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Initial Evaluation of Human Supervised Automated Breast Cancer Screening Using Thermography

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Abstract

Breast cancer has the highest incidence among cancers in women, in India and world-wide. Screening and early detection play a large role in reducing mortality as breast cancer can be cured if it is detected in the early stages. Mammography is considered the gold standard in screening, but it is not useful for younger women due to low sensitivity with denser breasts and its harmful X-rays can cause an increase in the risk of cancer if used frequently. Sono-mammography is typically used in correlation. Incidence rates are rising in younger women as compared to previous decades, due to changes from environmental pollutants and socio-economic reasons. This is causing a relook at thermography for low cost and non-harmful screening. In this paper, an automated thermographic screening tool is used to classify 108 subjects from the patient database of Central Diagnostic Research Foundation, a diagnostic clinic. In addition to classification, the location of the suspected tumor is also highlighted on the thermography images. The results are promising with 100% sensitivity and 73% specificity. The algorithm used is novel, which combines features obtained from the temperature distribution of the subject, in a personalized manner, to classify as well as localize the tumor.

1. Introduction

Breast cancer is the leading cause of cancer deaths for women worldwide as well as in India, with around 5,00,000 and 70,000 in the world and India, respectively, in 2012. It also has the highest incidence among cancers in women, with 1.7 million and 145,000 diagnosed worldwide and in India, respectively, during 2012 [1]. Breast cancer is curable, with a high survival rate of 97%, if diagnosed in the early stage [6]. This can be achieved by regular screening. Mammography is the current gold standard for breast cancer screening. However, mammograms not only are less sensitive at detecting tumors in young women due to denser breast tissue, but also are harmful enough to cause cancer in young women due to the radiation exposure [6]. The sensitivity of mammography falls from 83% in less dense tissue to 55% in the highest density tissue [6]. While no empirical studies have directly measured the risk of developing breast cancer due to regular mammographic screening, many simulation models have been used to estimate risk depending on the dosage of radiation, frequency of screening and age when screening started[3-5]. The most recent estimate was of 125 breast cancers and 16 deaths per 100,000 women in US screened annually from 40 years to 74 years [3]. For women with BRCA mutations who have a high risk of developing breast cancer at a young age (<40 years) and are recommended to undergo screening from as early as 25 years, mammography's risk of inducing cancer negates its benefits of detecting cancer if used for annual screening below 35 years[4]. Even for a single screening mammogram at 35 years, the lifetime risk of radiation-induced breast cancer is 11 per 100,000 women [5]. Sono-mammography is another commonly used modality, which is typically used in correlation with mammography as its standalone approach has too many false positives and false negatives for screening [7]. In general, there have been insufficient large scale studies on other modalities of screening [8]. Thermography is evaluated here as an alternative imaging modality for breast cancer screening.

Breast cancer incidence is increasing in younger women presently as compared to previous decades. Due to excessive use of chemicals in our modern society, that causes adverse effects on our bodies, we are seeing problems that were not heard of a hundred years ago. One such risk factor is xeno-hormones, a group of man-made laboratory synthesized chemicals that are hormonally active agents [9,10]. Many of these xeno-hormones are proven carcinogens [9,10]. They are also well known for their ability to damage the immune system and interrupt hormonal balance. Our cells can't always distinguish fully between our own hormones and xeno- hormones. The xeno-hormones that mimic the female hormones, estrogen and progesterone, increase the risk of breast cancer. Synthetic estrogens and progestins are found in oral contraceptives and conventional synthetic hormone replacement therapies [11]. Estrogen dominance is probably the leading cause of breast cancer risk from hormones [10]. All American-grown, non-organic livestock are fed estrogenic drugs to fatten them. Also, the grains they are fed are laden with chemical sprays that accumulate in animal tissue and promote hormone disruption in the person consuming them. Petro chemically-derived pesticides, herbicides and fungicides are also sources of xeno-hormones [9]. The chemical Bisphenol A (BPA) used in plastic bottles, containers and almost all food-can liners is also a xeno-hormone [12]. Exposure to Bisphenol A has shown an increased incidence of breast and prostate cancers. Solvents found in fingernail polish and polish remover, glue, have been found

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to have the same cell proliferative properties and endocrine disruption. Emulsifiers found in soaps and cosmetics of the past and present are also risk factors. Skin being the largest organ is very capable of transferring chemical through it at a highly efficient rate.

Thermography is useful in screening for breast cancers that are affected by hormonal activity[6]. Thermography measures the infra-red radiation emitted by the body [6]. The increased metabolic rate of malignant cells and the neo-vascularity and angio-genesis caused by cancer, increases the temperature compared to the surrounding tissue, which is visible in thermographic images. There was research in the 1970's and 1980's on thermography for breast cancer screening [13,14] and thermography got approval by FDA since 1982 as a risk predictor for cancer [6]. However, the lower sensitivity and specificity compared to mammography reported in a study in 1977 [15] resulted in a decline in its usage. With the advent of high resolution thermal cameras, there is a relook at thermography [16]. In a study of 100 subjects with carcinoma [16], the sensitivity of thermography was 83%, and its value is in signaling abnormality in younger subjects with carcinoma where mammograms or clinical examination did not detect malignancy. Thermography may be able to detect malignant tumors 5 years before mammography [14]. Breast cancers that grow due to hormones have abnormal thermograms[17]. Their progression is also faster. Thermography can help in detecting women at high risk for cancer. The thermal cameras are also of lower cost, small and mobile, enabling non-contact and non-invasive screening for large populations in non-hospital settings. These advantages could be useful especially in less developed countries like India where cost and availability of hospitals play a vital role in screening.

