# Ultrasound and Thermographic Assessment of Upper Limb Alterations in Women with Breast Cancer-Related Lymphedema

## ABSTRACT

**Aims:**
To associate the results of thermography and ultrasound of the upper limb with lymphedema in women after breast cancer.

**Study Design:**
Cross-sectional study.

**Place and Duration of Study:**
Conducted in Recife, Brazil, from September 2022 to July 2024.

**Methodology:**
A total of 43 women with breast cancer-related lymphedema were included. Each participant underwent frontal thermography using a Thermovision FLIR Systems C5 camera. Minimum, mean, and maximum temperatures were evaluated at specific points on the forearm (TA) and arm (TB) using the FLIR Tools software. The same points were analyzed using ultrasound to identify fibrosis, fat infiltration, thickening of the dermo epidermal layer (DEC), and loss of differentiation between layers. Statistical analysis was performed using JASP software.

**Results:**
The study identified a higher prevalence of DEC thickening in the arm (68.5%) and forearm (57.9%). However, no significant correlation was observed between skin temperature and tissue alterations ($P > .05$), with a small effect size ($g < 0.46$) and limited clinical relevance (<0.2).

**Conclusion:**
The findings indicate that ultrasound-detected alterations in the upper limb are not associated with changes in skin temperature in women with secondary lymphedema due to breast cancer.

*Keywords: Lymphedema; Breast Cancer; Ultrasound; Thermography*

## 1. INTRODUCTION

Lymphedema is characterized by the accumulation of protein-rich fluid in the interstitial space due to lymphatic system failure. It is a chronic, progressive, and currently incurable condition (*Shen et al., 2023*). The prevalence of lymphedema is high among women diagnosed with breast cancer. The main causes of this condition include treatments such as radiotherapy and lymph node removal, which can reduce lymphatic reabsorption and transport capacity. The management of lymphedema is challenging due to diagnostic difficulties and various associated tissue alterations (*Levenhagen et al., 2017*).

There is no single tool to assess lymphedema; instead, a combination of methods is employed for more accurate conclusions. The most common diagnosis is based on clinical analysis and increased volume of the affected limb. The lack of standardization limits understanding of the disease's incidence and the effectiveness of available treatments (*Donahue et al., 2023*). An effective tool for diagnosing lymphedema should go beyond simply detecting arm volume increase after surgery. It should be cost-effective, highly accurate, and assist clinicians in understanding the tissue changes associated with the condition. Additionally, it should facilitate the detection of lymphedema in subclinical stages, when arm volume changes are not yet measurable (*Shavit et al., 2018*).

Lymphedema classification is done in stages, with stage 0 characterized by sensations of heaviness and fatigue in the limb without visible swelling, which, like stage 1, is reversible (*Denlinger et al., 2018*). However, diagnostic methods often focus on arm circumference measurement, water displacement, and bioimpedance analysis, comparing the limbs (*Yusof et al., 2012*). Therefore, imaging and functional methods are becoming increasingly important in research and clinical practice, rather than relying solely on circumference measurements to quantify arm volume increase, despite their simplicity. Thermographic devices, for example, capture infrared radiation emitted by the body and convert it into electrical signals, generating a thermogram that displays temperatures using colors. Although this method is effective in detecting various vascular conditions, skin and tissue problems, and lymphedema, there is still a lack of comprehensive evidence-based insights to support its application in different areas of medicine (*Kelly-Hope et al., 2021; Kesztyüs et al., 2023*).

While thermography results for diagnosing lymphedema are promising and suggest benefits in identifying patterns associated with tissue changes in lymphedema, such as edema, fibrosis, and liposubstitution (*Ibarra Estupiñán et al., 2020*), caution is essential, and the accuracy of these documented associations must be evaluated.

Ultrasound, on the other hand, can more accurately detect pathologies in superficial tissues. Studies comparing physical examination with ultrasound imaging reveal that physical examination is ineffective in identifying the more advanced stages of lymphedema, unlike ultrasound images (*Ricci et al., 2022*). Changes in stages two and three, considered irreversible, go beyond swelling and include morphological changes in the skin, subcutaneous tissue, and muscles, requiring a trained professional to properly identify them through ultrasound (*Goudarzi et al., 2023*).

