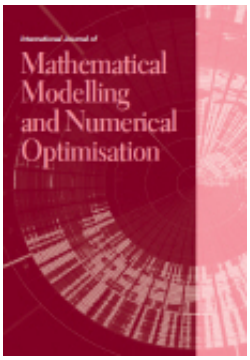

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A numerical analysis of temperature variation in a breast tumour with varying ages

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A numerical analysis of temperature variation in a breast tumour with varying ages

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Abstract: Breast cells grow abnormally and uncontrollably leading to the development of breast tumours. Tumour size is determined by its age. Tumours develop quickly in the early stages of growth and slowly after 250 days (Gautherie, 1980). New blood vessels sprout for the fulfillment of nutrients and oxygen when a tumour expands. These new vessels increase blood flow and metabolism in tumour than in healthy tissue. This increases the tumour's temperature. At a particular tumour age, the temperature distribution in the breast has been investigated by some researchers Afify and Osman (1988) and Ng and Sudarshan (2001); however, no research has been done throughout breast tumour development. To approximate the temperature change of breast tumour, the finite element approach is applied. The temperature variation of breast tumour is observed over a period of 50 to 700 days at various blood perfusion and metabolic rate. The tumour temperature is maximum at 50 days and drops gradually. Since blood flow and metabolic rate both decline with age, the temperature does not vary as the tumour grows. However, the temperature of breast skin surface is increased with tumour age.

Keywords: tumour age; female breast; temperature variation; FEM.

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1 Introduction

A human being is a multicellular organism. Biological tissue is the organisation of similar cells with specific functions. Each cell contains more than 30,000 different genes that regulate its functions (Guyton and Hall, 2020; Weerasinghe et al., 2019). The cell cycle involves the birth, reproduction, and death of cells. When they expire or get damaged, a new one is replaced in their place. From the parent cell, two daughter cells are created. Cells are instructed by the specific signals (genetic codes) when to divide and stop. Cell division is not interrupted and continued as a result of gene damage. A tumour is a collection of cells that are developing abnormally and out of control. Breast tumour develops in the breast cells. Breast cancer, a malignant tumour, leads to the highest mortality rate for women worldwide (Zou et al., 2023).

Gautherie (1980) developed the growth rate and metabolic rate of tumour with their experimental result. The tumour growth was exponential and valid in size up to 40 mm in breast carcinomas. Afify and Osman (1988) developed a thermal model of malignant women's breasts with tumour ages 50, 325, 515 and 650 days. Sudarshan and Ng (1999) developed the numerical breast model with various tumour sizes. They investigated the surface temperature variation based on the various tumour depths and sizes. Thermographic patterns in female breasts caused by uniformly perfused tumours and the menstrual cycle were explored by Makrariya and Adlakha (2019). Wei (2019) developed a tumour growth model based on MCF-7 cell growth in contact with tumour cells. The impact of tumour size and location on the temperature variation of female breast was discussed by Shrestha and Gurung (2017) and Shrestha et al. (2020). They observed that the skin surface temperature of the tumourous breast is higher when the tumour is closest to the areola and vice-versa.

Numerous researchers studied the constant breast tumour size. Several of them investigated the temperature variation of tumourous breast tissue at particular tumour age. According to the literature review, there has been no research on the temperature variation in breast tissue throughout tumour development. The objective of this study is to observe the temperature variation in breast tissue with various tumour ages at different blood perfusion and metabolism. So, a two-dimensional finite element model for temperature variation in breast tissue has been developed, with tumour ages ranging from 50 days to 700 days. For this tumour age, the tumour size has been estimated to be

10–40 mm. This investigation is focused on the glandular layer (known as the breast), whose average size is 45 mm (Sudarshan and Ng, 1999). The findings will be beneficial to researchers and others working in biomedicine.

