About the Evolution of the Thermographic Profile In Breast Cancer - A Case Report

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SUMMARY

INTRODUCTION: Patients suffering from lobular breast cancer bear a high risk of a metastasising disease. Since this type of neoplasia often presents with an asymptomatic and therefore insidious growth, establishing the diagnosis through imaging may be difficult.

STUDY AIM: To report the clinical course of a patient who presented with a lobular breast carcinoma and to illustrate the contribution of infrared thermography in monitoring this lesion.

METHODS: P.L.S, a female patient 57 years old, was diagnosed with invasive lobular carcinoma in the lower right breast quadrant. A neoadjuvant chemotherapy was initiated to increase the chances of success of radical surgical therapy followed by radiation therapy. Before, during and after the completion of chemotherapy, infrared thermal images were taken of the patient's breasts in a private clinic by a physiotherapist who had been trained to record and evaluate infrared thermal images.

RESULTS: During chemotherapy, the temperatures both above the tumour and on the contralateral breast decreased by 3° C, but the side difference in breast temperature remained unchanged at 2 °C. These temperature changes were paralleled by a decrease in tumour size.

CONCLUSION: This case report suggests that infrared thermal imaging technique can be a helpful complementary diagnostic tool to follow-up tumour development or involution in patients undergoing chemotherapy. The main advantages of the technique are real-time imaging, easy handling and the possibility of performing multiple examinations that are harmless to the patient, since neither painful procedures are applied nor the patient is exposed to ionizing radiation.

KEYWORDS: Neoplasms; Breast Cancer; Infrared thermography.

ÜBER DIE ENTWICKLUNG DES THERMOGRAPHISCHEN PROFILS BEI BRUST KREBS - EIN FALLBERICHT

EINLEITUNG: Patientinnen mit lobulärem Brustkrebs haben ein hohes Risiko für eines metastasierende Erkrankung. Da diese Art von Neoplasie oft ein heimtückisches, weil symptomfreies Wachstum zeigt, kann die Bestätigung der Diagnose durch Bildgebung schwierig sein.

ZIEL DER STUDIE: Darstellung des klinischen Krankheitsverlaufs einer Patientin mit lobulärem Mammakarzinom und Veranschaulichung des Beitrags der Infrarot-Thermographie bei der Überwachung dieser Läsion.

METHODE: Bei der 57 Jahre alten Patientin P.L.S. wurde ein invasives lobuläres Karzinom im unteren rechten Brustquadranten diagnostiziert und eine neoadjuvante Chemotherapie eingeleitet, um die Erfolgschancen einer radikalen chirurgische Therapie mit anschließender Strahlentherapie zu erhöhen. Bevor, während und nach Abschluss der Chemotherapie wurden in einer Privatklinik Infrarot-Wärmebilder von den Brüsten der Patientin von einer für Aufnahme und Auswertung von Infrarot-Wärmebildern ausgebildeten Physiotherapeutin angefertigt.

ERGEBNISSE: Während der Chemotherapie verringerten sich die Temperaturen sowohl über dem Tumor als auch an der kontralateralen Brust um jeweils 3°C, der Seitenunterschied der Brusttemperatur blieb jedoch mit 2°C unverändert.

SCHLUSSFOLGERUNG: Dieser Fallbericht legt nahe, dass die Infrarot -Thermografie ein hilfreiches ergänzendes diagnostisches Werkzeug sein kann, um die Entwicklung oder Involution von Tumoren bei Patienten zu verfolgen, die sich einer Chemotherapie unterziehen. Die Hauptvorteile der Technik sind eine Echtzeit-Bildgebung, einfache Handhabung und die Möglichkeit, zahlreiche Untersuchungen durchzuführen, die für die Patienten unschädlich sind, da weder schmerzhafte Prozeduren angewendet werden noch der Patient einer ionisierenden Strahlung ausgesetzt ist.

SCHLÜSSELWÖRTER: Neoplasma. Brustkrebs, Infrarot-Thermographie

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Introduction

Invasive lobular carcinoma (ILC) comprises approximately 10% of breast cancers and appears to have a distinct biology [1]. It is less common than infiltrating ductal carcinoma (IDC) and few data have been reported that address the biologic features of ILC in the context of their clinical outcome. ILC responds to 28% of new cases a year and is responsible for most female's cancer deaths [2]. Although common in women, IDC is the predominant histologic type causing breast cancer in men [3].