The evaluation of skin and tissue changes by ultrasound is crucial for monitoring and managing women with secondary lymphedema due to breast cancer (*Mander et al., 2023*). This imaging technique provides a detailed view of the skin layers and underlying tissue, enabling early detection of structural changes such as skin thickening, fibrosis, and fat accumulation (*Polat et al., 2020*). Identifying these tissue changes allows for a more accurate classification of lymphedema severity. However, no studies to date have related these changes to superficial skin temperature measured by thermography.

This article generally aimed to verify the association between upper limb ultrasound alterations and superficial skin temperature in women with lymphedema, assessed through infrared thermography. Specifically, it aimed to clinically characterize the sample of women with lymphedema; identify qualitative ultrasound alterations (fibrosis, fat infiltration, fluid presence, and loss of subcutaneous tissue differentiation) in the upper limb; and identify the maximum, mean, and minimum superficial skin temperatures of the upper limb through thermography.

## 2. METHODOLOGY

This was a cross-sectional study analyzing ultrasound and thermographic exams of women with a history of breast cancer, with and without breast cancer-related lymphedema (BCRL). This study is part of a larger research project aimed at evaluating the diagnostic accuracy of thermography in diagnosing BCRL. The research was conducted at the Laboratory of Women's Health and Pelvic Floor Physical Therapy (LAFISMA), Department of Physical Therapy, Federal University of Pernambuco (UFPE), from September 2022 to July 2024. The research protocol was reviewed and approved by the UFPE Research Ethics Committee under protocol no. 5.434.586. All participants provided informed consent by signing the written Informed Consent Form.

For this study, all women with available ultrasound and thermographic exams were included. Eligibility criteria for the primary study included women aged 40 to 70 years with a history of unilateral mastectomy. Exclusion criteria included women with bilateral breast cancer, bilateral mastectomy, primary lymphedema, edema related to other causes (e.g., rheumatologic, renal, neurological, orthopedic problems, or prior vascular disease), skin conditions (erysipelas, intertrigo, or ulcers), and those undergoing chemotherapy or radiotherapy treatment.

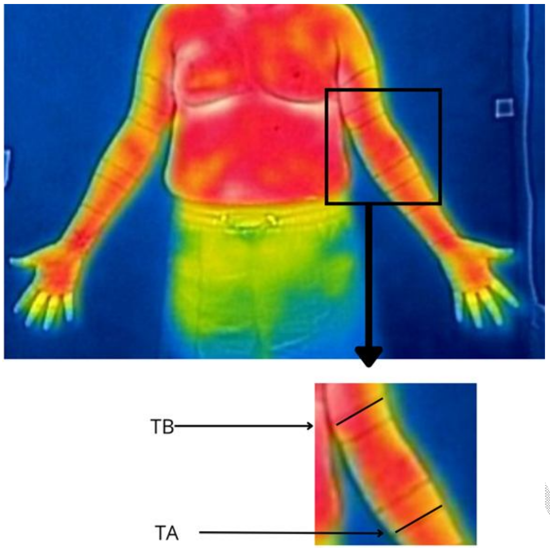
BCRL assessment was conducted following the guidelines of the International Society of Lymphology (*International Society of Lymphology*, 2016). The standard method for lymphedema evaluation consisted of indirect volumetry using the truncated cone volume calculation. This method is characterized by good diagnostic accuracy, excellent reproducibility, and is based on the calculation of the total volume of the affected limb and its comparison with the unaffected limb (*Levenhagen et al., 2017*).

Data collection was performed at the LAFISMA-UFPE facilities, and evaluators were previously trained and calibrated for all assessments included in the project, which comprised thermographic imaging acquisition, clinical lymphedema examination, and ultrasound evaluation of lymphedema. The use of thermography as an alternative diagnostic method for lymphedema followed the recommendations of the American Academy of Thermology. The thermography process involved four steps: image acquisition, image processing, delimitation of regions of interest, and analysis (*Fernández-Cuevas et al., 2017*).

Thermograms were obtained in a windowless room at a controlled temperature of 22°C and 60% humidity, regulated by a digital weather station. The room was free from direct sunlight, air drafts, and electrical equipment generating heat. Prior to the examination, participants were instructed to avoid applying creams or perfumes to the skin, consuming stimulants or caffeinated substances, using nasal decongestants, or engaging in vigorous physical exercise within two hours before the exam. Upon arrival, participants remained seated in the room for 20 minutes with exposed upper limbs positioned on their laps to achieve thermal equilibrium with the room temperature (*International Society of Lymphology*, 2016).