Automatic screening algorithms can help in outreach to large populations, as doctors can focus on a fewer number of suspicious cases for further analysis. There have been several semi-automated algorithms for breast cancer screening with thermography [18,19] whose specificity and sensitivity is comparable with that of mammography, but have been tested on only a small number of subjects. Ng et al [20] report a sensitivity of 86% and specificity of 91% on 25 normal subjects and 25 subjects with malignant tumors in stage 2 or stage 3 cancer. Most of these approaches use textural features and temperature moments for classification with standard classifiers. In this paper, we use a feature fusion based segmentation algorithm designed in our previous work [21] for high sensitivity to determine the specificity in a dataset consisting mostly of normal subjects and benign tumor subjects.

2. Data description

Anonymized subject data has been obtained from the diagnostic clinic of Central Diagnostic Research Foundation through a collaboration. This data has been obtained from a subset of the subjects coming to the clinic over the past four years for breast examination. These subjects had come either for regular breast cancer screening or for diagnosing a clinical condition of the breast. The data included thermal images, and the radiologist/thermographer's report having thermography and sono-mammography (ultrasound) findings and conclusions obtained from combining the findings from both modalities. It also included subject demographic data, including age, gender, medical history of the subject such as pregnant or lactating, clinical complaints, as well as personal history and family history of cancer.

The thermographic data has been obtained from the Meditherm camera, with a resolution of 690×478 pixels. There is a specific protocol for capturing the thermography images of the subject. The subject is asked to wear a loose fitting gown and wait in an AC room for 15 minutes so that there is normalization of body temperature and external heat conditions are minimized. The subject is then seated on a swivel chair at a fixed distance from the thermography camera. The camera focus is zoomed in so that only the relevant region of the subject's body is captured; from below the neck to just below the infra-mammary fold. The subject's chair is also swiveled so that the angle of capture is exactly frontal, at ±45° oblique, i.e. right and left oblique, and right/left lateral. The thermography camera temperature range is also calibrated within 8°C range for each subject, with the maximum temperature of this range corresponding to the maximum body temperature of the person. This would allow the maximum body temperature of the person to be observed at the color corresponding to the image's maximum temperature (in this case white). This is to assist in visual interpretation of the image by the radiologist/ thermographer. Figure 1 shows sample images of a normal subject. In this paper, the default view of the Meditherm camera is used, which shows the isotherm view, where pixels within every 0.5°C range are shown in a different color. The default views of the same subject are shown in figure 2. The thermographers/radiologists find this isotherm view helpful and typically make most of their observations based on this view.

The data used in the paper consists of 108 subjects, with statistics as given in table 1. Mostly normal subjects are presented in this data, with a significant percentage of subjects with benign tumors, such as simple cysts, fibroadenoma, and fibrocystic disease. There are five cases of cancer. Among normal subjects, there are a few cases of subjects who have a high hormonal response that places them at a higher risk of breast cancer, as well as faster growing cancerous cells, if breast cancer develops. There is one case of infection in the ribs. In screening the general population of women, it is expected that mostly normal subjects would be observed, with a significant percentage of women having benign tumors and/or inflammatory/infectious conditions, and a few subjects with malignancy that depends on the breast cancer incidence rates of that country/population.

3. Automated screening software features

The breast cancer screening tool (figure 3 to 7) allows the user to analyse thermal images for semi-automatic detection and classification of breast tumours. The tool consists of three sections: 1) patient data acquisition, 2) thermal data analysis, and 3) conclusion, data storage, and report generation.

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3.1. Patient data acquisition

This section of the software tool captures relevant information needed as a pre-requisite for patient classification and conclusion. The section allows the user to enter patient demographic information, patient cancer history, family cancer history, patient medical history, patient complaints, and clinical examination. The information captured in this section helps to evaluate the probability of a patient developing breast cancer. For example, history of cancer present in patient and/or her family increases the chances of developing cancer in the future. Patient medical history plays an important role in final diagnosis of the patient; for e.g. medical history like pregnant or lactating mothers suggests that it might lead to temperature increase seen in the thermal images. Moreover, medical history of patient gives insight into any benign conditions that may lead to cancer. Patient complaints and clinical/physical examination give relevant information on the present condition of the patient, which include important data on hormonal levels, breast nodules, and other factors. The entire acquisition section captures data to help evaluate the patient condition in a holistic manner.