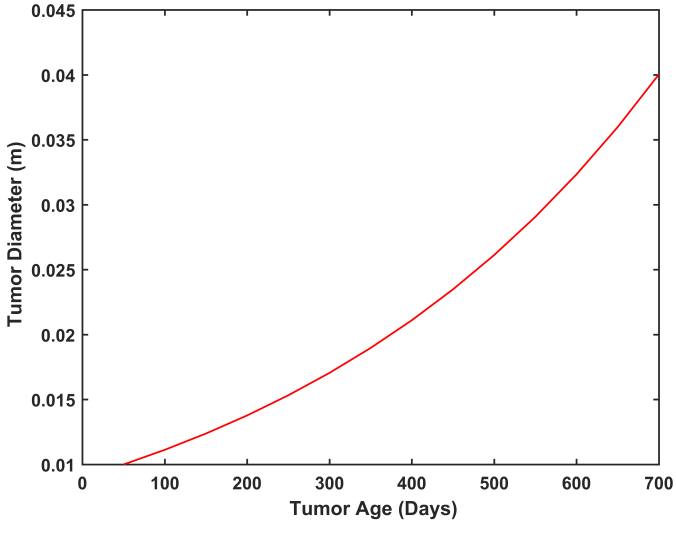
1.1 Tumour growth

Tumour needs more nutrients and oxygen for its growth. In the early stage of growth, nutrients and oxygen are supplied by the host vasculature (Saxena and Pardasani, 1991). It develops new blood vessels as it grows. According to Gautherie (1980), the growth rate of a malignant tumour is dependent on tumour doubling time (tumour needs time to double its volume). The range of tumour doubling time is about 50–700 days. Afify and Osman (1988) treated tumour doubling time as tumour age. The tumour size used by Osman and Afify with tumour age is same as the tumour size determined by Gautherie with tumour doubling time. On the basis of experimental result, Gautherie et al. (1975) developed a formula for finding tumour size valid for up to 30–40 mm in breast carcinomas (Wahab et al., 2015) is:

$$D = \alpha e^{\beta(t_a - 50)} \tag{1}$$

where D is diameter of the tumour [m], $\alpha = 0.01$ [m], $\beta = 21.34 \times 10^{-4}$ [day^{-1}], t_a is tumour doubling time/ tumour age [day]. The relation between tumour age and its size is determined by the relation (1) as shown in Figure 1.

Figure 1 Tumour age vs. tumour diameter (see online version for colours)



1.2 Metabolism

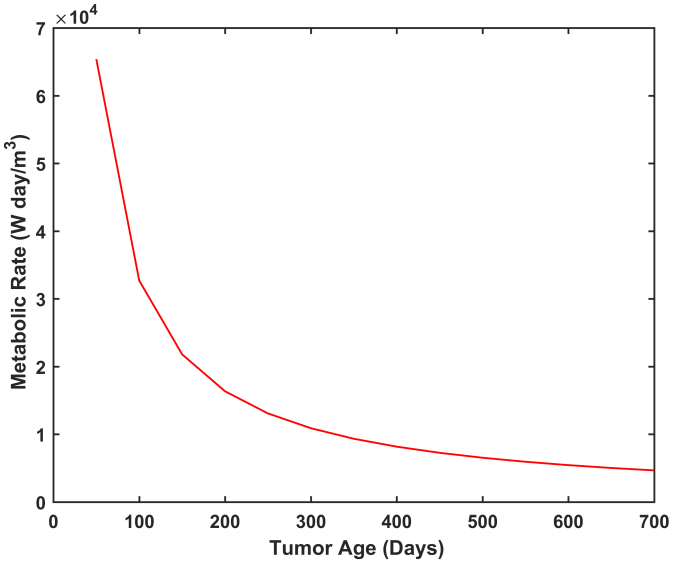
Metabolism is an important factor in the temperature variation of tumourous breast tissue. Previous researchers Sudarshan and Ng (1999) and Shrestha et al. (2020) used two times metabolic rate in the tumour than normal tissue. Gautherie et al. (1975)

developed the formula of metabolism corresponding to tumour doubling time/tumour age as:

$$\text{Tumour's metabolic rate} = \frac{C}{t_a} \tag{2}$$

where $C = 3.27 \times 10^6$ is a constant [W day/m^3]. The metabolic rates at various tumour ages calculated by the relation (2) are given in Table 1. An increase in tumour age decreases the metabolic rate (Figure 2).

Figure 2 Tumour age vs. metabolic rate (see online version for colours)



1.3 Blood perfusion

Blood perfusion is an essential factor in the breast temperature change. Compared to healthy tissue, the blood flow in the tumour region is different. Tumour is a heavily perfused tissue. Sudarshan and Ng (1999) estimated that the blood perfusion of a tumour is 20 times more than that of a muscle. Blood perfusion during the early stages of tumour formation is 50 times greater than average (Das and Mishra, 2013). The literatur also reveals that the growth of necrotic cells in the tumour's core causes the blood flow rate to decrease with tumour age. The blood perfusion rate varies from 0.0053 to 0.053 s^{-1} in breast tumour (Soni et al., 2015). Das and Mishra (2013) used 0.001 s^{-1} blood perfusion rate for breast tumour having metabolism 4,000 W/m^3. The parameter values related to tumour size as well as tumour age are displayed in Table 1.

Table 1 Relation of metabolism and blood perfusion for increasing tumour ages

Tumour age (days)	*Tumour size (mm)*	*Metabolic rate (W/m^3)*	*Blood perfusion (s^{-1})*
50	10	65,400	0.053
100	11	32,700	0.0265
150	12	21,800	0.0177
200	14	16,350	0.0133
250	15	13,080	0.0106
300	17	10,900	0.0088
350	19	9,343	0.0075
400	21	8,175	0.0066
450	24	7,267	0.0058
500	26	6,540	0.0052
550	29	5,945	0.0047
600	32	5,450	0.0043
650	36	5,031	0.0040
700	40	4,671	0.0037

Notes: Blood perfusion is calculated according as decreasing ratio of metabolism.

