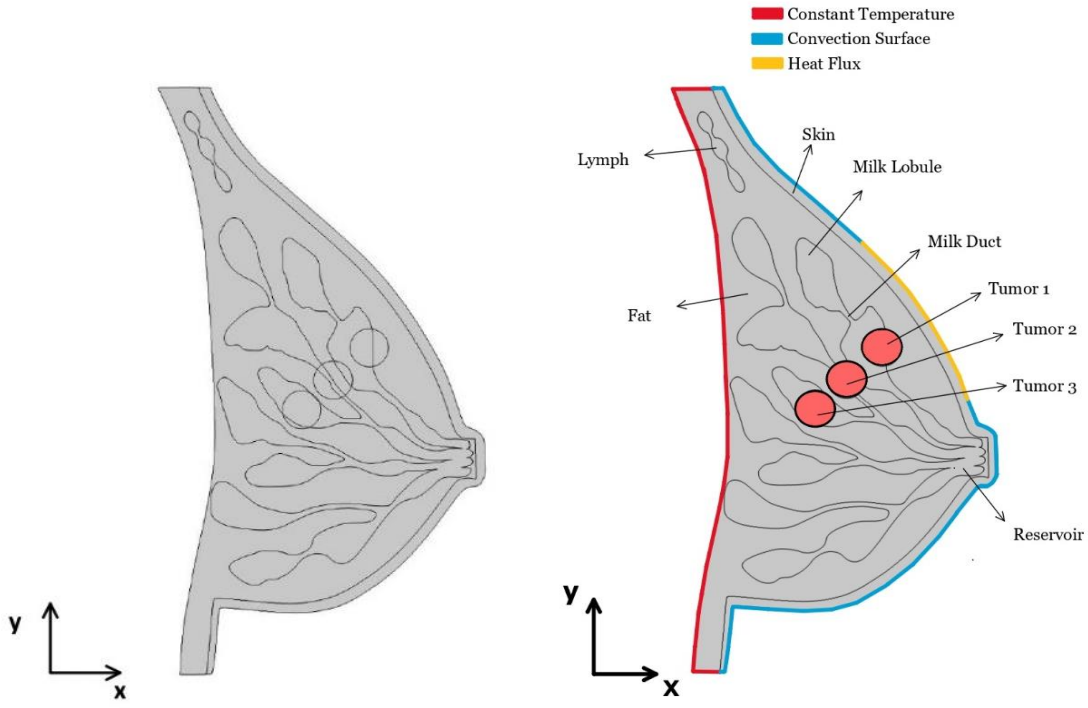
Damasceno and Figueiredo (2021) performed an analysis of the temperature distribution on the breast surface during hypothermic conditions in order to observe the stages of dynamic thermography. The numerical model was developed considering real physical conditions of the breast during cold stress. The results show that for a cold stress of 5 ºC and cooling of 60 s, the increase in the thermal contrast between the superficial temperatures of breasts with and without tumor occurs from the thermal recovery of 360 s, exhibiting thermal contrast gains up to 1440 s.

In this work, a two-dimensional numerical breast model was used to assess temperature distribution and tissue thermal damage during hyperthermia. The heating of the breast surface is performed using a heat flux with intensity and exposure time limited by thermal damage for dynamic thermography analysis. The 2D model was developed using COMSOL commercial software considering thermophysical properties. The results obtained aim to increase the efficiency of tumor estimation by infrared thermography.

2. MATERIALS AND METHODS

2.1 Mathematical and physical model

Physical geometry is a two-dimensional structure of the breast composed of healthy tissue and three common types of tumors arranged in different locations, as shown in Figure 1a. Tumors 1, 2, and 3 with a diameter of 0.8 cm are described as Invasive Lobular Carcinoma (ILC-1), Invasive Ductal Carcinoma (IDC), and Invasive Lobular Carcinoma (ILC-2), respectively. The numerical model assumes convection boundary conditions, known temperature and heat flux, highlighted by Figure 1b.



(a) (b)

Figure 1. Numerical model of breast: (a) Breast 2D, and (b) Boundary conditions.

The Pennes's equation (1948) was used to model bioheat transfer, as described in Eq. (1).