3.2. Thermal Analysis

This section of the tool focuses on performing thermal analysis on the captured thermal images of the patient. The following operations summarizes the thermal analysis section:

Load: The thermal images of the patient are captured in different views like frontal view, lateral view, oblique view etc. The tool allows the user to load all those thermal images, browse through them, view them in infrared view or 2D contour view (contour view is created by temperature separation of 0.5 degree Celsius).

Crop: Once all the thermal images are loaded, the tool allows the user to crop the regions of interest from all the images. These cropped regions will be input for the auto-detect tumor algorithm as well as the manual-select process.

Auto-detect: After the cropping operation is over, the tool enables the auto-detect button which when clicked by the user will initiate the tumor auto-detection algorithm. If any suspected tumor detected, the algorithm highlights the tumor region, displays it in the best possible view and displays a message saying “suspected malignancy detected”. If no suspected tumor is detected, then it just displays the frontal view thermal image with a message “no tumor present”. The tool provides the user the facility to confirm whether the output of auto-detect algorithm is correct or not. This is important to improve the accuracy of the auto-detect tumor algorithm.

Manual-select: After the auto-detect tumor process is done, the tool enables the manual-select process. The user chooses the desired cropped region and clicks on the manual-select button. The cropped region is displayed in 2D contour view and allows the user to mark the suspected tumor regions. The manual-select algorithm is then processed and the best possible thermal image view along with the highlighted suspected tumor region is displayed. The user perform the manual-select process only when the user suspects any tumor is present.

Comments: The tool provides the facility for the user to enter the thermobiological score of the patient and quadrant-wise comments for right breast and left breast with respect to the captured thermal images and above mentioned processes.

3.3. Patient evaluation, data storage and report generation

This section of the tool concludes the patient evaluation, persists all data collected from other sections of the tool, and generates report for documentation purposes. It evaluates the acquired patient and thermal information to classify the patient as normal, benign, malignant, or bilateral. All this data is then stored in a database that contains records of all breast cancer screening patients; the information can be captured from the database and edited and analysed further using the tool. Also, report containing all the relevant data is generated for doctor’s reference.

4. Automated screening algorithm

In this paper, we are using human supervision through the screening software for locating the breast regions, i.e. our Regions of Interest (ROI). Fully automated ROI location is difficult, as the region is amorphous and needs to be located at different angles in the different images. Current approaches to automate ROI segmentation have been generally done on just frontal images [19] through heuristic approaches and hence are very noisy, as the body shape of subjects vary. Our approaches to ROI selection through human supervision and automated algorithms for classification & localizing the tumor are described in the following sub-sections.

4.1. Regions of Interest selection through human supervision

The right and left breast regions from the thermograms are the Regions of Interest (ROI) to us here to determine the presence/absence of cancer or any abnormality. The infra-mammary folds are hot normally due to friction, and hence were not considered in the ROI. The lymph nodes in the axilla regions are also possible regions where there may be metastasis of breast cancer and are typically examined in sono-mammograms. In thermograms, the axilla regions are generally hot due to friction and the presence of lymph nodes. Detection of abnormalities in the axilla regions from thermography are out of scope in this study, although it is an interesting topic for future research.

http://dx.doi.org/10.21611/qirt.2015.0074

Six thermal images are captured for each cancer subject. The right/left breast region is then manually segmented using a free-form selection in the software described in Section 3. Figure 8 shows the segmented ROIs from a sample subject.

4.2. Automated localization and classification algorithm on ROIs

The temperature map of the ROIs is obtained from the camera's temperature colorbar. From the ROIs, the tumor detection and location is done automatically using a multi-feature fusion algorithm [21]. The split-and-merge segmentation approach is used to detect/locate the tumors, although other segmentation approaches could be used. The novelty lies in the usage of multiple features, their decision-based fusion and in using subject specific thresholds based on their temperature distribution.

Cancerous tumors are typically "hot", and are significantly hotter than the surrounding tissue. Small tumors in the earlier stages of cancer growth are "warm." As the surface body temperature is observed to vary by a few degree centigrade across subjects, the temperature thresholds to determine "hot" areas need to be subject-dependent, and based on the temperature distribution over the ROIs. Weak edges in the temperature map can also be obtained around the tumors, but may not have closed boundaries. Temperature thresholds based on the temperature distribution and edges around the tumor may be used to detect the tumor region. The following set of features are used to decide if a particular block in the ROI belongs to a tumor or not.

1) The temperature threshold θ_1 based on the temperature distribution in the ROIs: If k_1% of the block has temperature above threshold θ_1, decide as tumor.
2) Another temperature threshold θ_2 based on the maximum temperature in the ROIs: If k_2% of the block has temperature above threshold θ_2, decide as tumor.
3) A temperature threshold θ_3 based on normal body surface temperature: If k_3% of block has temperature below θ_3, decide as normal.
4) Edges around the tumor: If the edge length is k_4% of the block perimeter, decide as tumor.

These block decisions are combined using a decision fusion rule to maximize cancerous tumor detection and minimize false positives. The optimal decision fusion is based on the inter-dependence of these features in tumor detection. More details on selecting the optimal fusion rule is found in [22]. Figure 3 and 4 shows the tumor location on sample subjects with cancer.