According to Borchartt there are more than twenty types of breast cancer and among them, the ductal carcinoma, lobular and inflammatory cancer are the most common ones [4]. The most prevalent histological kind of invasive breast cancer is ductal carcinoma comprising 80% to 85% of all cases. About 15% of breast neoplasms are non-invasive "in situ" carcinomas, in situ ductal carcinoma (ISDC) appear in 80% of cases and in situ lobular carcinoma in approximately 20% [5].

By definition, an in situ ductal carcinoma represents the proliferation of neoplastic cells, limited to the ductal epithelium without invasion of the basal membrane and stroma.When the neoplastic cells break through the ductal wall and proliferate into the breast adipose tissue, this might result in metastasis and the tumour is named invasive or infiltrating ductal carcinoma.

Breast lobular neoplasm refer to a group of lesions mainly characterized by atypical lobular hyperplasia (ALH) and by in situ lobular carcinoma (ISLC) [6]. They also include the whole spectrum of atypical epithelium lesions which may evolve in the terminal ductal lobular unit. It is characterized by cells proliferation and those cells are small, uniform, round, without cellular cohesion and with or without pagetoid extension for terminal ducts. [7]. ILC has great risk of metastasizing [8]. Since this type of neoplasia often presents with an asymptomatic and therefore insidious growth, establishing the diagnosis through imaging may be difficult [7].

The National Institute of Cancer (INCA) in Brazil expected for the period 2018-2019 six hundred thousand incident cancer cases per year with breast lobular cancer being the most common among women (about sixty thousand) becoming a huge public health problem [2]. In this context, early detection and early diagnosis appear as the key actions for optimal prevention facilitating all methods for treatment and tumour control.

Infrared thermography or digital infrared thermal imaging exam has a high potential to detect circulatory changes triggered by tumour induced angiogenesis or any other breast cancer signals in the earlier stage [9]. It is possible to identify thermal signals that suggest the presence of pre-cancer cells or an initial breast lobular tumor, even if it is too small in size to be detected by physical exam, mammography or any other types of structural imaging modalities [10].

Thermography technique consists of catching infrared radiation emitted from the skin with an infrared camera, which converts the registered radiation into temperature values creating thereby a map of temperature distribution on the surface of the imaged object. On the presence of mammary tissue anomalies, like a malignant tumour or some benign alteration, the breast surface temperature can significantly change [11]. Such phenomenon may be observed in cases of malignant neoplasms where cancer cells absorbs more glycose and reproduce themselves in an unordered way. In 1994, Anbar has pointed out that cancerous breast hyperthermia is seemingly associated with non-neurological vasodilation modulated by nitric oxide (NO) [12]. 20 years later the potential roles of NO in tumour growth are much better understood as it seems well established that nitric oxide is involved in angiogenesis and promoting thereby increased blood flow in breast cancer [13]. Due to the detection of thermal signals, infrared thermography becomes a promising technique as a complementary diagnostic tool for the evaluation of lesions suspicious for cancer and to follow up thermal signs that suggest the presence of a tumour.

This study aimed to report a case of a patient who had a lobular breast cancer and to illustrate the contribution of infrared thermography in follow up of this lesion.

Case history

This case report was submitted to and approved by the Human Ethic Committee of Science Institute from Federal University of Bahia under the protocol number 3.580.028.

The patient P.L.S., a fifty-seven years old female reported a painful sensation in her right breast in July 2016. She went to a mastologist who detected at breast palpation a nodular lesion in the lower quadrant of the right breast. It was required a colour doppler ultrasonography (USG) of the breasts. Image evaluation suggested a solid neoplasm of benign pattern (Bi-RADS II). It was also observed bilateral ductal ectasia and bilateral simple cysts. A fine needle biopsy was performed with negative results for cysts or neoplastic cells. Twenty days after the first imaging exam, she returned to the mastologist complaining about pain in the right breast. On that occasion, it was required new complementary exams such as digital mammography. A normal breast´s contour and volume were identified like in the previous sonographic finding (Bi-RADS II classification).

In February 2017, seven months after her first medical consultation, the pain complaint continued, and the patient was again submitted to ultrasonography and digital mammography. Enlarged lymph nodes were observed, and the mammography findings revealed a nodule with undefinable bounds in the right breast. Its size was about 8.0 x 6.0 x 3.2 cm in the lower quadrant (Bi-RADS IV). In addition, it was suggested a new core biopsy which confirmed the diagnosis of invasive lobular carcinoma.