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

where the properties k, c, ω and ρ are the thermal conductivity, specific heat, blood perfusion, and density of tissue, respectively. The subscript b represents blood properties. The heat generation and tissue temperature are Q and T, respectively. The numerical simulations consider the internal and blood temperatures equal to *Tblood, Tbody* = 37 °C. The external surface is exposed to the environment, characterizing a natural convection condition, where thermal convection coefficient is equal to h = 5 W/(m²K), and the ambient temperature corresponding to $T \infty$ = 22 °C. The hyperthermia was characterized as a heat flux applied to a limited region on the breast external surface according to prior knowledge of the tumor location. Table 1 shows the thermal biological properties of the breast used in the simulations.

Table 1. Thermal properties of biological tissues.

Properties	**Skin, Fat**	**Lymph node, Duct and lobule**	**Tumor**
Thermal Conductivity, W/ m²K	0.21	0.52	0.62
Blood Perfusion, 1/s	0.00022	0.00052	0.01600
Specific Mass, kg/ m³	1000	1000	1000
Specific Heat, J/ kgK	4186	4186	4186
Heat Source, W/ m³	420	420	70000

2.2 Thermal damage

The Arrhenius model was used to evaluating the thermal damage degree to breast tissue as a function of exposure time during hyperthermia as described in Eq. (2).

$$\Theta = \frac{C_D(t)}{C_0} = 1 - exp\left\{-\int_0^{\tau} A e^{-E_a/R_g T(\tau)}\, dt\right\} \quad (2)$$

where A is frequency factor, Ea is activation energy for cell denaturation, Rg is universal gas constant, T is tissue temperature, and τ is time of hyperthermia. $CD(t)$ is concentration of damaged cells, and $C0$ is the concentration of intact cells before the application of thermal therapy, therefore, $C0$ = 1.0 or 100%. The maximum thermal damage degree is 1.0, which represents approximately 63% of the minimum damaged cells (Singh *et al*., 2016). Table 2 shows the Arrhenius parameters used in computer simulation.

Table 2. Arrhenius equation Parameters.

Properties	**Symbol**	**Breast Tissue**
Activation Energy, J/mole	E_a	$6.03\ x\ 10^5$
Frequency Factor, 1/s	A	$3.1\ x\ 10^{98}$

2.3 Numerical simulation

The heat transfer model and boundary conditions in the breast tissue were solved using the commercial software COMSOL Multiphysics by the finite element method. Figure 2 shows the mesh used in the simulation composed of 19,582 triangular elements.

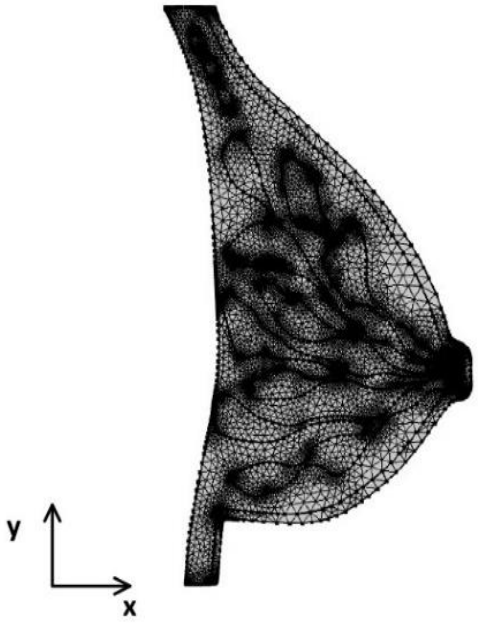


Figure 2. Numerical mesh used in COMSOL.

In this study, tumors 1, 2, and 3 were individually simulated at different depths modifying specific breast structures such as the duct and lobe, as shown in Figure 1b. A heat flux was applied, q" = 400 W/m², simulating a laser heating of the breast tissue with exposure times of 180 s, 220 s, and 230 s for the respective tumors. The heat flux exposure times were obtained based on the thermal damage degree limit of 0.7 chosen as a tissue control parameter.

