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FEASIBILITY STUDY OF BREAST CANCER RISK MONITORING USING THERMOGRAPHY TECHNIQUE IN MALAYSIA

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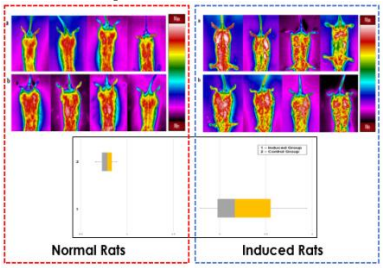
Graphical abstract



Abstract

Breast cancer remains as a serious health issue in Malaysia and most presentation of breast cancer incidences are at the later stage which will reduce the survival rate. Breast Self-Examination for all women (BSE), Clinical Breast Examination for women above 40 years old (CBE) and Mammography for the older and high-risk groups are the current policies that are available in the government hospitals and selected clinics. However, BSE and CBE could not detect the early stage breast cancer while Mammography is less sensitive in detecting tumor in high dense breast tissue. Both factors have caused an increase in the overall percentage of later stage presentation of breast cancer in Malaysia. In this paper, a feasibility study of breast cancer screening and risk monitoring using Thermography technique is presented. Thermography technique is capable in identifying any physiological changes occur prior to lump formation. This technique is simple, cheaper, and produce no radiation which will allow a safe regular screening. In this study, a series of screenings has been performed on carcinogenic induced rats and thermal images acquired were then analyzed for risk monitoring. Visual analysis shown that the presence of hotspot and asymmetrical temperature profile could be an indicator of a high risk patient while temperature measurement on both induced and control groups shows a significant difference in standard deviation of the surface temperature with smaller deviation of 0.31±0.08 observed in control group while bigger deviation of 2.23±0.78 observed in the induced group. Hence, it is shown that Thermography technique could be a potential modality for upfront breast screening in Malaysia.

Keywords: Breast cancer, thermography, risk monitoring, regular screening

Abstrak

Kanser Payudara adalah isu yang serius di Malaysia dan kebanyakan pengesana insiden kanser payudara adalah pada peringkat akhir dan boleh mengurangkan peluang hidup. Pemeriksaan Payuara Sendiri (BSE), Peperiksaan Klinikal Payudara (CBE) dan Mamografi untuk wanita berisiko tinggi dan selepas 50 tahun adalah kaedah semasa yang terdapat di hospital kerajaan dan klinik terpilih. Walau bagaimanapun, BSE dan CBE tidak dapat mengesan kanser di peringkat awal manakala Mamografi kurang sensitif dalam mengesan tumor pada wanita muda. Kedua-dua faktor ini telah menyebabkan peningkatan dalam peratusan keseluruhan persembahan peringkat akhir kanser payudara di Malaysia. Dalam kertas kerja ini, kajian kemungkinan pemeriksaan kanser payudara dan pemantauan risiko menggunakan teknik Termografi dibentangkan. Teknik Termografi mampu mengenal pasti sebarang perubahan fisiologi yang berlaku dengan lebih awal. Teknik ini lebih mudah, murah, dan tiada radiasi membolehkan pemeriksaan berkala dialkukan dengan selamat. Satu siri pemeriksaan telah dilakukan ke atas tikus teraruh karsinogenik dan imej haba yang diperolehi kemudiannya dianalisis untuk memantau risiko. Analisis visual menunjukkan bahawa kehadiran kawasan panas dan profil suhu

simetri boleh menjadi penunjuk pesakit berisiko tinggi manakala pengukuran suhu di kedua-dua kumpulan karsinogenik dan kawalan menunjukkan perbezaan yang signifikan dalam sisihan piawai suhu permukaan dengan sisihan kecil iaitu 0.31 ± 0.08 dalam kumpulan kawalan manakala sisihan yang lebih besar iaitu 2.23 ± 0.78dalam kumpulan teraruh. Ini menunjukkan bahawa teknik Termografi boleh menjadi modaliti potensi untuk pemeriksaan payudara pendahuluan di Malaysia.