Superficial skin temperature measurements were obtained using a thermographic camera (Thermovision FLIR Systems C5, resolution 160 x 120, 19,200 pixels). The camera was positioned 1 meter from the participant to capture all regions of interest. Participants were positioned frontally in an anatomical position, with the chest and upper limbs uncovered. Two equidistant points from the elbow joint line were marked: TB (arm point) and TA (forearm point)(Figure 1).

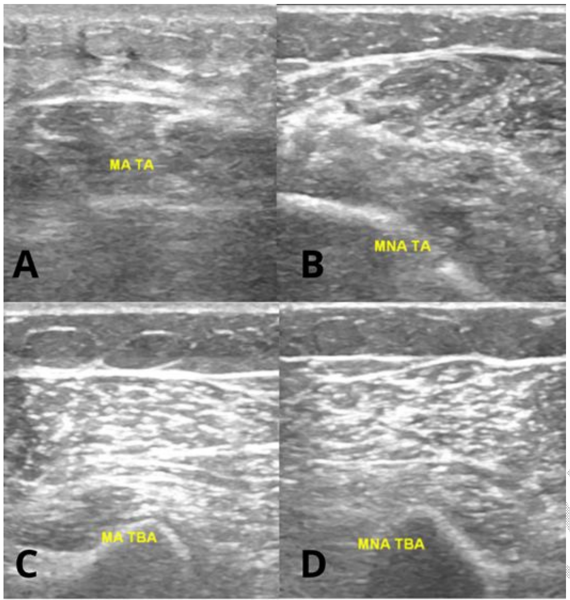
**Figure 1.Schematic thermographic image in the frontal plane, showing the location of the pointsTA: forearm point and TB: arm point.**



Thermograms were processed using FLIR Tools software, with a standard emissivity of .98, Rainbow scale, and a temperature range from 23°C to 37.7°C. Each region of interest (ROI) was analyzed using the line measurement tool, with trained evaluators marking 10 cm below and above the cubital crease, referred to as TA and TB, respectively (*Polat et al., 2020*). For each ROI, the software provided maximum, mean, and minimum temperatures in degrees Celsius (°C). Thermograms were quantitatively interpreted based on the minimum, maximum, and mean temperatures measured, comparing the affected and contralateral limbs, while considering the theoretical framework of thermoregulation (*Fernández-Cuevas et al., 2017*) and the pathophysiological process of lymphedema (*Cohen, 2009*).

Ultrasound images were acquired using GE's LOGIC V5 equipment with a 7–12 MHz linear transducer in B-mode at a depth of 4 cm. The transducer with gel was positioned on the anterior surface of the arm and forearm, following the same orientation as the thermography. The images (Figure 2) were qualitatively analyzed by a trained evaluator to identify fibrosis, fat infiltration, dermoepidermal layer thickening, and loss of differentiation between the dermis and epidermis at the same points where temperatures were collected (*Mander et al., 2019*).