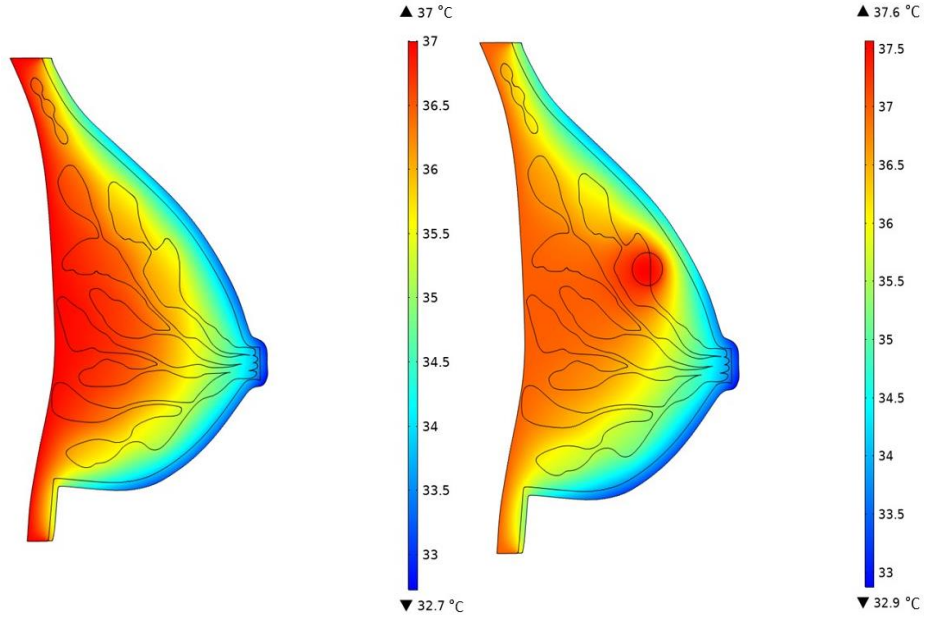
The problem modeling uses a dynamic thermography simulation to aid in the early detection of breast cancer. The analysis was performed on the breast with and without tumor and consists of three well-defined steps. The stationary stage, where the breast reaches thermal equilibrium considering the time-invariant properties, submitted only to natural convection on the external surface. The second step was the heating of a limited region on the external surface using a laser with defined intensity and exposure time. The last step was the thermal recovery, which used only natural convection as a boundary condition on the external surface for a period of 10 minutes.

3. RESULTS AND DISCUSSIONS

Temperature distribution was analyzed in the breast from three studies: stationary, hyperthermia (laser heating), and thermal recovery. Three tumor cases were analyzed, ILC-1, IDC, and ILC-2.

3.1 Tumor 1: Invasive lobular carcinoma (ILC-1)

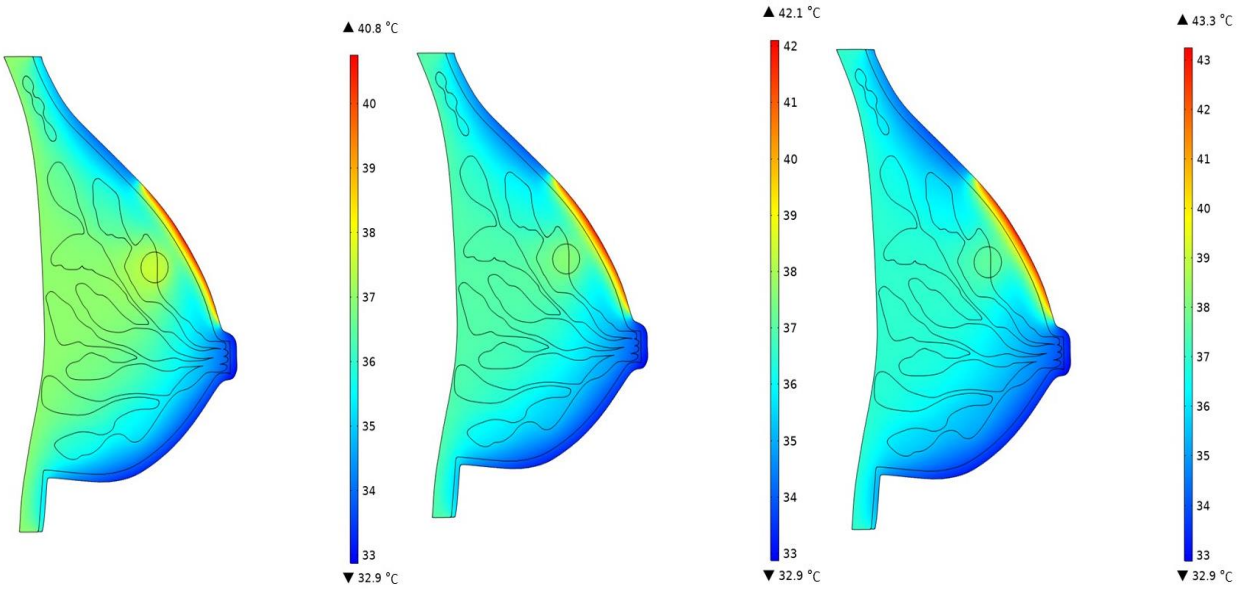
Initially, the breast case was analyzed for the healthy breast in a steady state, where the normal temperature distribution is shown in Figure 3a. The breast with invasive lobular carcinoma (ILC-1) is shown in Figure 3b, where a change in temperatures is observed, especially close to the tumor region due to greater heat generation at the site.



