ORIGINAL ARTICLE

Thermal Profiling Analysis for Asymmetrically Embedded Tumour with Different Breast Densities

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ABSTRACT

Introduction: Detecting breast cancer at earlier stage is crucial to increase the survival rate. Mammography as the golden screening tool has shown to be less effective for younger women due to denser breast tissue. Infrared Thermography has been touted as an adjunct modality to mammography. Further investigation of thermal distribution in breast cancer patient is important prior to its clinical interpretation. Therefore, thermal profiling using 3D computational simulation was carried out to understand the effect of changes in size and location of tumour embedded in breast to the surface temperature distribution at different breast densities. **Methods:** Extremely dense (ED) and predominantly fatty dense (PF) breast models were developed and simulated using finite element analysis (FEA). Pennes' bioheat equation was adapted to show the heat transfer mechanism by providing appropriate thermophysical properties in each tissue layer. 20 case studies with various tumour size embedded at two asymmetrical positions in the breast models were analysed. Quantitative and qualitative analyses were performed by recording the temperature values along the arc of breast, calculating of temperature difference at the peaks and comparing multiple thermal images. **Results:** Bigger size of tumour demands a larger increase in breast surface temperatures. As tumour is located far from the centre of the breast or near to the edge, there was a greater shift of temperature peak. **Conclusion:** Size and location of tumour in various levels of breast density should be considered as a notable factor to thermal profile on breast when using thermography for early breast cancer detection.

Keywords: Breast cancer, Breast density, Bioheat transfer, Breast modelling, Thermography

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INTRODUCTION

The number of breast cancer incidence in women increases every year worldwide. Breast cancer is the second leading cause of all cancer death (1) and the most commonly diagnosed cancer as well as the major cause of death among women (2). Cases are less frequent in younger women than the older adults, but studies showed cancer cells exhibit more aggressive features and a worse prognosis for the young age (3, 4). Early detection of breast cancer is crucial in the diagnosis of the disease thus improves the expectancy of survival. Meanwhile, recent advancement in cancer treatment also contributes to the chance of survival. To conclude, early detection of breast cancer is believed to improve the chances of survival and provide options for curative treatment while effective breast screening method remains the most population health strategy in reducing the number of breast cancer cases related to morbidity and mortality (5). This suggests that detecting breast cancer at the earliest stage is crucial to improve one's life.

Breast screening aims to detect the disease early and to date, mammography remains the most promising technique used by radiologist worldwide. However, annual mammography is only recommended for women starting at the age of 40 and above due to the lower breast density of breast tissue compared to younger women (6, 7). A high proportion of fibro glandular tissue in young women breast than fat that make the breast denser. These fibro glandular tissues which appear white on mammograms has a higher coefficient of X-ray attenuation than fat (8), therefore, cause a reduction in sensitivity and specificity of mammography. The white appearance of dense tissue from mammogram also may mistakenly obscure a cancer (9). According to Albert et

al., there were higher levels of mammographic breast density, background parenchymal enhancement and fibro glandular tissues seen in women at higher risk of breast cancer (dense breasts) compared to women who already diagnosed with breast cancer (10).
Infrared Thermography is a non-invasive, contactless screening method that is economical, quick and does not cause any pain to the patient (11, 12). It uses a higher sensitive infrared thermal camera to map a high resolution of thermal images that shows the temperature variations (11-13). Future improvement by researchers can help in reducing the high false positive and false negative values in thermography imaging by using appropriate combinations of segmentation, feature extraction and classification in computer simulation (14). Physiologically, metabolic rate and blood perfusion area of the tumour is higher than the healthy breast tissue thus increases breast surface temperature. The surface temperature distribution of tumorous breast is affected by several parameters such as tumour size and location, metabolic heat generation and blood perfusion rate. Generally, tumour located closer to the breast surface is easily identified by the thermal camera while deep tumour may not be detected. Besides, bigger size of tumour may show significant temperature variations on breast surface when detected by the camera compared to a smaller size of tumour. Therefore, while mammography detects anatomical changes and thermography provides physiological information on breast condition, the combination of these two imaging methods actually able to perform better in detection of invasive cancer and multifocal diseases (15).