2 Mathematical modelling

2.1 Discretisation of breast

A female breast has a hemisphere geometrical shape with a radius of 72 mm (Ng and Sudarshan, 2001). It is symmetrical about the breast's central line (X-axis). Epidermis (1.5 mm), dermis (2 mm), subcutaneous tissue (1.5 mm), glandular layer (45 mm), and muscle with thoracic wall (22 mm) are multilayer structures of a breast (Shrestha et al., 2020). A breast tumour can develop on any layer of the breast, although the majority begins in the milk ducts and milk-producing glands of the glandular layer. In this study, a tumour develops at the glandular layer in the breast's central line, which has a fixed centre (27.5, 0) and expands with age. Figure 3 represents the portion of the breast that is vertically cross-sectioned from the areola to the thoracic wall. The various shades in Figure 3 signify the various sizes of a tumour that is spreading from the centre.

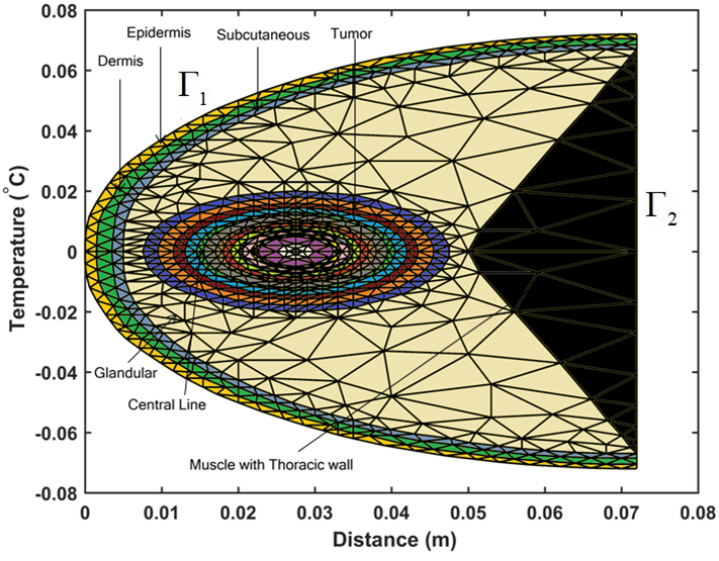
2.2 Model equation

The steady-state Pennes (1948) bio-heat equation is used for the investigation of breast tissue's temperature variation. This equation addresses the energy balance in living tissue due to metabolism and blood perfusion, which is given by:

$$\text{div}(k\ grad\ u) + w_b c_b \rho_b (u_b - u) + S_m = 0 \tag{3}$$

where k [W/m°C] = tissue's thermal conductivity, w_b [s^{-1}] = volumetric blood perfusion rate per unit volume, c_b [J/kg°C] = blood's specific heat, ρ_b [kg/m^3] = blood's density, u_b [°C] = arterial blood temperature, u [°C] = local tissue temperature, and S_m [W/m^3] = tissue's metabolic heat generation rate.

Figure 3 2D discretisation of breast tissue with tumour (see online version for colours)



2.3 Boundary conditions

Human body skin is in contact with the environment. It protects the body from external fluctuations and helps to maintain body temperature regulation. The convection, radiation and sweat evaporation cause the heat loss from breast skin. On the outer part of the breast, the mixed boundary condition (Shrestha et al., 2020) is applied as follows:

$$\Gamma_1 : \; k\frac{\partial u}{\partial \eta} = h_c(u - u_\infty) + le \tag{4}$$

where η = normal direction to the surface boundary, h_c = 13.5 W/m^2°C (Shrestha et al., 2020) is combined heat transfer coefficient (convection and radiation), u_∞ [°C] = room temperature, l = 2.4 × 10^6 J/kg (Acharya et al., 2013) is latent heat of evaporation, and e [kg/m^{2}s] = sweat evaporation rate.

On the interface between thoracic wall and breast base, the Dirichlet boundary condition is applied. The body's core temperature is kept at 37°C (±0.6°C). Therefore, the boundary condition on inner surface of breast is:

$$\Gamma_2 : \; 37°C \tag{5}$$

2.4 Variational form

The variational form of the model equation (3) with boundary condition (4) is given in equation (6).

$$I = \frac{1}{2}\int\int_\Omega \left[k\left(\left(\frac{\partial u}{\partial x}\right)^2 + \left(\frac{\partial u}{\partial y}\right)^2\right) + w_b c_b \rho_b (u_b - u)^2 - 2S_m u\right] dxdy$$
$$+ \frac{1}{2}\int_{\Gamma_1} \left[h_c(u - u_\infty)^2 + leu\right] d\Gamma_1 \tag{6}$$

where Ω is the breast domain.
For minimisation,

$$\frac{\partial I}{\partial u_i} = 0 \tag{7}$$

where $u_i = i^{\text{th}}$ triangular mesh's temperature.