**Figure 2**. **Ultrasound images of the upper limb with lymphedema (A and C) and without lymphedema (B and D).**



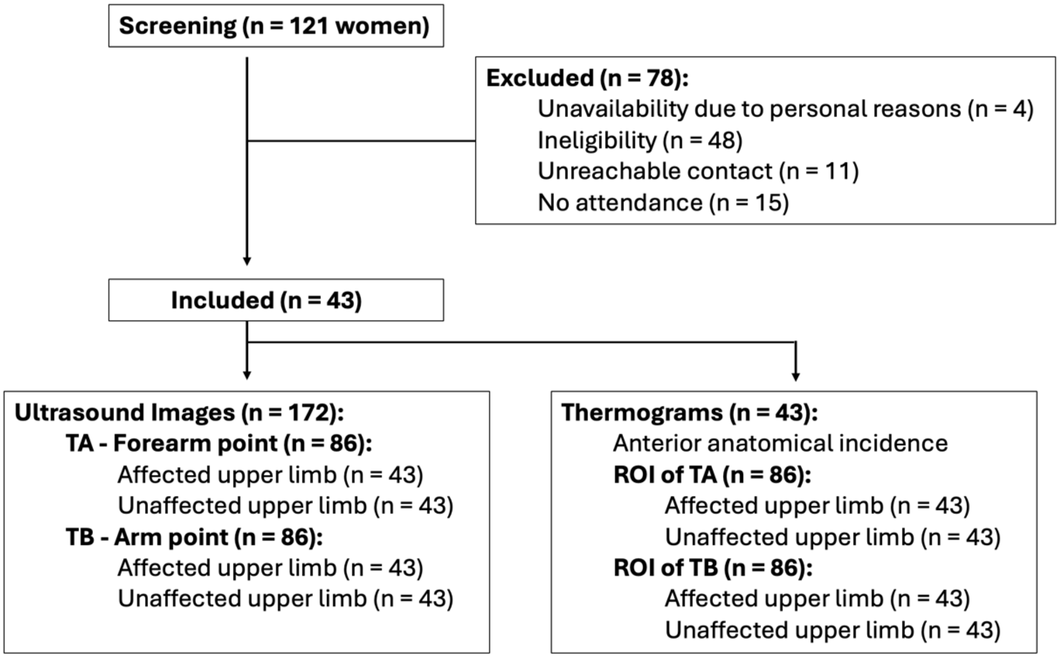
A: affected limb, forearm point; thickening of the dermoepidermal layer and loss of differentiation between the layers can be observed through the blurring effect, as well as fibrosis represented by hyperechoic lines. B: unaffected limb, forearm point. C: affected limb, arm point; fat infiltration is visible, surrounded by hyperechoic lines in a circular arrangement. D: unaffected limb, arm point.

Data were stored and processed using JASP software, version 0.18.3.0. Central tendency measures were described using means and standard deviations. Data normality was assessed using the Kolmogorov-Smirnov test. The prevalence ratio for ultrasound findings was calculated using the Odds Ratio (95% CI). The confidence interval (95%) for non-parametric data used to associate thermography with ultrasound was calculated using the Hodges-Lehmann method. Comparisons of skin temperatures according to the ultrasound findings were conducted using the Mann-Whitney test for non-parametric data, and effect sizes were estimated using Hedges' *g*, where values between 0.2 and 0.5 are considered small, 0.5 to 0.8 moderate, and above 0.8 large (*Cohen, 2009*). Results were presented with their respective confidence intervals and considered statistically significant at $P<.05$ for both the analysis of findings and their association with temperatures.

## 3. RESULTS AND DISCUSSION

A total of 121 women were screened, of whom 43 met the inclusion criteria as women who had unilateral breast cancer and completed all their treatment. In the laboratory, a thermogram was obtained for each participant. From these thermograms, four regions of interest (ROIs) were analyzed at the arm and forearm points—two in the affected upper limb and two in the unaffected upper limb—totaling 172 ROIs. Subsequently, four ultrasound images were generated for each participant, corresponding to the same points—two in the affected upper limb and two in the unaffected upper limb—resulting in 172 images (Figure 3).

**Figure 3. Flowchart of sample screening and acquisition of ultrasound images and thermograms.**



The women included in the sample had a mean age of 54.14 years. Less than half of the sample (44.18%) presented lymphedema according to the volumetric evaluation. Most participants were married (48.84%) and had completed high school (44.19%). Among the clinical symptoms that may indicate the onset or presence of lymphedema, the most prevalent were a sensation of heaviness (67.45%), paresthesia (55.82%), and peaud'orange (44.19%) (Table 1).

**Table 1. Sociodemographic and clinical characteristics of the sample (n: 43).**

| **Variable** | **Mean (SD) or n (%)** |
|---|---|
| Age in years (mean, SD) | 54.14 (7.72) |
| Presence of lymphedema n (%) | 19 (44.18) |
| **Marital status n (%)** | |
| Single | 13 (30.24) |
| Married | 21 (48.84) |
| Widow | 3 (6.98) |
| Divorced | 6 (13.96) |

| **Variable** | **Mean (SD) or n (%)** |
|---|---|
| **Education n (%)** | |
| Incomplete elementary school | 3 (6.98) |
| Complete elementary school | 1 (2.33) |
| Incomplete high school | 2 (4.66) |
| Complete high school | 19 (44.19) |
| Undergraduate degree | 12 (27.91) |
| Graduate degree | 6 (13.96) |
| **Symptoms n (%)** | |
| Feeling of heaviness | 29 (67.45) |
| Paresthesia (numbness) | 24 (55.82) |
| Increased local temperature | 14 (32.56) |
| Erythema (redness) | 8 (18.61) |
| Peau d'orange (skin thickening resembling orange peel) | 19 (44.19) |

SD: standard deviation; n: sample size.