Computer-aided diagnosis contributes in detection of breast cancer from thermal images such as using adoption of deep convolution of neural network that can help to boost the performance of thermograms for early breast cancer detection (16). Artificial Neural Network (ANN) has performed 96.33% to testing data and 92.89% to validation data according to Wahab et al. in their study to approximate the localize tumour position from skin surface, therefore, ANN should be integrated in thermogram analysis (17). Many studies have been conducted regarding temperature distribution analysis on breast model by using Finite Element Method (FEM) such as using single-layer of a two-dimensional and three-dimensional model, homogenous breast phantom and single composition multi-layer breast model (18, 19). Based on one previous study, they has concluded that we can determine the behaviours of axisymmetric tumours at varies sizes and locations by using the breast surface temperature profile (20). Das and Mishra in their previous studies developed a two-dimensional homogeneous breast model to estimate the effect of size and location of tumour in thermal distribution at breast surface. To estimate the tumour size, location and blood perfusion of a cancerous breast lesion, Hatwar and Herman also has proposed a computational method by using the combination of transient and steady state data to make it possible (21). However, they did not consider factor such as breast density during the analysis (18, 19, 22). Studies performed by Wahab et al. concluded that different types of breast density produce varying breast surface temperature distribution profiles in the presence of cancerous tumour (23). The research suggested that dynamic thermal changes should be observed on various size at asymmetrical location of tumour for all breast density levels.

Breast tumour in different breast density levels namely extremely dense (ED), heterogeneously dense (HD), scattered fibro glandular (SF) and predominantly fatty (PF) produced different thermal effect on breast surface. A study performed by Singh S and Repaka R found that PF breast model having a higher composition of fatty tissues required a higher input voltage than ED breast model in their investigation on the effect of radiofrequency ablation at different breast compositions (24). Ramнrez-Torres et al. in their previous study obtained appreciable findings regarding role of cancerous tissues on temperature distribution which are: (a) tumour presence does affect the surface temperature distribution (b) low blood perfusion rates in glandular tissues cause a greater temperature difference in tumour area (c) the maximum breast surface temperature difference increases as tumour move closer to the surface in heterogeneous tissue (25). In addition to that, three-dimensional analysis for whole breast surface also has been done previously where the result has proven that tumour position affects the temperature maps more than its volume, therefore, providing essential hints for breast cancer detection (26). To show the heat mechanism in living tissues, Pennes' bioheat transfer equation (27) is the first and has been widely used as continuum model for many centuries (28). The equation has been adapted and explored in many studies related to breast cancer computational simulation (19-23, 29). In breast model analysis, Eq. (1) is used to model the heat transfer in breast tissue at nth layer as followed:

$$\rho_n c_n \frac{\partial T}{\partial t} = k_n \nabla^2 T + \rho_b c_b \omega_b (T_b - T_n) + Q_n \qquad (1)$$

where ρ_b, c_b, ω_b, T_b represents blood density, specific heat of blood, blood perfusion rate as well as the arterial temperature, respectively. Meanwhile for tissues density, specific heat, temperature, thermal conductivity and metabolic heat generation were also stated by Pennes' given by ρ_n, c_n, T_n, k_n, and Q_n, respectively.

Above that, this research aims to investigate the effect of changes in size of tumour which embedded at two different asymmetrical positions on the breast surface temperature distribution in ED and PF breast models.

MATERIALS AND METHODS

Breast Modelling

ED breast is frequently found in breasts of younger women while PF in older women. Breast tissues were categorized to several layers which are muscle (D1), gland (D2), fat (D3) while tumour is added to show the presence of cancerous tissues in the breast. The percentage of gland composition in ED breast is approximately 70% whereas in PF is only 20%. In addition, major tissue composition in PF is the fat layer with almost 70% compared to fat composition in ED which is only 10%. According to these percentage divisions, predominantly fatty breast density of woman breast composed almost entirely with fatty tissues thus make it less dense compared to ED breast density type.