In matrix form, equation (7) can be expressed as a system of linear equations:

$$fu = b \tag{8}$$

where $u = [u_i]$ is $m \times 1$ vectors, $b = [b_i]$ is $m \times 1$ load vector matrix, f is $m \times m$ conductance matrix, m is total number of nodal points.

3 Results and discussion

The finite element approach is applied to solve the two-dimensional bio-heat equation numerically. The breast tissue's temperature with tumour age from 50 days to 700 days is studied at various blood perfusion and metabolic rates, which are displayed in Table 2. The difference between two successive tumour ages is considered 50 days. The specific heat, blood density, sweat evaporation rate and room temperature are 1,060 J/kg°C (Shrestha et al., 2020), 4,200 kg/m^3 (Wahab et al., 2015), 3.0806 $\times$ 10^{-6} kg/m^{2}s (Park and Tamura, 1992) and 25°C (Park and Tamura, 1992), respectively. The other parameter values are shown in Table 3.

Table 2 Blood perfusion and metabolic rate of tumour region

Parameters	*Set I*	*Set II*	*Set III*
Blood perfusion (w_b) (s^{-1})	20 $\times$ normal (Sudarshan and Ng, 1999)	20 $\times$ normal (Sudarshan and Ng, 1999)	Table 1
Metabolism (m_t) (W/m^3)	2 $\times$ normal (Sudarshan and Ng, 1999)	Table 1 [relation (2)]	Table 1 [relation (2)]

Table 3 Parameter values used in model

Breast tissue's	*Thermal conductivity*	*Blood perfusion*	*Metabolism*
Layers	k [W/m°C]	w_b [s^{-1}]	S_m [W/m^3]
Epidermis	0.20934	0	0
Dermis	0.31401	1.7969 $\times$ 10^{-4}	400
Subcutaneous	0.41868	1.7969 $\times$ 10^{-4}	400
Glandular	0.48	5.3908 $\times$ 10^{-4}	700
Muscle with thoracic wall	0.48	5.3908 $\times$ 10^{-4}	700
Tumour	0.55 (Soni et al., 2015)	Table 2	Table 2

Source: Shrestha et al. (2020) and Sudarshan and Ng (1999)

3.1 Tumour region's temperature

The temperature profiles of the tumourous breast tissue associated with sets I, II, and III are shown in Figures 4–6, respectively. In our study, the tumour has a fixed centre at (27.5, 0), and its size increases with its age (Table 1).

Figure 4 Breast tumour temperature (set I) (see online version for colours)

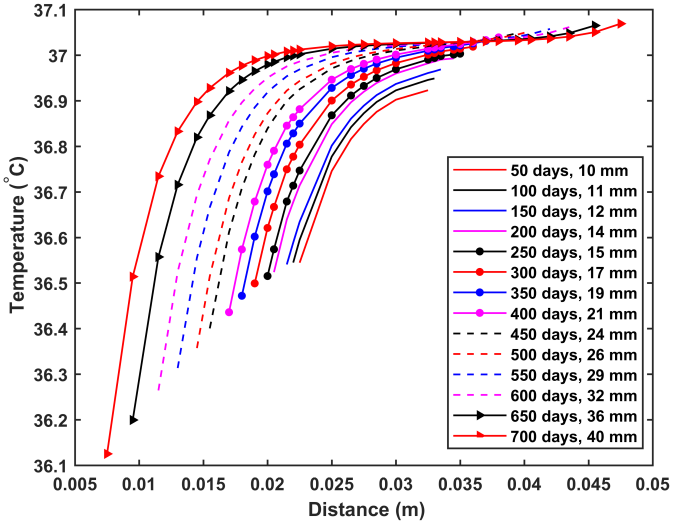


Figure 5 Breast tumour temperature (set II) (see online version for colours)