(a) (b)

Figure 3. Temperature distribution in steady state: (a) healthy breast, and (b) with tumor (ILC-1).

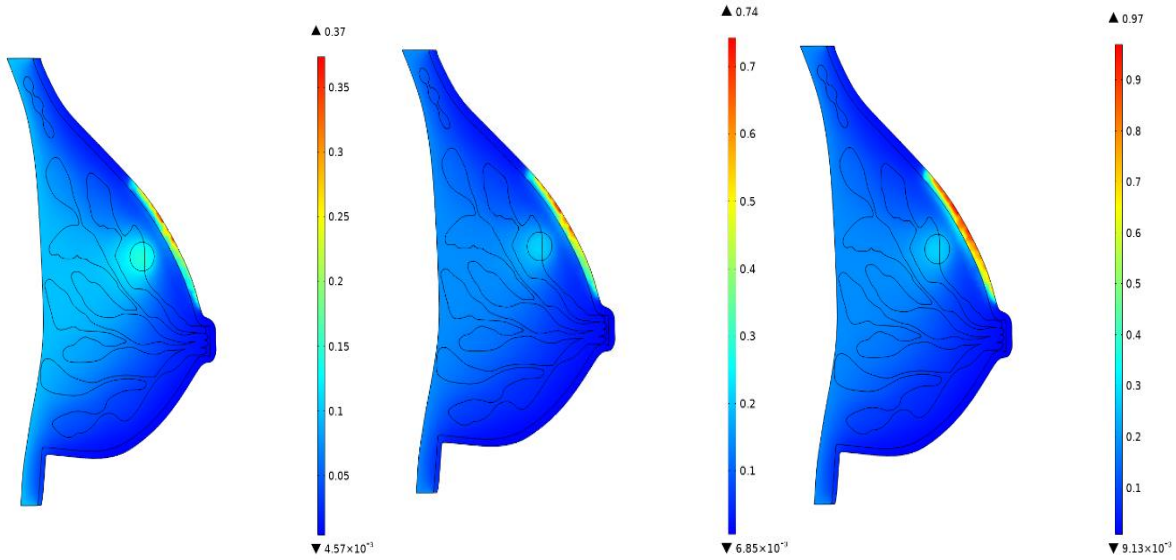
Then, the tumor was subjected to transient hyperthermia analysis for times 120 s (Figure 4a), 180 s (Figure 4b), and 240 s (Figure 4c). The application of thermal laser heats the breast surface layers, reaching temperatures above 37°C and diffusing the heat into the breast. The heat flux (q" = 400 W/m²) used for the thermal laser raises the breast temperature to 43.3 ºC during an exposure time of 240 s.



(a) (b) (c)

Figure 4. Hyperthermia condition in breast with ILC-1, (a) 120s, (b) 180s, and (c) 240s.