The breast was constructed as a hemisphere with a diameter, D = 14.4 cm. After that, another hemispherical shape with a much smaller size was drawn to build the glandular layer then a semi-ellipsoidal shape with a specific radius and height were added to mimic the muscle layer on the breast. Then, a line segment at the bottom part of the hemisphere is attached to the body core. In this study, areola, nipple and other small distortions were ignored. ED has a thicker glandular layer than PF meanwhile the amount of fats is higher in PF than in ED. These unique compositions made the temperature distribution on the breast surface to be different from each type of breast density.

Bioheat Transfer Mechanism and Thermophysical Properties

The transport of heat energy in living organisms required a complex biological process and mechanism such as heat conduction, convection by blood perfusion, radiation and heat metabolism. Any abnormality or sudden changes in the temperature distribution of a body may be connected to both biological and physiological processes, which is normally the first sign of a disease. This is strongly related to cancerous tissue since the rapid growth of cancer cells need an adequate amount of nutrients and it should be transported through blood vessels nearby the demanding area. In addition, the formation of new blood vessels known as angiogenesis would increase the metabolic rate of the surrounding tissues area that can cause a slight alteration on body temperature. The thermophysical properties of each tissue layer in this study were closely related to what have been suggested by Ng and Sudharsan (30) in Table I.

Table I: Thermophysical parameters in ED and PF

Thermophysical parameters	Muscle (D1)	Gland (D2)	Fat (D3)	Tumor (T1)
Thermal conductivity (W/m °C)	0.4	0.48	0.21	0.48
Metabolic heat generation (W/m³)	700	700	400	8720
Blood perfusion (1/s)	0.8e-3	0.5e-3	0.2e-3	0.1e-1
Specific heat blood (J/Kg °C)	4200	4200	4200	4200
Blood density (kg/m³)	1060	1060	1060	1060

Geometry

The improvement of this study compared to previous studies is that the position of tumour embedded in the breast is asymmetry. This involves study on the effect of changes in the size of the embedded tumour at an asymmetrical position inside the breast on the breast surface temperatures. There were ten case studies for each type of breast density including the case without tumour embedded (act as control) and the tumour size ranged from 0.25 cm until 1.25 cm. However, there is no case study for tumour size 1.25 cm at x = 5.4 cm in both types of breast density due to the bigger tumour extruded from the breast surface.

Two positions in x-axis (1.8 cm and 5.4 cm from the centre of breast) were studied while the tumour depth from breast surface is fixed. The reason of choosing position at x = 1.8 cm was to show the tumour is closer to breast centre while at position x = 5.4 cm, the tumour is nearer to breast edge. Next, the radius of tumour was changed by 0.25 cm for each case study.

Extremely Dense breast model and Predominantly Fatty breast model

Table II shows a total of 20 cases studied in these breast models. The tumour depth is fixed at 2 cm from the breast surface, and the tumour sizes were diverse. Fig. 1 shows the position of tumour embedded inside both ED and PF breast model in the simulation process at two different locations; nearer to breast centre and closer to breast edge.

Table II: 20 case studies in ED (Case 3.10 – Case 3.24) and PF (Case 6.10 – Case 6.24) breast density models at five different sizes of tumour and two positions inside the breast

SIZE (r, cm)	ED at x = 1.8 cm	ED at x = 5.4 cm	SIZE (r, cm)	PF at x = 1.8 cm	PF at x = 5.4 cm
0.25	3.11	3.21	0.25	6.11	6.21
0.50	3.12	3.22	0.50	6.12	6.22
0.75	3.13	3.23	0.75	6.13	6.23
1.00	3.14	3.24	1.00	6.14	6.24
1.25	3.15	-	1.25	6.15	-
No Tumor	3.10		No Tumor	6.10	

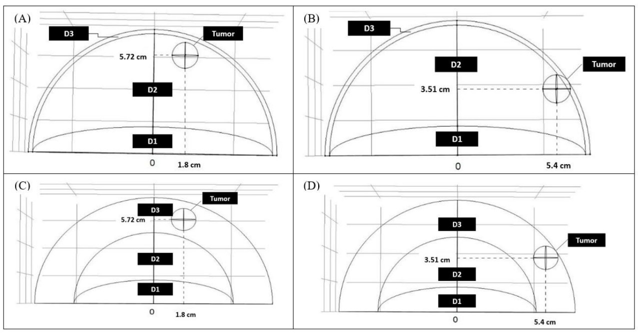

Figure 1: Examples varies position of tumour inside both models. (A). Case 3.15 (x=1.8 cm) (B). Case 3.24 (x=5.4 cm) (C). Case 6.15 (x=1.8 cm) (D). Case 6.24 (x=5.4 cm)