Consequently, the patient was undertaken to a complete investigation of the neoplasm that included a magnetic resonance imaging of breasts as well as ultrasonography, electrocardiogram (ECG), computer tomography (CT) of thorax and total abdomen and laboratory exams. The CT of the total abdomen revealed the presence of small hepatic and bilateral renal cysts and increased size of homolateral axillary ganglia on the right (lymph node enlargement in I and II levels). Laboratory findings did not show any breast change worthy to be mentioned except increased serum levels of CA15.3 (300U/l) and CEA (>10 ng/ml). Magnetic resonance images of the breasts showed a great nodule in the right breast with 8.5 x 6.9 x 3.7 cm. Its classification was described as BI-RADS VI. Regarding ECG, there were no significant alterations. Transvaginal US revealed a myoma nodule and polyps of the endometrial cavity. The oncogenetic analysis did not show any genetic mutations related to cancer.

By medical indication, the patient underwent neoadjuvant chemotherapy with paclitaxel and Doxorubicin intravenously every twenty-one days. This treatment started on March 2017 and aimed to reduce the size of the tumor mass for surgery and radiotherapy treatment. In this period, the first thermographic evaluation was already performed to follow up the development of the neoplasm.

The thermographic evaluation was done in a private clinic in preserved environment and was combined with a control exam by an oncologist. Such conditions assured comfort and security for the patient. Thermograms were recorded by a physiotherapist trained as thermography technician.

To perform thermal imaging, the environment was temperature controlled at 23ºC and 55% of relative humidity. The patient was undressed to the waist and waited fifteen minutes for thermal acclimation. It was used an infrared camera FLIR T430sc 2.0, serie number 62116523 (Sweden), with 320×240 (76,800) pixels of spatial resolution, spectral range 7,5-13 μm, uncooled microbolometer, 23o lens, 60 Hz of image frequency, dual temperature range -20°C to 120°C/0°C to 650°C, thermal sensitivity <30 mK. The patient stood in an upright position and the thermal image captured in the anterior view of the upper body allowed analysing both breasts.

Using dedicated software, circular regions of interest (ROI) were defined circumscribing each breast, in which mean, maximum and minimum temperature were determined. If necessary, spot temperature measurements were performed for describing the temperature level in the breast quadrants. The distribution of colours was used for gross estimation of temperature. Thermal assymetry was defined as a temperature difference between corresponding measurement points equal or greater than 0.5°C. Thermal asymmetry was estimated when corresponding areas varied by at least 30% size of differently coloured areas.

Results

Figure 1 shows a thermogram that exhibited asymmetry in the thorax upper region and between both breasts in the lower quadrant. In the lower quadrant of the right breast a large white coloured area can be identified where spot tem-

Figure 1.
Baseline thermal image after 1st session of chemotherapy (03/24/2017).

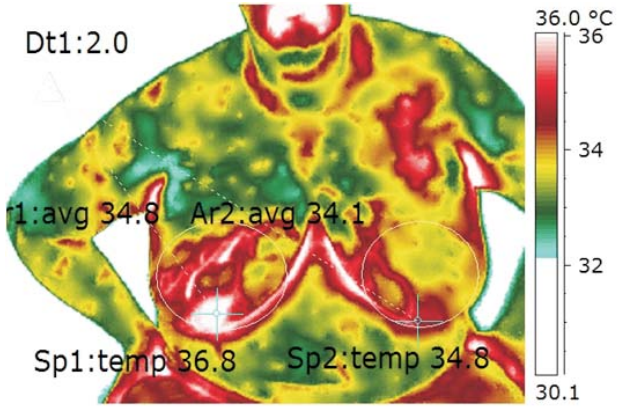

Figure 2.
Thermogram one month after the beginning of chemotherapy (04/23/2017).

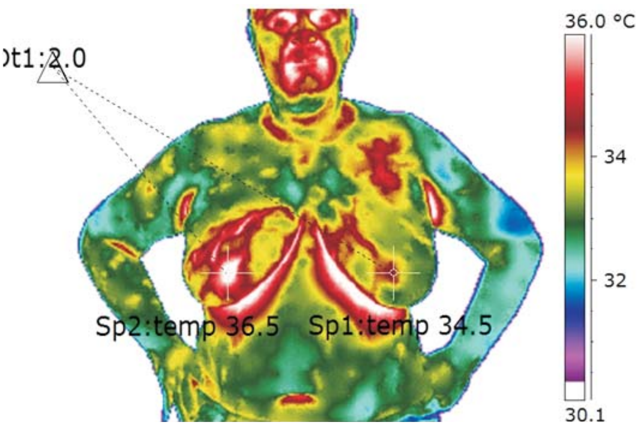

Figure 3.
Thermography after three months of neoadjuvant chemotherapy (06/06/2017).