The thermal damage degree of 0.7 was the maximum accepted limit for the breast tissue, assisting to select the thermal laser application time. The 120 s hyperthermia time generated thermal damage of 0.37, as shown in Figure 5a, which is below the adopted parameter. For an exposure time of 180 s the damage was 0.74, which is an appropriate value, as shown in Figure 5b. For the 240 s, the damage was 0.97 (Figure 5c), which represents a value close to 1, that is, unacceptable for the study. Thus, to analyze the ILC-1 exposed to a 400 W/m² thermal laser, the time 180 s was selected for the proper application of hyperthermia.



(a) (b) (c)

Figure 5. The heat damage degree after hyperthermia in breast with ILC-1: (a) 120s, (b) 180s, and (c) 240s.

The last step consists was the thermal recovery study of the breast tissue, where the thermal laser is no longer applied to the external surface, only heat exchange occurs by natural convection. Figure 6 shows the difference between the external surface temperatures (only the region where the thermal laser was applied) of the breast with and without tumor after the application of the same hyperthermia (180 s) and during some thermal recovery times. The steady state represents the temperature variation in the thermal balance with the external environment, i.e, considered before the application of the thermal laser. The curves positioned above the steady state represent gains in thermal contrast, while the curves below show lower performance. After hyperthermia, a maximum thermal contrast of 1.3 ºC was obtained between the breasts with and without tumor. During thermal recovery there was no increase in thermal contrast. For a time of 270 s of thermal recovery, the thermal contrast was lower compared to the stationary study. Therefore, for this case, the thermal contrast during the thermal recovery period does not increase.

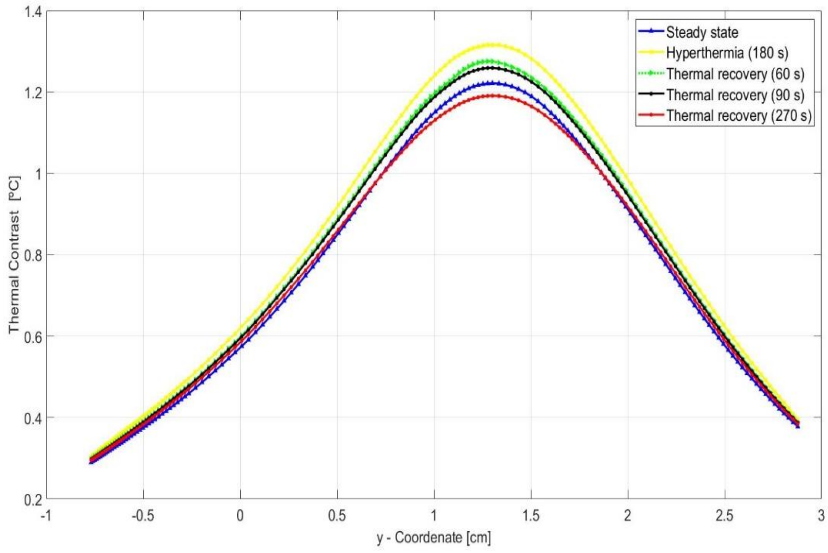


Figure 6. Thermal contrast for hyperthermia of 180s (ILC-1).

3.2 Tumor 2: Invasive ductal carcinoma (IDC)

The numerical breast model was simulated for the case of invasive ductal carcinoma, where the 0.8 cm diameter tumor is located in the breast duct structure. Figure 7 shows the temperature distribution in breast with tumor, where a thermal change compared to the healthy breast can be observed.