5. Results of automated thermal screening with human supervised ROI selection

The algorithm described in Section 4.2 is tuned to maximize tumor detection in cancerous subjects. In this dataset, θ_1=mode+0.5(max-mode), θ_2=max-2°C, with max denoting the maximum temperature, k_1=k_2=k_3=100%, and with the global decision as tumor block if decisions 1) and 2) and 3) decide as tumor block. The results of automatic tumor localization and classification is shown in table 2 and figure 9. There is 100% sensitivity as all cancerous cases and the suspicious case were declared as suspicious by the automated screening, and the tumor regions were correctly localized. There is 73% specificity. Among the errors, i.e. normal/benign tumor cases declared suspicious by the automated algorithm are in a)12 of the 14 cases where the radiologist required a repeat study after 3 months, 6 months, or over a year, as he felt they needed regular monitoring to rule out malignancy, b) 9 cases where external heat conditions caused a rise in temperature in parts of the body, c) 3 high risk subjects who had a high hormonal response. It is better to have additional stages of automated classification after this automated algorithm to re-classify the suspected subjects into those that are at high risk for cancer and/or require regular monitoring. The imaging protocols can be modified or additional questions to the subject can be asked to rule out external heat conditions. The imaging protocols can include an additional cooling step, where cool air is blown on the subjects to normalize the external heat conditions. This can be done even after an initial evaluation. If the heat persists after this additional cooling protocol, then it would be due to malignancy, inflammation or infection. Questions could include whether the subject was exposed to some external conditions causing heat generation.

5. Conclusions and Future Work

A subset of 108 subjects from the patient data of Central Diagnostic Research Foundation were categorized by the radiologist using age, gender, medical history, history of cancer in the patient and her family, thermography and sono-mammography data findings. We have demonstrated an automatic breast cancer screening tool on thermography data from this clinic. This tool also has visualization features to assist the doctors or thermographers in their diagnosis. Using automated thermographic breast cancer screening on 108 subjects consisting of normal subjects, benign tumor and malignant tumor subjects, promising results of 100% sensitivity and 73% specificity was obtained. The specificity of automated screening could be improved in future with better imaging protocols, such as cooling the subject to remove heat generated by external causes. The specificity can also be improved with additional algorithms that determine high risk subjects with excessive hormonal responses and that separate borderline suspicious cases into different categories. The screening tool will also be modified in future to take into account the age and medical history along with thermography data to improve sensitivity and specificity. Further tests on larger number of subjects needs to be done to

http://dx.doi.org/10.21611/qirt.2015.0074

determine the possibility of using thermography as a first line breast cancer screening modality, followed by additional tests to diagnose breast cancer.

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Table 1. *Statistics of the subject data used in this paper*

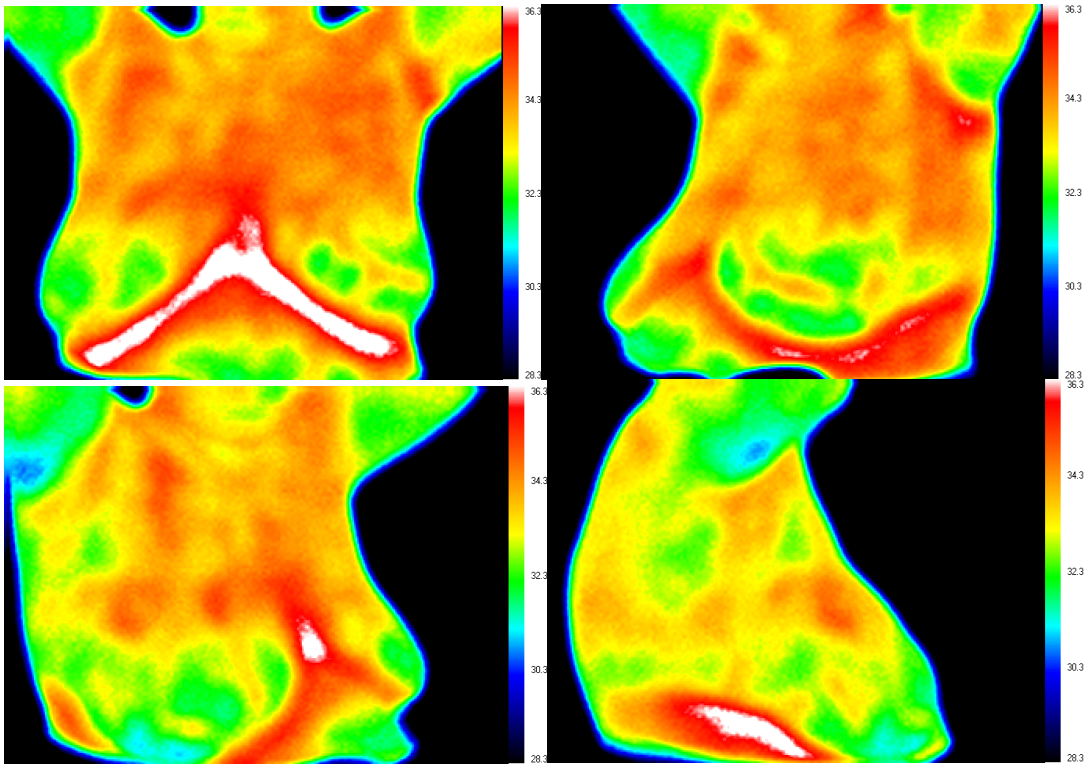
Subject category	**Number of subjects**
Cancerous tumor	5
Benign tumor	38
Normal subjects	60
Suspicious	1
Infection	1
Lactating	2