Finite Element Analysis

Numerical simulation in this study was performed using FEM available in COMSOL Multiphysics 4.4. Each breast model was meshed into a predefined number of finite elements as the first step of FEM for spatial discretization. Then, tetrahedral meshing was selected in this study. According to the test conducted on normal and finite element size meshing setting in previous study, there was an insignificant difference in breast surface temperature. However, in some case studies, the tissues and tumour gather in small spaces and cause overlapping. To overcome this issue, both fine element and normal element were used. The area nearer to boundaries of tissues and the edge of the breast looks darker after the meshing process because more elements were needed in that area.

RESULTS

Data collection was performed by recording the temperature values extracted along the arc of the breast surface. The temperature values in each point along the surface with and without tumour embedded inside were then compared. Next, thermal profiling analyses were performed where significant factors such as peak temperature in each case and the peak temperature differences were further observed and discussed in this study.

Thermal Profiling along breast surface on ED breast

Fig. 2 presents the distribution of breast surface temperatures extracted from ED breast when tumour was embedded at x = 1.8 cm (case 6.11 until case 6.15) and at x = 5.4 cm (case 6.21 until case 6.24). The graphs show the breast skin temperature (°C) against the arc length (cm).

Based on Fig. 2 (A), peaks appeared at the arc length was about 13 cm as tumour was nearer to the centre while in Fig. 2 (B), peaks are shown at arc length was about 19 cm due to tumour situated at the breast edge. The different of peaks location were derived from the two different location of tumour. So, based on the appearance of peaks we could estimate the position and size of tumour presence in the breast. Based on the graphs, breast with a bigger size of tumour seemed to have larger increment in breast skin surface temperature for each location of tumour.

At position x = 1.8 cm, the maximum temperature peak obtained was 31.65 °C while at x = 5.4 cm, the maximum peak was about 33.65 °C. The temperatures on the breast surface increases linearly along the increment of tumour sizes. The maximum altitude of temperature was demonstrated when the tumour is located at x = 5.4 cm from the centre of breast, which is nearer to edge of breast.

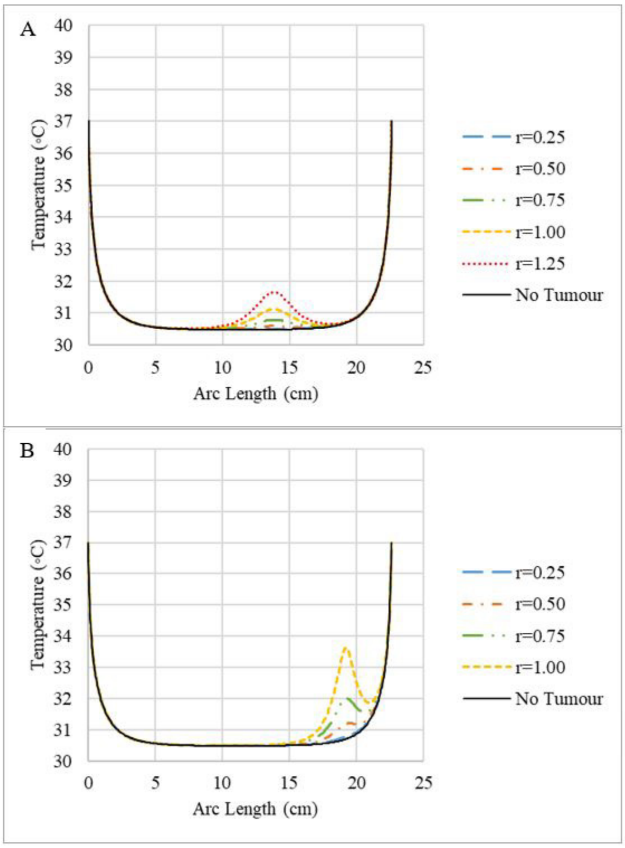

Figure 2: Analysis in ED breast models. (A). All cases in ED breast at x = 1.8 cm (B). All cases in ED breast at x = 5.4 cm