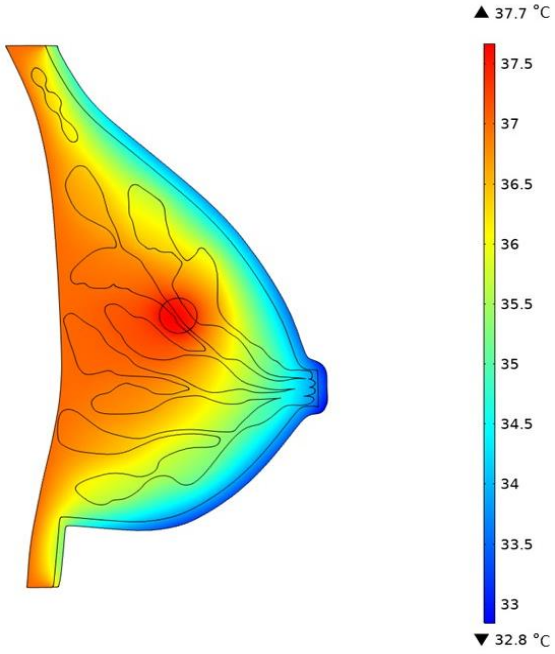
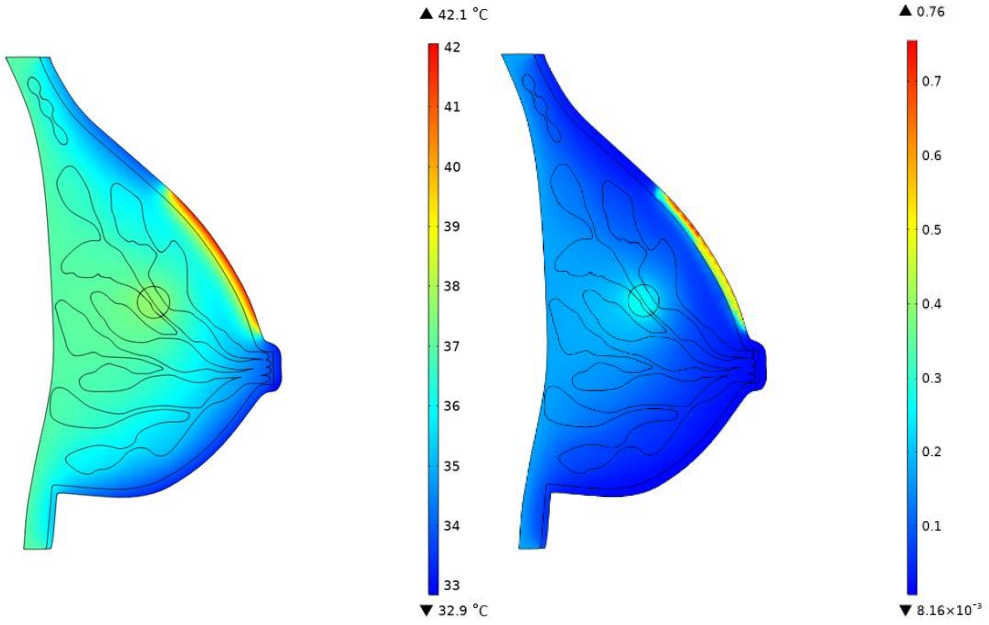


Figure 7. Temperature distribution in steady state for IDC.

The transient hyperthermia conditions for times of 150 s, 220 s, and 300 s were considered. The times of 150 s, 220 s, and 300 s resulted in thermal damage of 0.4, 0.76, and 1.0, respectively. Thus, the exposure time of 220 s was chosen for thermal laser application. Figure 8 shows the temperature distribution and thermal damage degree after the application of thermal laser with a duration of 220 s.



(a) (b)

Figure 8. Numeric breast simulation with IDC: (a) hyperthermia of 220s, (b) thermal damage degree.

Fig 9 shows the main thermal recovery times, allowing the evaluation of the thermal contrast evolution after a heating period of 220 s. The analysis did not return during the recovery of heat values higher contrast compared with the end of hyperthermia. Therefore, for the IDC, evaluation of thermal contrast during thermal recovery is not necessary.