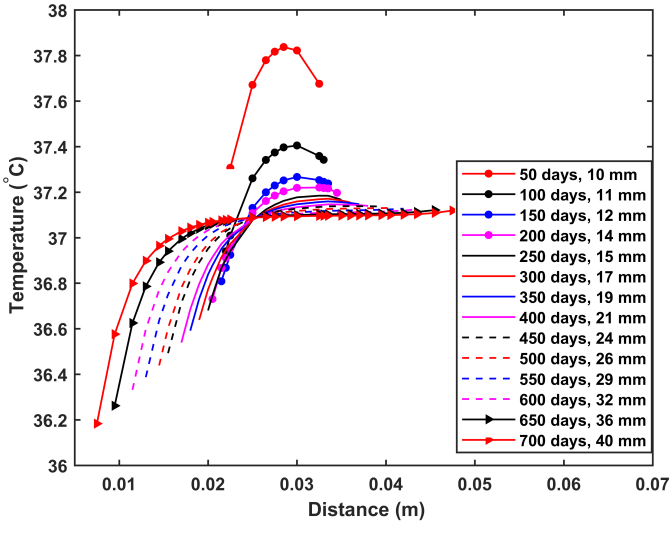
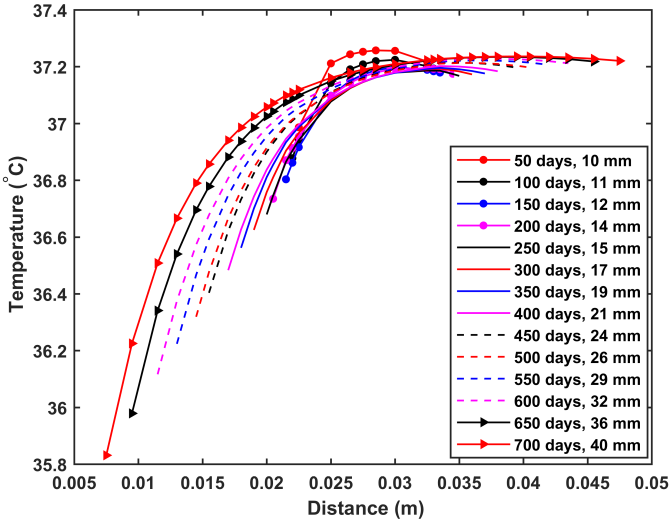


Figure 4 displays the temperature profile of the tumour regions using blood perfusion and metabolism defined in set I. The results show that the tumour temperature slightly increases with increased age.

Figure 6 Breast tumour temperature (set III) (see online version for colours)



The temperature profile of the breast tumour at blood perfusion and metabolic rate using set II is shown in Figure 5. The findings indicate that the tumour's temperature reaches its maximum at 50 days then decreases with its increasing age. It is observed that when tumour age increases from 50 days to 100 days, the average tumour temperature decreases by 0.39°C. Similarly, when tumour age increases from 100 days to 150 days, the average tumour temperature decreases by 0.13°C. According to the findings, the tumour temperature rapidly decreases up to the age of 150 days, then slightly decreases with age.

After the rapid growth of a tumour, the necrotic cells develop in the core, which decreases the blood vessels (Song et al., 1980). Generally, the tumour blood flow decreases with its growth (Song, 1984). Soni et al. (2015) used the blood perfusion rate 0.053 s^{-1} for high perfused tumour and 0.001 s^{-1} used by Das and Mishra (2013) for breast tumour. So, blood perfusion rate within the range 0.001 s^{-1}–0.053 s^{-1} is used in set III. The blood perfusion rate 0.053 s^{-1} is assumed for 50 days tumour and decreases accordingly as metabolism, which is presented in Table 1. This results the tumour temperature of 50 days using set III (Figure 6) being lower than the temperature using set II (Figure 5).

The temperature profile of breast tumour using set III is shown in Figure 6. According to the findings, tumour temperature slightly decreases up to 200 days then slightly increases. So, there is no variation in tumour temperature due to high blood perfusion in 50 days tumour compared to 700 days however metabolic rate decreases for various tumour ages.

3.2 Tumour's anterior, central and posterior temperature

The graphs of anterior, central, and posterior temperature of tumour with varying ages are displayed in Figures 7, 8 and 9 using sets I, II, and III. Figure 7 shows that the tumour's anterior temperature drops with increasing tumour ages. The anterior

temperature using set III at 50 days tumour is higher than set I by 0.45°C and lower than set II by 0.32°C. Similarly, the anterior temperature at 700 days using set III is lower by 0.30°C and 0.35°C than sets I and II, respectively.

Figure 7 Anterior temperature of tumour with its age (see online version for colours)

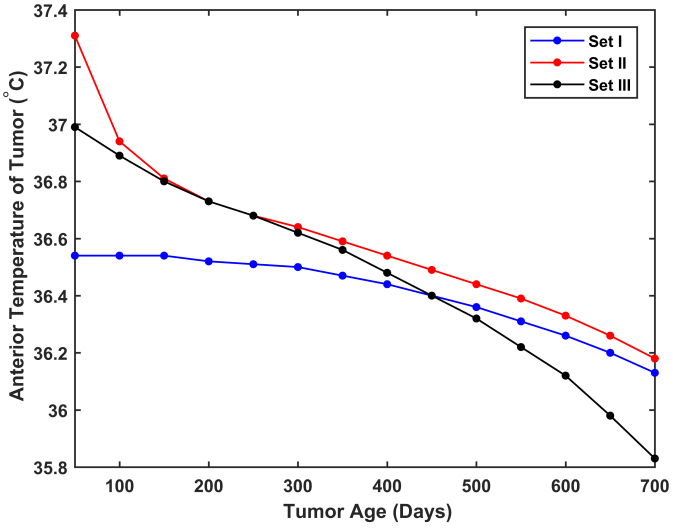


Figure 8 Central temperature of tumour with its age (see online version for colours)