http://dx.doi.org/10.21611/qirt.2015.0074

Repeat study requested among normal/benign tumor cases	14 out of 98
High risk due to hormonal responses among normal/benign tumor subjects	3 out of 98

Table 2. *Results of automated screening on human supervised ROI selection.*

Subject category	**Number of subjects**	**Classified as suspicious through automated screening**
Cancerous tumor	5	5 out of 5
Benign tumor	38	13 out of 38
Normal subjects	60	12 out of 38
Suspicious	1	1 out of 1
Infection	1	0 out of 1
Lactating	2	1 out of 2
Repeat study requested among normal/benign tumor cases	14 out of 98	12 out of 14
High risk due to hormonal responses among normal/benign tumor subjects	3 out of 98	3 out of 3



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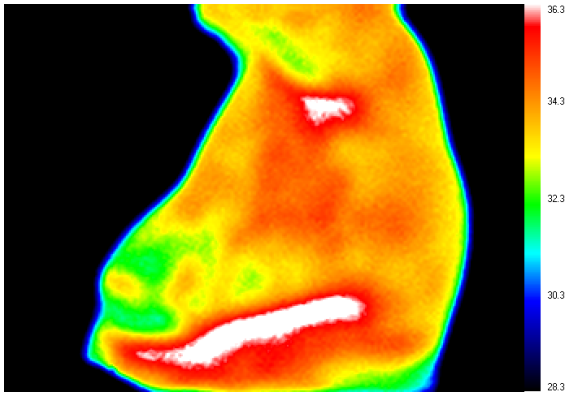
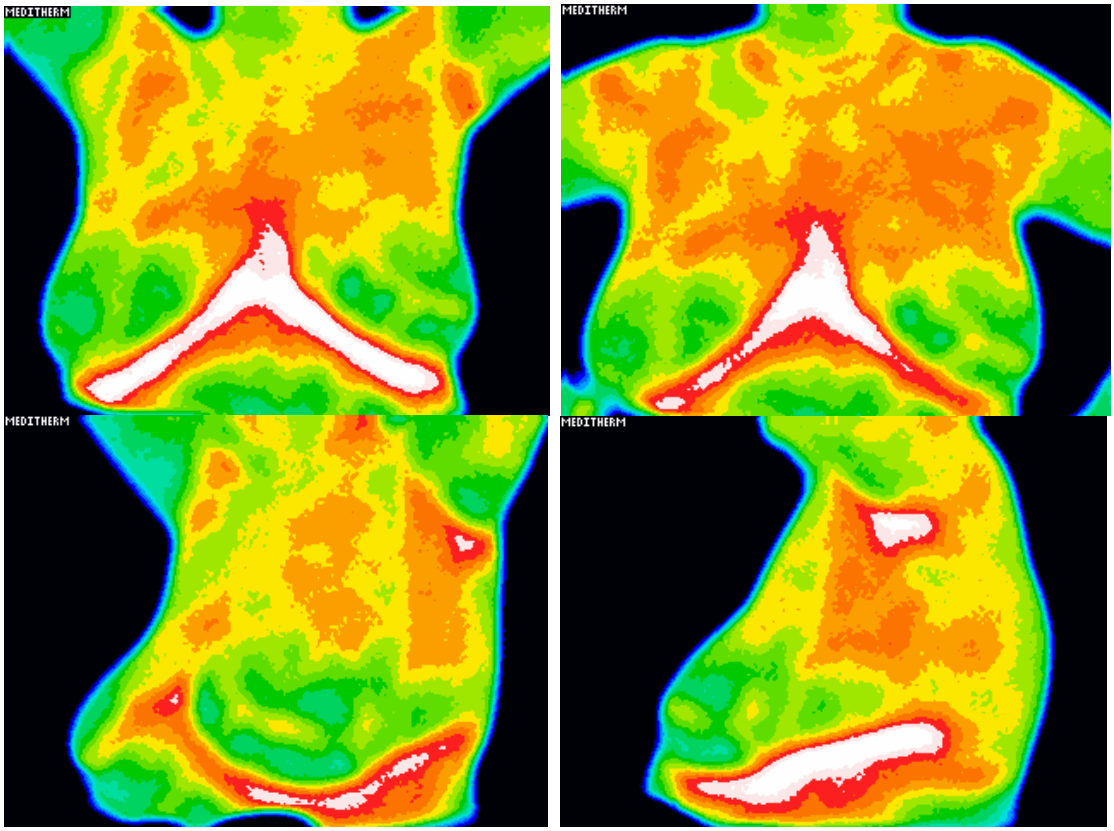