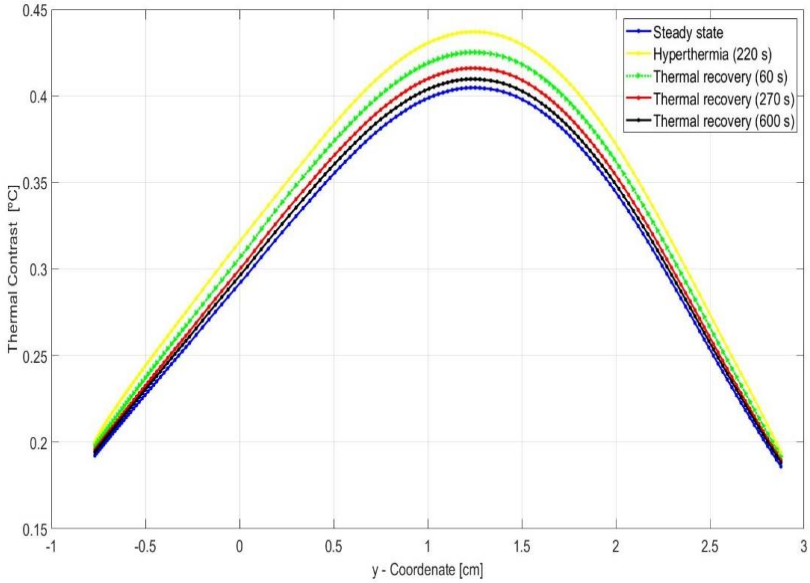


Figure 9. Thermal contrast for hyperthermia of 220s (IDC).

3.3 Tumor 3: Invasive lobular carcinoma (ILC-2)

The breast model was simulated for the second case of invasive lobular carcinoma (ILC-2), where the 0.8 cm diameter tumor was inserted deeper into the breast. Figure 10 shows the temperature distribution for the tumor breast, where a change in the thermal profile close to the tumor is also observed in relation to the healthy breast.

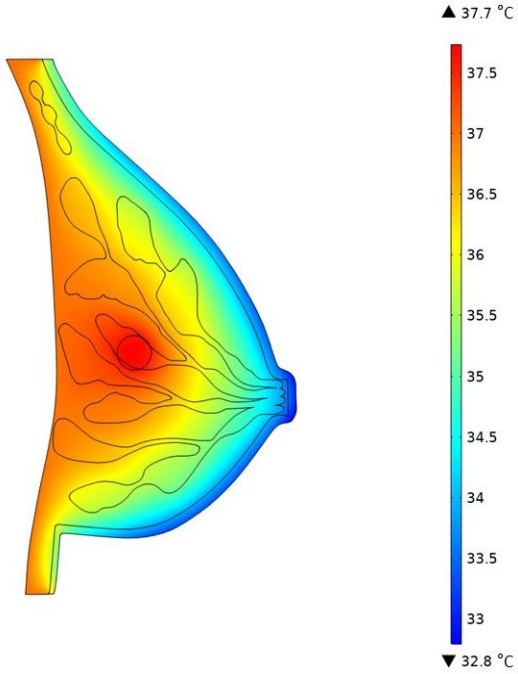
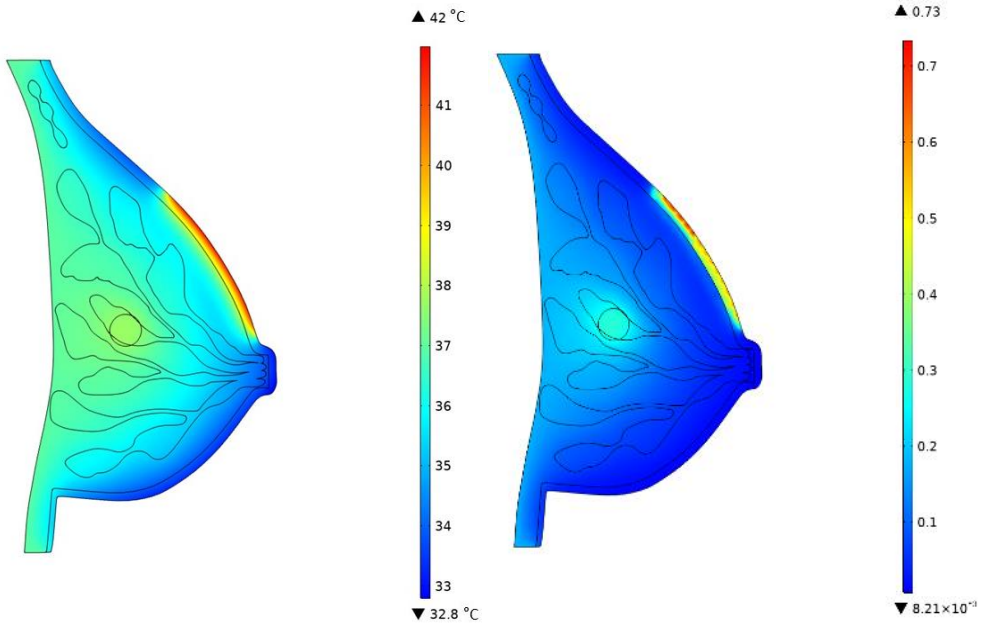


Figure 10. Temperature distribution in steady state for ILC-2.