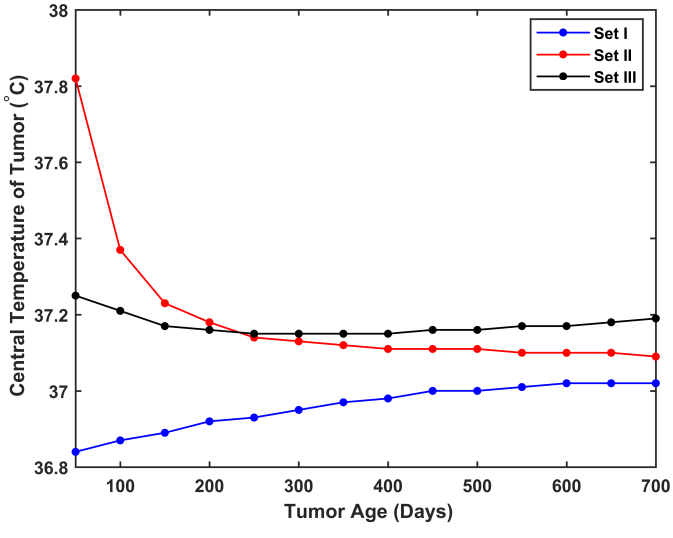
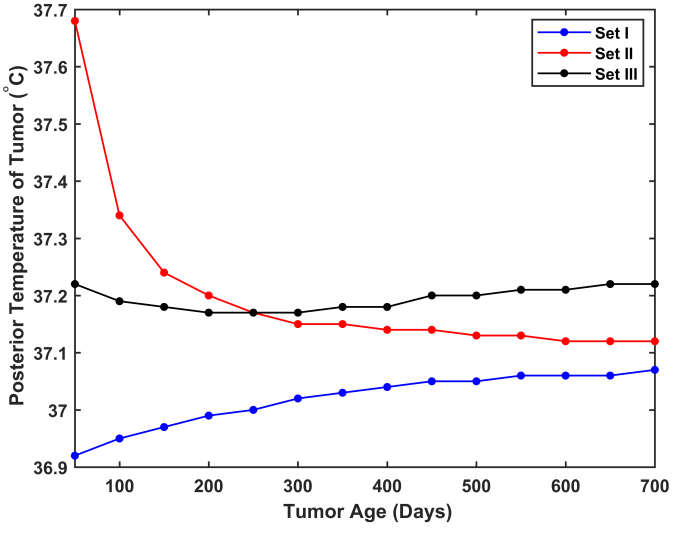


Figure 8 represents the graph of the tumour's central temperature. The results exhibit that the central temperature rises in set I but drops in set II. Since the metabolic rate is very high in the 50 days tumour in set II, the temperature drops rapidly from 50 days to 150 days then slowly to 700 days. The graph of set III shows that the central temperature decreases slightly from 50 days to 250 days then it rises slowly to 700 days. Similar temperature behaviour is exhibited in the posterior part of the tumour region (Figure 9).

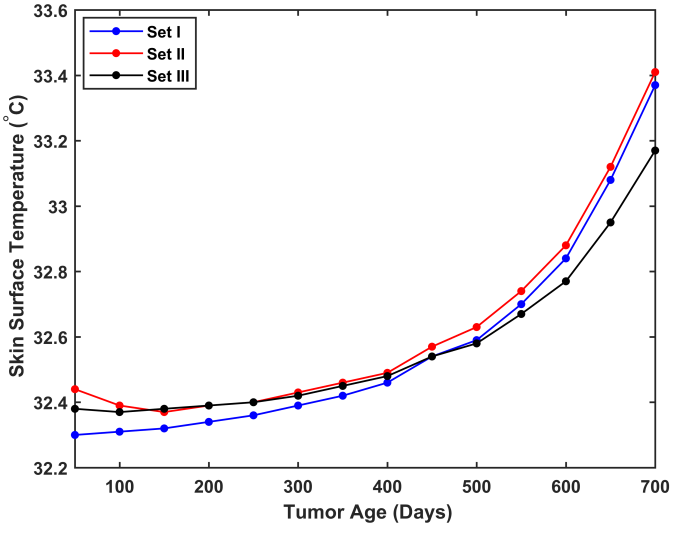
Figure 9 Posterior temperature of tumour with its age (see online version for colours)



3.3 Skin surface temperature

The breast skin surface temperature profile with increasing tumour age is exhibited in Figure 10 using sets I, II, and III. The results show that the breast skin surface temperature rises with its age in sets I and III. In set II, the breast skin surface temperature decreases from 50 days to 150 days then increases gradually.