Fig. 1. *Images of a normal subject from the Meditherm camera at a resolution of 690×478 pixels. There is high temperature in the root of the neck and upper part of the chest due to external heat exposure.*



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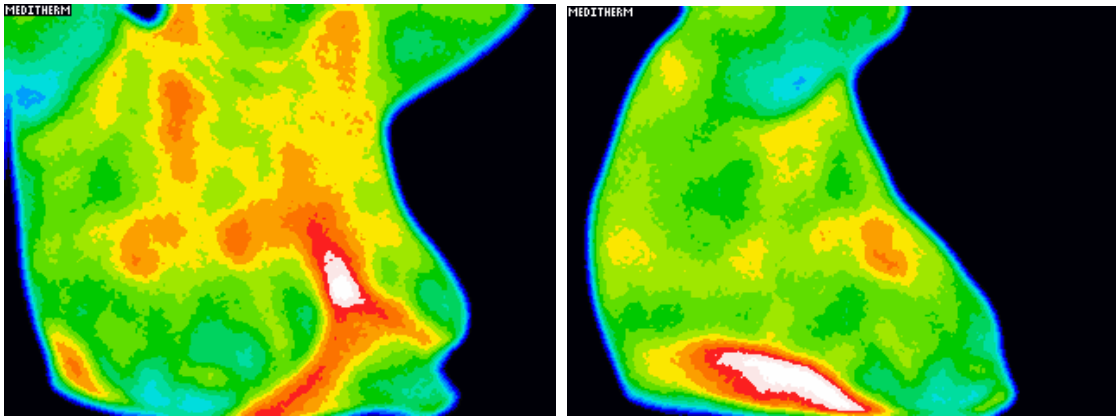

Fig. 2. *Images of a normal subject in figure 1 in the isotherm view, with each color representing a 0.5°C change.*

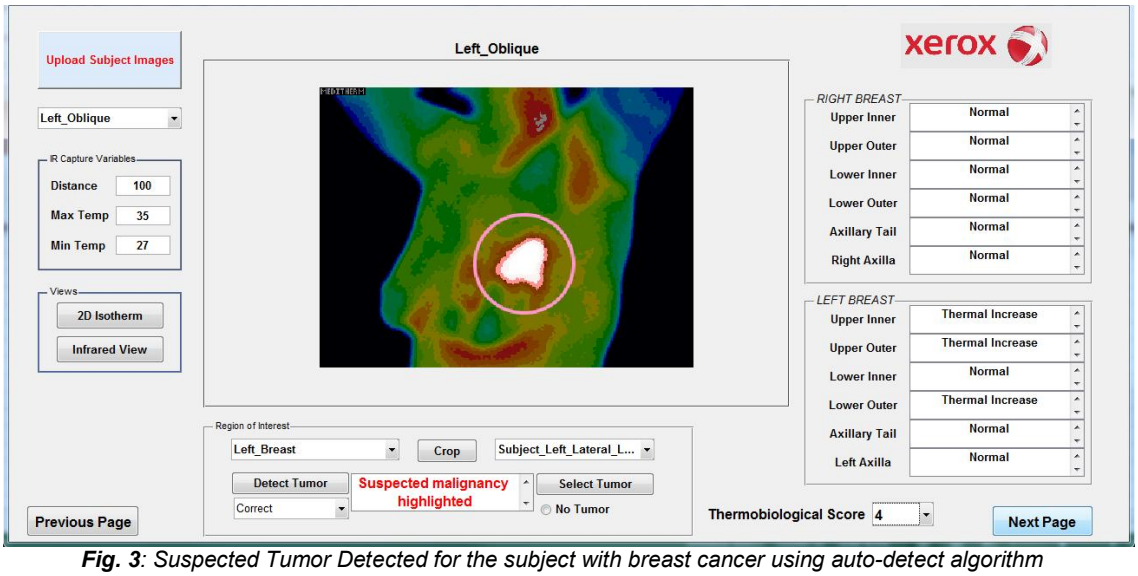

Fig. 3*: Suspected Tumor Detected for the subject with breast cancer using auto-detect algorithm*