Kata kunci: Kanser payudara, termografi , pemantauan risiko, pemeriksaan berkala

1.0 INTRODUCTION

Breast cancer is the most common cancer among women worldwide. In Malaysia, based on the National Cancer Registry report in 2007 shows that breast cancer is the top leading cancers (18.1%) in overall population across all ethnic groups [1,2]. With a cumulative risk at 5.0, Malaysian women had a 1 over 20 chance of developing breast cancer in their lifetime. Early detection of tumor is one of the important determinants for better survival rate and early treatment [3]. However, Malaysian women are generally diagnosed with breast cancer at later stages of breast cancer compared to other developing countries where 30-40% of the total reported were at Stage 3 and Stage 4 and most of the cases reported (90%) were due to the presence of lump in the breast with the mean size of 4.2cm [4,5]. Currently, there are common three procedures available in Malaysia namely breast self-examination (BSE) , clinical breast examination (CBE) and regular mammography screening that have to be carried out by the women especially those in high-risk category with family history to monitor their risk of having breast cancer [6] . While BSE and CBE procedures are only effective when the tumor has grown to a later stage where lump palpation is possible, mammography screening shown to be less effective for younger and pregnant women due to high dense breast tissue and excessive exposure to radiation respectively [7–11].

On the other hand, previous studies on breast cancer incidence in Malaysia have shown that Malaysian women diagnosed with cancer are those in their early age compared to Western countries where approximately 50% of women were diagnosed before reaching 50 years old due to the younger demographic profile of Malaysian population [12]. Besides that, different lifestyles these days have caused an increase in risk of breast cancer cases [13–16]. These 2 factors viz. detection in young women and detection in low-risk women are essential to be addressed in order to allow an early breast cancer screening among Malaysian women for better risk monitoring and prevention.

Thermography technique has shown to be a potential adjunctive modality in detecting early stage breast cancer for all women regardless of their age groups. This technique is capable of providing a functional information on physiological aspect of the breasts due to the changes of their thermal and vascular properties prior to lump formation. In addition, thermography also has other advantages such as non-invasive, radiation-less and low cost which allow this technique to be a safe and friendly screening modality [17–19]. Although, some studies showed that thermography could not replace the current gold standard modality, a lot of studies have been carried out to improve the total accuracy of this technique with concurrent advancement in the hardware development [20–22]. Thus, the aim of this study is to investigate the feasibility of thermography technique used for breast cancer risk monitoring in Malaysia context.

1.1 Thermal Breast Imaging

Physiologically, breast with developing cancerous cells will appear warmer compared to the surrounding healthy tissues due to increase in metabolic heat generation and angiogenesis which have eventually contribute to the skin surface temperature alteration via the heat conduction and convection processes occurring within the tissues and the blood vessels. The overall bioheat transfer mechanism occur in the biological tissue can be represented by Pennes bioheat transfer model (PBHT) as shown in equation (1) [23].

$$pc\frac{dT}{dt} = -\nabla.k\nabla T + p_b c_b w_b(T_a - T) + Q_m \quad (1)$$

where p and c are the density and specific heat capacity of the tissue respectively, T represents the tissue temperature, k is the thermal conductivity while Q_m represents the volumetric metabolic heat generation rate. w_b is the blood perfusion rate, p_b and c_b denote the density and specific heat capacity of blood respectively and $T_a$represents the arterial blood temperature.

On the other hand, thermal images obtained by the infrared thermography camera captured the total infrared radiation emitted by the objects (as shown in equation (2) whose temperature is above absolute zero Kelvin at a different wavelength distribution and

converted them into a visual thermal image format [25,26].

$$E_{total} = E_{emitted} + E_{reflected} + E_{transmitted} \quad (2)$$

Hence, different temperature profile obtained via these images were used to detect and analyze the abnormalities presence underlying the skin surface.

2.0 MATERIALS AND METHODS

2.1 Sample Preparation

The use of animal models in this study has been approved by the institutional review board of Universiti Kebangsaan Malaysia, Animal Ethics Committee (UKMAEC), Selangor, Malaysia with the ethical endorsement approval reference number Utm/FBME/2014/Jasmy/21-May/583-May-2014-Dec 2015. The entire experiment was conducted in the Animal Laboratory, Faculty of Bioscience and Medical Engineering, Universiti Teknologi Malaysia (FBME, UTM), Johor, Malaysia

Two groups of female Sprague-Dawley rats weighing between 180-250g were used in this study. First group consists of fifteen rats were used for control purposes while another fifteen rats were induced with 7,12-dimethylbenx(a)anthracene (DMBA) via subcutaneous injection beneath the mammary gland of either side. All rats were regularly monitored for water consumption and food and they also underwent weekly weigh in and palpation. The induced rats were also allow for 2 weeks adaptation before the weekly screening begin. All rats were housed in polypropylene cages with wood shavings as bedding at an ambient room temperature, as well as access to water and food *ad libitum* with a 12 hour light/dark cycle.