Figure 10 Temperature profile of skin surface with tumour age (see online version for colours)



3.4 Breast temperature

Figures 11–13 compare the temperature variation of normal and tumourous breast tissue at the tumour age of 50, 250, 500, 600 and 700 days. It observes that the tumourous breast temperature at various tumour ages is higher than normal. Using set I, Figure 11 shows that each layer's temperature of the tumourous breast increases with increasing tumour age. The tumourous breast's skin surface temperature is higher than normal by 0.06°C, 0.12°C, 0.35°C, 0.60°C and 1.13°C at the tumour age of 50, 250, 500, 600 and 700 days, respectively. This concludes that the tumourous breast's skin surface temperature increases with increasing tumour age.

Figure 11 Breast temperature (set I) (see online version for colours)

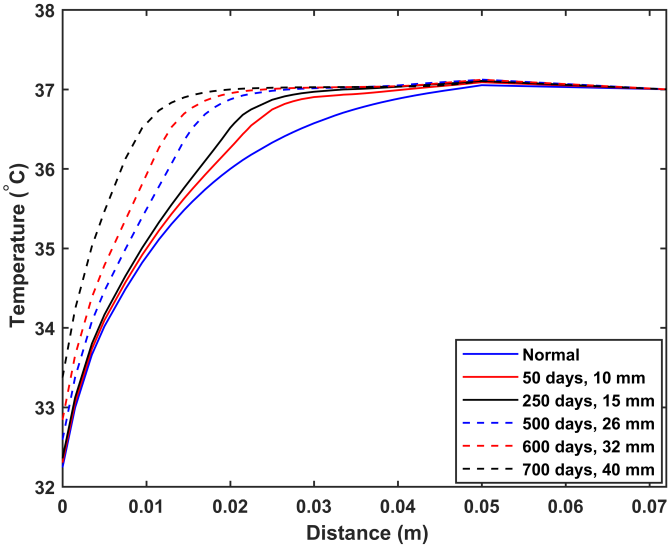


Figure 12 uses set II's metabolic rate and blood perfusion to show the temperature change of breast tissue. A 250 days tumour has 5 times lower metabolic rate than a 50 days. So, the tumourous breast has a maximum tumour temperature of 37.82°C at 50 days, then it rapidly decreases to 37.14°C at 250 days, and then gradually decreases to 700 days. Using set III, Figure 13 shows that the tumourous breast has the highest temperature of 37.25°C at 50 days, then it gradually decreases with increasing age.

3.5 Discussion

The tumour region, skin surface, and breast tissue temperature profiles of varying tumour ages are investigated at various levels of blood perfusion and metabolism (sets I, II, and III). At various tumour ages, the temperature in tumourous breast is higher than normal due to the high blood perfusion and metabolism in the tumour than in healthy breast. When a tumour expands, the tumour's posterior part moves closer to the thoracic wall, and the anterior part moves closer to the skin surface. The breast temperature continuously rises from the skin surface to the body core in normal and tumourous breasts due to the consideration of a lower environmental temperature (25°C) than the

body core temperature (37°C). However, the tumour region exhibits unusual temperature behaviour. Because of these facts, the tumour's anterior temperature decreases with increasing age.

Figure 12 Breast temperature (set II) (see online version for colours)

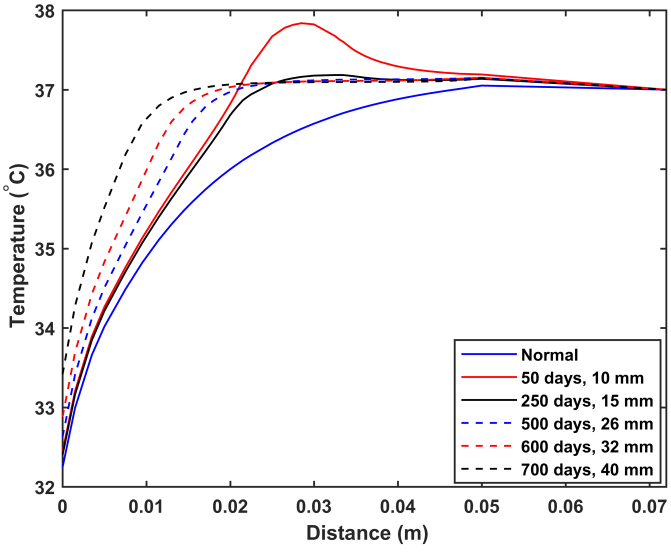
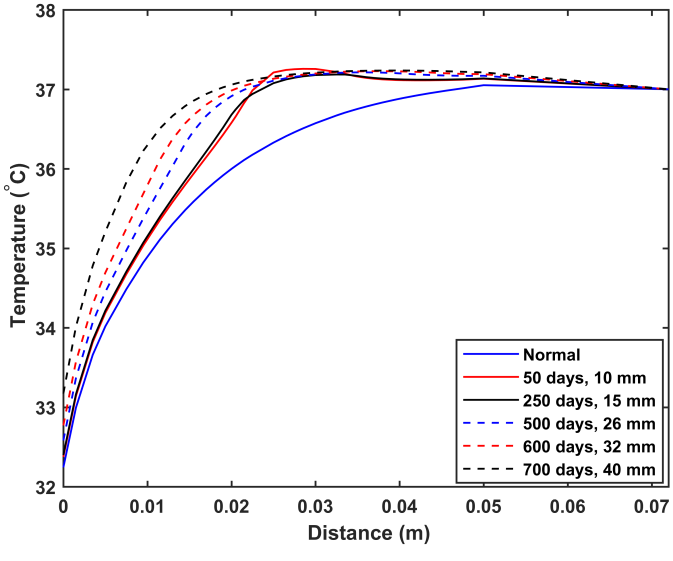