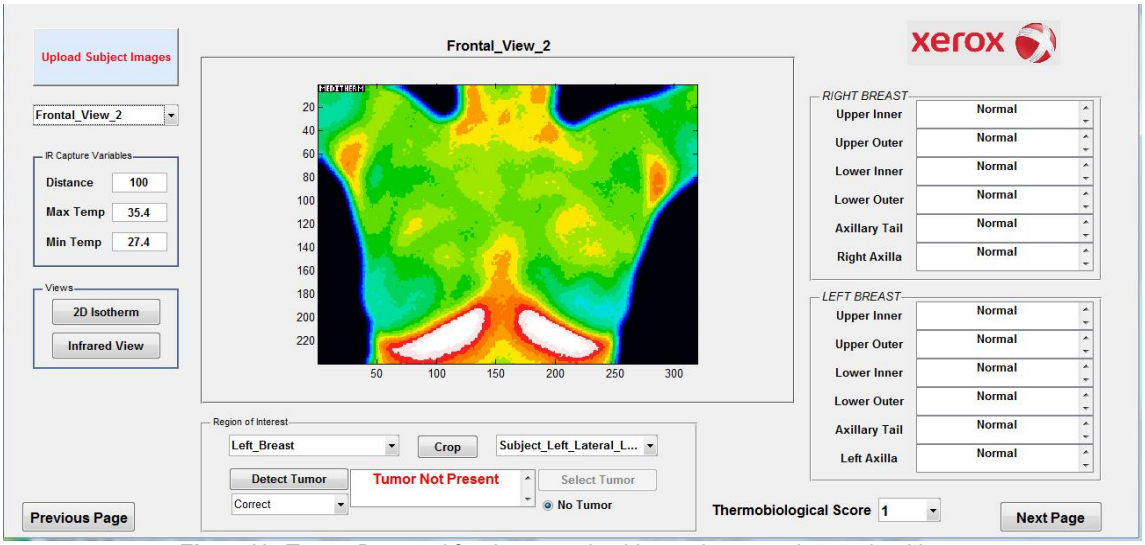

Fig. 4. *No Tumor Detected for the normal subject using auto-detect algorithm*

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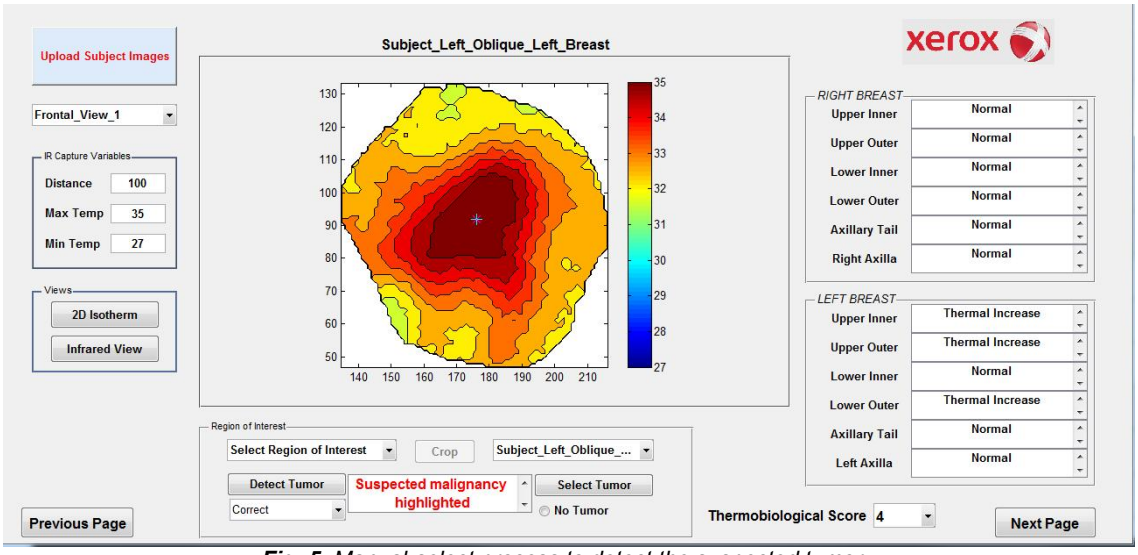