2.2 Image Acquisition

A 12-weeks weekly screening has been conducted using an Epidermal Thermal Imaging Professional (ETIP) infrared imaging camera system model 7640 P-Series, manufactured by Infrared Camera Incorporation, Texas USA. The camera is fixed-mounted on the flexible metal bar and connected to the display monitor. The distance of the camera to the sample was manually controlled to obtain the best display output. The room temperature was controlled and maintained between at 20 – 22 degree Celcius with a relative humidity of 60-65%. The fluorescent lights available in the room were turned off during screening procedure. The rats were allowed to acclimate at room temperature for 15 minutes before screening. Rats were then placed in front of the camera in their anterior position for image capturing. A set of protocols has been developed and followed before, during and after the screening processes [24].

2.3 Image Comparison and Analysis

A total of 120 thermal images obtained from the screening sessions were compared from both qualitative and quantitative aspects. Manual region segmentation and selection were carried out to identify the possible hotspot regions for both analyses focusing on mammary gland area.

For qualitative analysis, visual comparison for both control and induced rats were made for at least 4 selected consecutive weeks of screening period. Factors such as asymmetrical surface temperature contour, hotspot identification and hotspot position were observed from the thermal images alone. Next, a quantitative analysis was carried out to measure the maximum temperature, mean temperature and standard deviation of surface temperature using both thermal images and data temperature output from the system. Finally, a comparative analysis was made using the identified features between both induced and normal rats.

At the end of the experimental works, rats were then euthanized by using drug overdose method to harvest the breast tissue sample which were then send to Pathology and Clinical Laboratory (PATH Lab) in Johor, Malaysia for disease identification by a certified pathologist. Based on the result obtained, the samples were diagnosed with high grade invasive ductal carcinoma.

3.0 RESULTS AND DISCUSSION

3.1 Visual Analysis

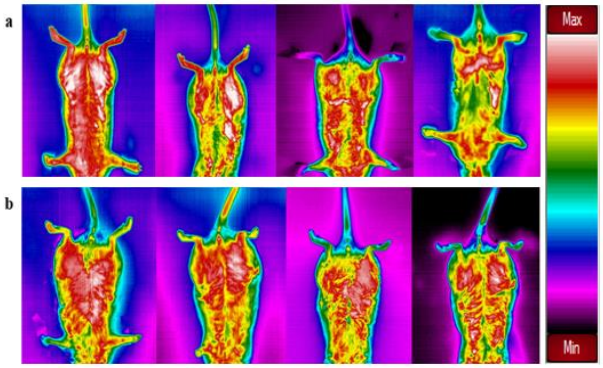


Figure 1 Four consecutive weeks of Thermal Images output for a) Induced rat sample 1 and b) Induced rat sample 2

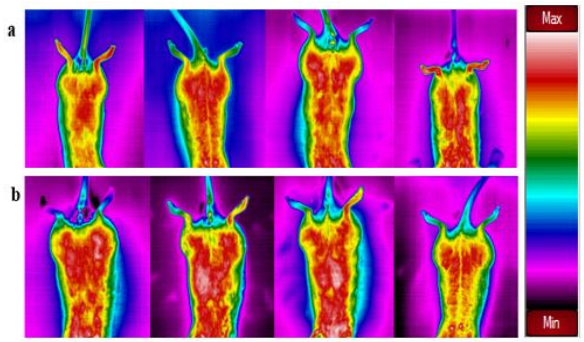


Figure 2 Four consecutive weeks of Thermal Images output for a) Control rat sample 1 and b) Control rat sample 2

Figure 1 and 2 show the output of a series of thermal images obtained for both induced and control rats. Induced rat sample 1 images were taken from week 6 to week 9 while for induced rat sample 2, the images were taken from week 2 until week 5. On the other hand, for control rat sample 1, the images were taken from week 1 until week 4 and control rat sample 2 images were taken from week 5 until week 8. Visual analysis shown that for induced rats, a clear asymmetrical temperature profile can be seen in all screening session and contrarily to the control group, where their symmetrical temperature profile can be observe throughout the 4 weeks screening. Besides that, it can also be seen that as the tumor grows in in the induced group ,the overall skin surface has appeared to have higher temperature difference compared to control group where no obvious physiological changes occurred. Finally, by observing the thermal images, the analyst would be able to pre-locate the position of the hotspot easily. For example, in the thermal images of induced rat sample 1, a consistent hotspot appears on bottom right breast. Table 1 shows the summary of visual observation and physical assessment made on both groups. Note that physical assessment is not for the analyst to consider during image observation.