Figure 13 Breast temperature (set III) (see online version for colours)



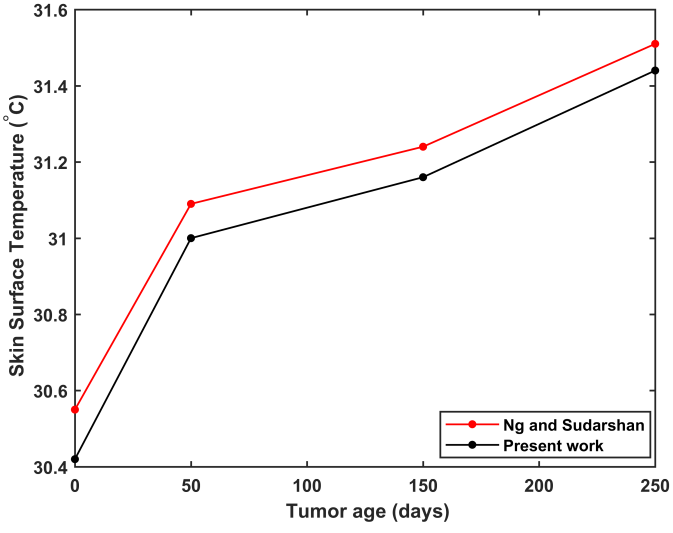
Using set I, the tumour's central and posterior temperatures increase with increasing age due to constant blood perfusion and metabolic rates. In set II, the tumour's metabolic rate reaches a peak at 50 days and declines with tumour growth. So, the tumour's central and posterior temperatures reach their maximum at 50 days and then decrease

to 700 days. Due to decreased blood perfusion and metabolism with increasing tumour age in set III, the tumour's central and posterior temperatures decrease slightly from 50 days to 250 days then it rises slowly to 700 days. The tumourous breast's skin surface temperature rises with increasing tumour age due to the effects of blood perfusion and metabolism in the tumour region, and skin proximity to the tumour surface is shortened as tumour size increases. As a result of high metabolism and constant blood perfusion in set II, the skin surface temperature decreases from 50 days to 150 days and then rises with increasing tumour age.

3.6 Validity of the model

For validity, the present work is compared with work of Sudarshan and Ng (1999). The physical parameters, tumour size, and tumour location are used same as in Sudarshan and Ng. The tumour sizes 10, 12 and 15 mm with centre (15, 0) are used for comparison. Figure 14 represents the normal and tumourous breast's skin surface temperatures with tumour age 50, 150 and 250 days.

Figure 14 Comparison of present work with Sudarshan and Ng (1999) (see online version for colours)



Ng and Sudarshan considered the entire SST region as a single layer, whereas we separated it into three layers with different thermal properties. The absence of blood circulation and metabolic activity is considered in the epidermis layer of the SST region. This is the reason why our model's temperature is just slightly different from Sudarshan and Ng's. Therefore, our results agree with those of Sudarshan and Ng.

According to Kwok and Krzyspiak (2007), the breast's skin surface temperature with 10 mm tumour size was 31.96°C at the metabolic rate of 65,400 W/m^3. Using the same parameter values and tumour size as Kwok and Krzyspiak, it is observed at 31.28°C temperature for a 50 days tumour. The skin surface temperature varies slightly due to differences in breast size and tumour location. Kwok and Krzyspiak used a breast radius

of 47.5 mm with a tumour centre (17.5, 0) whereas a breast radius of 72 mm with a tumour centre (27.5, 0) is used in our study.

4 Conclusions

The temperature variation in breast tissue is investigated by increasing tumour age at varied blood perfusion and metabolic rates. Tumourous breast temperatures are higher than those of a normal breast with increasing tumour age. When applying the blood perfusion and metabolism described in set I, the breast temperature gradually increases with varying tumour ages. The tumour temperature rises to its maximum at 50 days and rapidly decreases until 150 days, then gradually decreases with increasing tumour age, using set II. When using set III, the tumour temperature slightly decreases from 50 days to 250 days and then stays stable as the tumour enlarges. It is observed that the breast tumour temperature using blood perfusion and metabolism defined in set II is realistic than set I, and set III is more realistic than set II.

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