Thermal Profiling along breast surface on PF breast model

Meanwhile, Fig. 3 show graphs obtained from the simulation of PF breast model when the tumour is embedded at x = 1.8 cm and x = 5.4 cm, respectively. In Fig. 3 (A), the peaks appeared at where the arc length was about 13 cm while Fig. 3 (B) shows peaks appeared at where arc length was 19 cm due to different position of tumour in the breast. The graphs proved that breast with bigger size of tumour possessed a larger increment in breast surface temperatures.
The fat composition in PF breast in nature is greater than in ED breast that make it less dense. At x = 1.8 cm, the maximum peak was 27.9 °C while at x = 5.4 cm, maximum peak temperature was 28.85 °C. This suggests that temperature of breast surface increases following the increment in size of tumour. The significant temperature peaks obtained from tumour embedded nearer to breast edge.

DISCUSSION

Comparison of Temperature Peaks Difference in ED and PF breast model

Temperature peaks in all case studies were compared between ED and PF, for tumour located at x = 1.8 cm

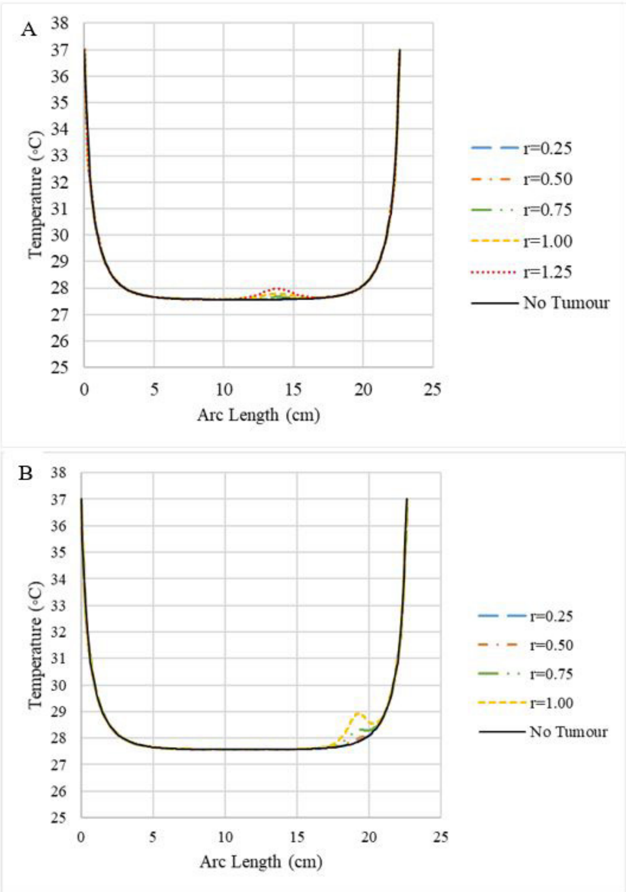

Figure 3: Analysis in PF breast models. (A). All cases in PF breast at x = 1.8 cm (B). All cases in PF breast at x = 5.4 cm

and x = 5.4 cm as shown in the following figure. Fig. 4 shows the difference of temperature peaks on breast surface when the size of tumour was varied for both breast models. Peak temperature difference was attained by calculating the differences in temperature at the highest peak at with and without tumour cases.

The finding shows that the bigger the size of asymmetry tumour embedded at the breast in both ED and PF breast levels, the larger the increase on breast skin temperature. Based on Fig. 4, the largest increment in breast surface temperature is shown in “ED x = 5.4 cm” among the five curves in both breast densities. The smallest increment was at “PF x = 1.8 cm”.