The numerical model was simulated for the hyperthermia conditions for the times of 160 s, 230 s and 300 s in a similar way to the previous case. The thermal damage condition suggested in the study was 0.7, obtained with a time of 230 s of exposure to the thermal laser. The hyperthermia times of 160 s and 300 s resulted in thermal tissue damage of 0.39 and 0.97, respectively. Figure 11 shows the temperature distribution and thermal damage degree after the application of thermal laser with a duration of 230 s.



(a) (b)

Figure 11. Numeric breast simulation with ILC-2: (a) hyperthermia of 230s, (b) thermal damage degree.

Figure 12 shows the thermal contrast on the breast external surface. During recovery, it was not possible to increase the thermal contrast in relation to the end of hyperthermia. All thermal contrasts are approximately 0.1 °C. Therefore, it was not possible to obtain significant thermal contrast gains for ILC-2.

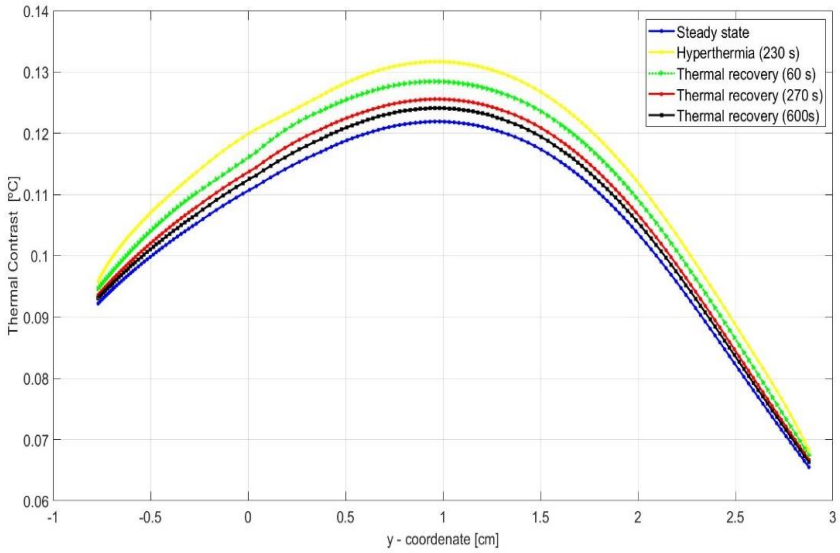


Figure 12. Thermal contrast for hyperthermia of 230s (ILC-2).

4. CONCLUSÃO

In this work, a two-dimensional breast composed of several layers was simulated using the commercial software COMSOL Multiphysics for three different cases of 0.8 cm diameter tumors at different depths within the tissue. Steady state analyzes identified changes between the temperature distribution of breasts with and without tumors. In order to analyze the increase in thermal contrast in thermal images, hyperthermia and thermal recovery analyzes were added to the study, where the application of a constant heat flux thermal laser was limited to the thermal damage degree generated in the breast tissue.

For ILC-1, the maximum allowed of application time of the thermal laser was 180 s because the thermal damage degree was limited to 0.7. The breast was also evaluated during thermal recovery, where the breast was exposed to the

natural convection condition. For IDC and ILC-2, the exposure times of the heat flux applied during hyperthermia were limited to 220 s and 230 s, respectively.

Considering that the applied heat flux was constant, the maximum thermal contrast occurs after the end of the hyperthermia. During thermal recovery, no greater thermal contrasts were obtained due to the thermal laser application method. However, it is observed that the analysis of thermal damage during hyperthermia is essential for optimizing the heat flux application and maintaining the integrity of living tissue.

To improve future analysis, it is possible to apply different forms of heat flux during hyperthermia and monitor the thermal damage generated in the tissue. The application of hypothermia therapy can also be evaluated to investigate improvements in thermal contrast for different tumor cases.

5. ACKNOWLEDGEMENTS

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