Table 1 Summary of images features observation and physical assessment on both groups

1) Image Features	**Induced**	**Control**
Symmetrical profile	No	Yes
Obvious hotspot	Yes	No
Overall changes	Yes	No
2) Physical Assessment	**Induced**	**Control**
Palpation (Vary in weeks)	Yes	No
Weight	Reduces	Increases
Daily routine	Reduces	Active

3.2 Temperature Data Analysis

Although visual analysis alone could provide the initial observation between these 2 groups, temperature data analysis is required to clearly verify their significant difference as visual analysis might be prone to human error. As explained in Section 2.3 , a manual segmentation has been adopted to retrieve the temperature data from the system. Figure 3, 4 and 5 show the boxplot of maximum temperature, mean temperature and standard deviation of temperature respectively for all samples used in this study.

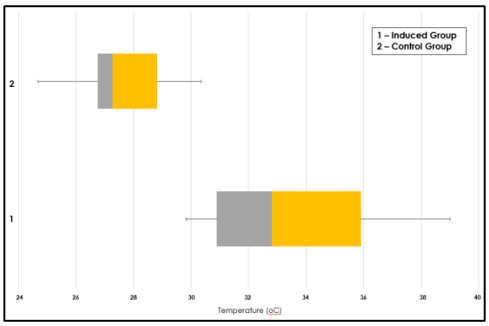


Figure 3 Maximum temperature for both groups

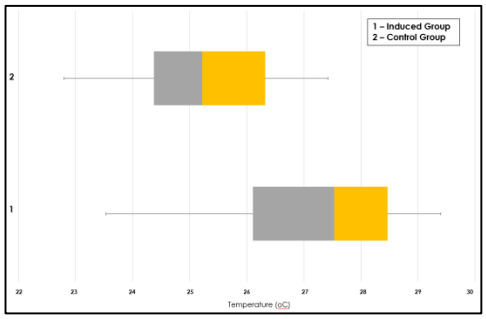


Figure 4 Mean temperature for both groups

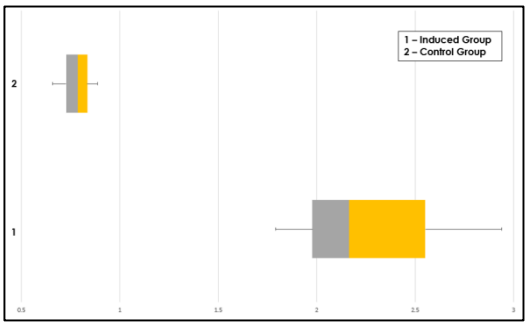


Figure 5 Standard deviation of surface temperature for both groups

Out of these 3 temperature measurements made on the induced and control rats, mean temperature distribution shown to be the least significant feature that could distinguish between high risk and low risk categories as shown in Figure 4, while maximum temperature distribution portrayed a better profile that could be used as one of the differentiator between both groups with minimal error. However, part of quartile 3 of the maximum temperature in control group could be inaccurately measured in the first

quartile of maximum temperature of the induced group. Nevertheless, the last factor which is the standard deviation of the temperature shown to be very significant where smaller deviation (0.31±0.08) noticed in control group while bigger deviation (2.23±0.78) can be observed in the induced group. This is due to the hotspot area presence on the surface which has caused an increment in the local temperature difference. Hence, for quantitative analysis, standard deviation measurement range could be used as a robust indicator for risk monitoring purposes. Other types of analysis could also be integrated for better result however, high computational load and time might be required [21,27–29].

4.0 CONCLUSION

As a conclusion, this feasibility study has shown that thermography technique could be a potential breast cancer risk monitoring modality that can be positioned as an upfront screening tool prior to other advanced procedures or early intervention. In Malaysia specifically where there are still a lot rural areas with minimal facilities, mammography shown to have more drawbacks in term of cost and its complicated procedures which eventually reduced the possibility of carrying out mass screening to the low-risk population group. Although, there is still improvement in its technical and image processing aspects, thermography technique has proven to be a simple modality, cheaper and suitable for regular screening due to its non-radiation exposure. After all, biopsy is the ultimate procedure that will determine whether one can be diagnosed with cancer or otherwise. This study also suggests that beside visual analysis, a significant standard deviation of the surface temperature value obtained could be used to monitor the risk of each thermal image. However, since animal model is used in this study, the data range presented is not meant for human data comparison and reference. A further study on human need to be conducted in future to obtain the real data range for clinical application.

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