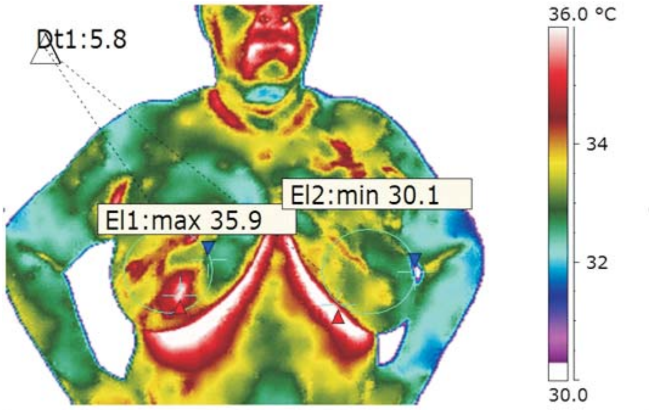

Figure 4
Thermography after last session of chemotherapy (08/12/2017).

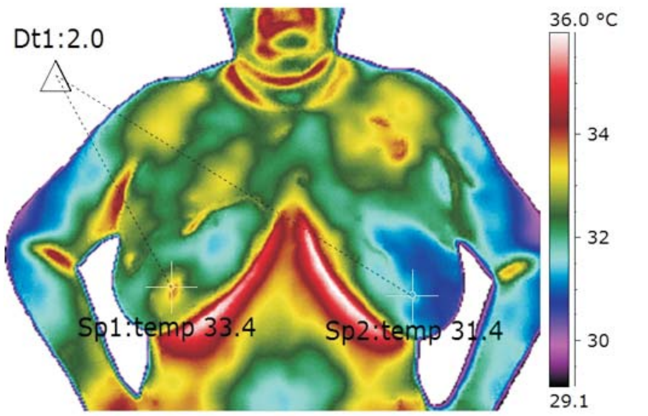

Table 1
Evolution of Spot Temperatures SP1 and SP2 throughout the period of observation.

Temperature	Figure 1 03/24/2017	Figure 2 04/23/2017	Figure 4 08/12/2017
SP1	36.8	36.5	33.4
SP2	34.8	34.5	31.4
Delta T (SP1-SP2)	2.0	2.0	2.0

perature measurement (SP1) indicated high temperature (36.8ºC). The same quadrant of the left breast showed an area of red color with a spot temperature (SP2) of 34.8ºC, resulting in a difference (ΔT) between the spot temperatures of 2.0ºC. In the region of axillary lymph nodes, a symmetric colour distribution was noted with estimated temperatures between 35 and 36ºC.

Figure 2 shows thermography at the second medical examination (04/23/2017) exactly one month after first investigation. When comparing to the first thermogram, it was noticed at the breasts that the asymmetry of temperature distribution continued. However, it was verified a quantitative and qualitative improvement of the thermal image of the lower breast quadrant showing a reduction in size of the red coloured area that had changed to yellow colour. Temperature in the spot SP1 at the right breast was 36.5ºC while in the SP2 (left breast) was 34.5ºC. The temperature difference (ΔT) between Sp1 and Sp2 was 2.0ºC. According to the colour scale, the breast temperatures presented slightly reduced compared to the baseline investigation.

Figure 3 shows the third thermographic evaluation (06/13/2017). The circular area 1 represents the right breast and the other circle 2, the left one. A thermal difference of 5.8ºC was observed between the maximal temperature of area 1 and the minimal temperature of area 2.

The last thermography evaluation (Figure 4) was done at the same date as the last neoadjuvant chemotherapy session (08/12/2017). The temperature in SP1 was 33.4ºC and 31.4ºC in Sp2, the temperature difference between the breasts remained unchanged (ΔT) = 2.0ºC). Table 1 shows the temperature evolution throughout the entire period of observation, which was equal to the time of chemotherapy.

Bilateral total mastectomy was performed due to the positive response to the neoadjuvant chemotherapy. Twenty days after the surgery, the patient underwent twenty-five sessions of radiotherapy with a total cumulated dose of 50 Grays. Currently, the woman is under medical observation, makes use of anastrozole 1mg/day and now two years after the surgical procedure, she is in good health condition.

Discussion

Global and Brazilian scenarios estimate an increase in the incidence of cases of breast neoplasm and the corresponding number of deaths in women [2]. So, this report aimed to describe the use of infrared imaging as complementary exam to follow up development of neoplasms in breast. This imaging tool shows high sensitivity and may detect tumour induced alterations even in the initial stage and the method may be helpful to follow up such condition over time [14].