Fig. 5. *Manual-select process to detect the suspected tumor*

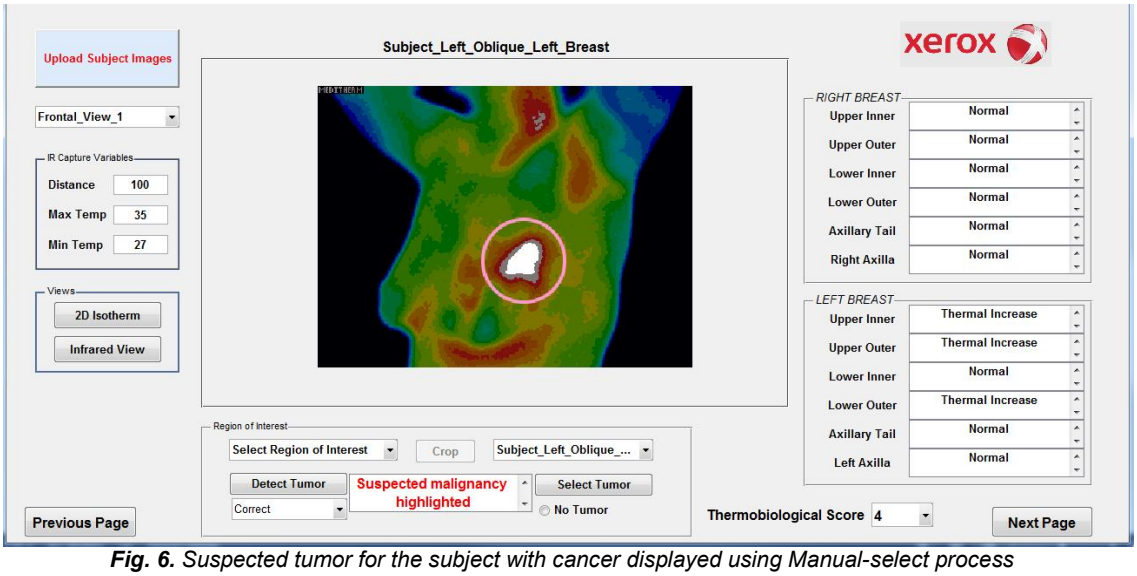

Fig. 6. *Suspected tumor for the subject with cancer displayed using Manual-select process*

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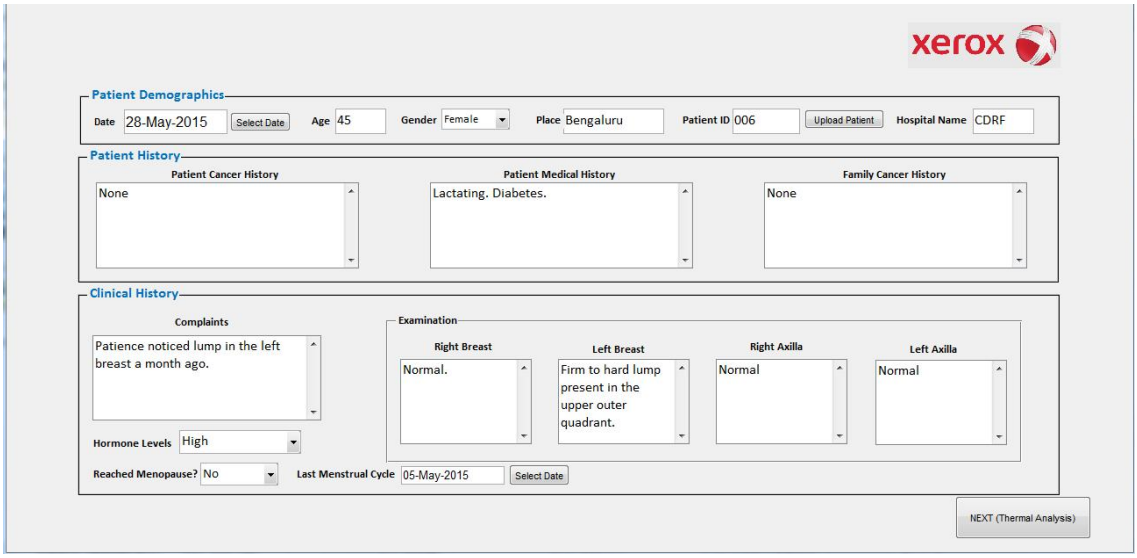

Fig. 7. *Patient data acquisition*

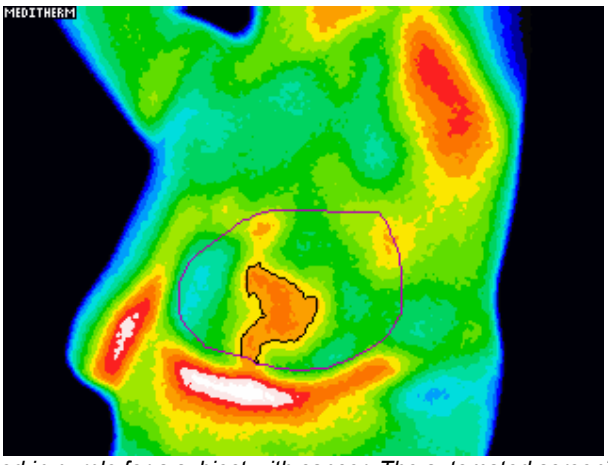

Fig. 8. *Segmented ROI outlined in purple for a subject with cancer. The automated screening located the tumor outlined in black.*

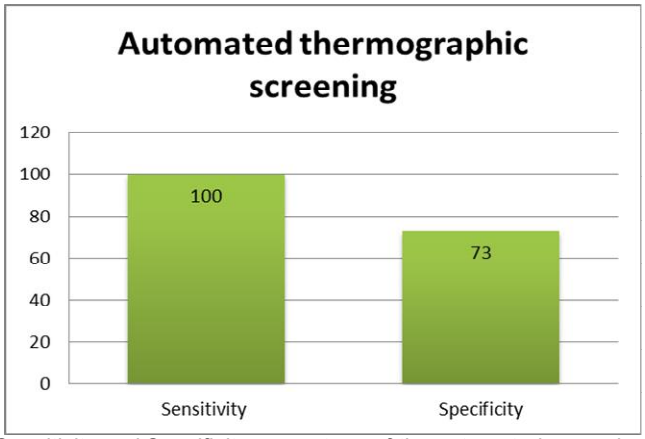

Fig. 9. *Sensitivity and Specificity percentage of the automated screening results.*