For a more comprehensive and better understanding, we could compare how significant the peak of temperature increased while the size of tumour (radius) changed by 1 cm. When tumour size was increased, greater peak temperature was the most dynamic in “ED x = 5.4 cm”. The temperature was increased by 2.92 °C as the radius increased to 1 cm. The increase in temperature peaks was the lowest at “PF x=1.8 cm” with only 0.21 °C. There are higher dynamical changes in breast surface temperature occurs when tumour is approaching the nearest end of the edge of breast in an extremely dense breast of women.

Case studies at “ED x = 5.4 cm” shows more dynamic changes in the thermal profile of breast surface compared to others. This proves that tumour embedded nearer to the edge of breast has significant temperature changes compared to tumour embedded near the centre of breast. It is because the tumour is getting closer to the breast skin surface. Besides, ED has higher thermal conductivity than PF thus produce noticeable changes in breast surface temperature. Since PF has thicker fatty layer than ED therefore the thermal conductivity is lower. The amount of heat distributed in layers of PF breast are lesser. As a result, the temperature difference or changes in breast surface is less significant.

Comparison of Thermal Images

Fig. 5 shows series of thermal images gained from the simulation on ED and PF breast models. The images show different tumour location; closer to centre of breast and nearer to the edge of breast at the largest tumour size to show the significant contrast on colour and heat distribution on breast surface of the two types of breast density.

Based on the colour variations shown, the contrast between tumour and normal area in ED breast is more obvious than that in PF breast because ED performs

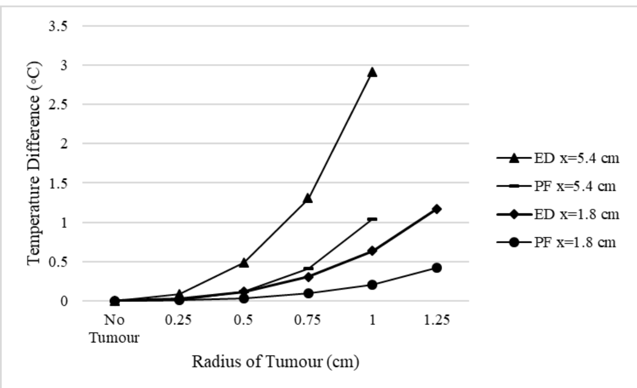

Figure 4: Comparison of Peak Temperatures Difference in both ED and PF breast models at varies tumour size and position

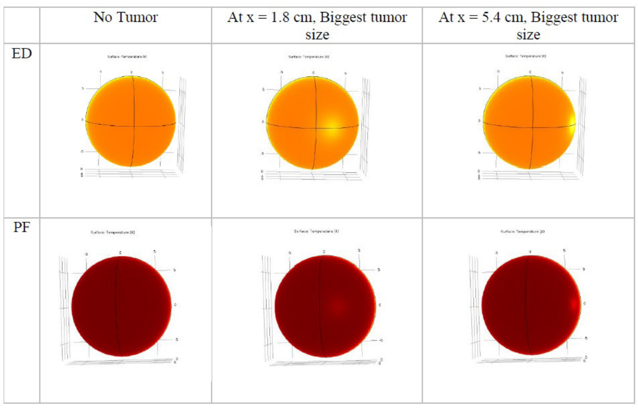

Figure 5: Series of thermal images obtained in ED and PF breast model simulation

higher thermal conductivity than PF breast allowing more heat to be distributed on breast surface, therefore, the temperature variations are more significant than PF breast model.

CONCLUSION

The increase in breast surface temperature is varies depending on the size of tumour presents and the position of tumour inside the breast. As the size of tumour increases, there is also an increment in breast surface temperature in ED and PF breast density levels. This study has confirmed that ED exhibits more significant dynamical changes of breast surface temperatures than PF breast. This finding suggests that when it is applied in medical examination for breast screening purpose, infrared breast thermography is highly recommended to younger women since ED breast density is more distributed in them. Larger tumour size made the width of peak wider while a closer tumour to skin surface made the peak narrower. Therefore, diagnosis using thermography may give higher accuracy on breast where the size of tumour is small (early stage) and nearer to breast skin than tumour that is large and embedded deep in breast. As a conclusion, the effect of tumour size and position in every breast density level should take an account as significant factors in considering the ability of thermography as an adjunctive tool to mammography in breast screening.

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