The choice of a patient with lobular breast cancer was based on the fact that such neoplasm shows risk of 7 to 12 times higher of having metastasis [14]. In addition, imaging diagnostic is of hard to achieve since this type of neoplasm shows an insidious and often asymptomatic growth. Thus, it has been suggested on literacy, a combination of image techniques such as ultrasonography, magnetic resonance and digital mammography in order to track the tumor in early stage and follow up patients who have genetic risk of developing breast cancer [15].

A case of a patient with lobular breast cancer was selected because such neoplasms show a 7 to 12 times higher risk of developing metastasis [15].Since this type of neoplasia often presents with an asymptomatic and therefore insidious growth, establishing the diagnosis through imaging may be difficult. It has been suggested in the literature to use a combination of imaging techniques such as ultrasonography, magnetic resonance and digital mammography in order to track the tumour in the early stage and follow up patients who have genetic risk of developing breast cancer [16].

In this study, the patient reported painful sensation in her right breast in July 2016 and such symptom are suspicious for a possible neoplasm. However, even though the neoplasm has been tracked through imaging exams as digital mammography, doppler ultrasonography, the diagnosis of a lobular invasive carcinoma was difficult to establish. Conclusive diagnosis was obtained as late as in February 2017 by core biopsy when the tumour was already measuring 8.0 x 6.0 x 3.2 cm and classified as BIRADS- IV.

Brazilian's health services have some barriers particularly regarding cancer diagnosis [17]. Thus, it is important to explore new techniques which allow tumour identification. Some imaging methods previously mentioned are very effective but have some limitations detection in an early stage. For instance, digital mammography, which is considered highly effective, might offer risks for women's health since it uses ionizing radiation. Another limitation is the low quantity of equipment available for population screening. These conditions make it difficult to interpret exams from patients for pro- gnosis [18].

In this context, infrared thermography, which can detect thermal asymmetries, might be a feasible tool for monitoring carcinomas without raising risks for women's health. This technique checks points with higher temperature on the body surface. Such areas with high temperature may indicate an increase in local blood flow resulting from neoangiogenesis or metabolic changes related to tumour growth [19].

This case report corroborates the sensitivity of infrared thermography for monitoring tumour development, since in this case focal hyperthermia visible in the breast thermogram was closely related to the location and area of the tumour invasion. A previous study found thermography not useful in the follow-up of breast cancer patients after breast-conserving treatment by tumourectomy and therapeutic irradiation [20]. However, these negative results might be explained by the fact, that high energy irradiation is followed by an increase in surface temperature of the treated breast.

A thermal asymmetry was noticed in the thermograms of the breast during chemotherapeutic treatment. The thermal difference ΔT between corresponding regions of right and left breast (Sp1-Sp2) did not change throughout the observation period. ΔT values of 2.0°C were understood as an indicator of ongoing tumour presence. It was also observed that there was a significant reduction in temperature of both SP1 and SP2, indicating a good response to the applied treatment that caused a reduction inflammatory activity of the tumour. The temperature of area of right breast decreased by 3.4°C and this finding might be explained by a possible reduction of microcirculation in tumour area. When doing imaging exams prior to surgery, it was observed that a significant reduction in size tumour occurred with a decrease in diameter from 8.5 to 0.6 cm. Thus, this case report description is relevant because it allowed patient's follow up through infrared image pattern during the entire period of neoadjuvant therapy.

The thermal difference between the maximum right breast temperature and the minimum temperature of the left breast was 5.8°C with Tmax right = 35.9°C and Tmin Left - 30.1°C. Regarding the left breast, a hot spot was present in the medial lower quadrant since the basal thermal image, but a tumour was not detected in this breast region by any of the conducted imaging exams. Thermography demonstrated temperature reduction in the hot spot of the left breast pointing to good response to chemotherapy. When looking on the initial thermography exams, the patient had already carried a high risk for breast cancer according to the breast thermography grading scale of the Ville Marie Women's Hospital in Montreal (Range of IR 5/5) [21]. This risk was found reduced after chemotherapy, but as it sustained on a moderate level, the patient opted for bilateral mastectomy. As a matter of fact, biopsy results from the left breast taken prior to mastectomy, were similar to that of the right one.

Conclusion

This case report recommends thermography as a valuable tool for monitoring patients who are under chemotherapy due to breast cancer. The advantages of this imaging method include the possibility to achieve results quickly, easy equipment handling, high image quality, multiple exam repetitions without exposing the patient to ionizing radiation or any painful procedure during the examination.

Conflict of Interest

The authors declare that they have no conflict of interest.

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