The qualitative findings observed in the ultrasound images of the upper limb with and without lymphedema (Table 2) indicated that, at the forearm point (TA), fibrosis was highly prevalent (47.4%), with individuals with lymphedema being 9.9 times more likely to present this dermal alteration (*P* = .01). Thickening of the dermoepidermal layer was observed in 57.9% of cases, with individuals with lymphedema having a 5.3 times higher likelihood of presenting this alteration (*P* = .02).

At the arm point (TB), fibrosis (42.1%) and dermoepidermal layer thickening (68.5%) were the most prevalent alterations. Among these, thickening of the dermoepidermal layer had the highest odds ratio, with individuals with lymphedema being 23.9 times more likely to present this alteration (*P*< .001). This was the only dermal alteration with a statistically significant association in the analyzed region of interest.

**Table 2.Tissue alterations in upper limbs identified in ultrasound images**

| Variable | With lymphedema<br>n (%) | Without lymphedema<br>n (%) | P value | Odds Ratio (95% CI) |
|---|---|---|---|---|
| **TA** | | | | |
| Fibrosis | 9 (47.4) | 2 (8.4) | .01 | 9.9 (1.8–54.5) |
| Fat infiltration | 5 (26.3) | 0 | .05 | 18.6 (0.9–361.3) |
| DEC thickening | 11 (57.9) | 5 (20.8) | .02 | 5.3 (1.4–20.0) |
| Loss of differentiation | 6 (31.6) | 1 (4.17) | .04 | 10.7 (1.2–98.1) |
| **TB** | | | | |
| Fibrosis | 8 (42.1) | 4 (16.7) | .07 | 3.7 (0.9–14.9) |
| Fat infiltration | 4 (21.1) | 0 | .08 | 14.3 (0.8–283.0) |
| DEC thickening | 13 (68.5) | 2 (8.4) | <.001 | 23.9 (4.2–136.0) |
| Loss of differentiation | 3 (15.8) | 0 | .13 | 10.4 (0.6–214.8) |

*P* values were calculated using the Chi-square test; DEC: dermoepidermal layer; TA: forearm assessment point; TB: arm assessment point.

The comparison of the mean maximum, mean, and minimum temperatures obtained through thermography with the qualitative findings identified via ultrasound (Table 3) showed that, in general, the mean temperatures recorded for all findings at the corresponding points on the arm and forearm ranged from 26.46°C to 30.41°C in the limb affected by lymphedema, with moderate standard deviations. The effect size, calculated using Hedges' *g*, was small for the following conditions: fat infiltration at the minimum temperature ($g = 0.31$) at TA; mean temperature ($g = 0.46$) and minimum temperature ($g = 0.44$) at TB. Similarly, for loss of differentiation at TA, the mean temperature ($g = 0.23$) and minimum temperature ($g = 0.23$) showed small effect sizes.

None of the analyzed variables presented statistically significant differences between groups ($P > .05$), suggesting the absence of significant temperature variations associated with the qualitative ultrasound findings.

**Table 3. Correlation between tissue alterations found in ultrasound and maximum, mean, and minimum temperatures of upper limbs**

| | **TA** | | | **TB** | | |
|---|---|---|---|---|---|---|
| **Tissue Alteration** | **Tmax** | **Tmean** | **Tmin** | **Tmax** | **Tmean** | **Tmin** |
| | Mean (SD) | Mean (SD) | Mean (SD) | Mean (SD) | Mean (SD) | Mean (SD) |
| **Fibrosis** | | | | | | |
| Present | 28.92 (2.52) | 29.69 (0.90) | 27.83 (1.36) | 30.23 (2.10) | 29.85 (1.40) | 28.78 (1.92) |
| Absent | 28.05 (3.97) | 29.88 (1.61) | 27.73 (2.47) | 29.49 (2.56) | 30.34 (1.42) | 28.98 (2.08) |
| *P* value | .48 | .57 | .67 | .44 | .41 | .70 |
| Hedges' *g* | -0.13 | 0.10 | 0.08 | -0.14 | 0.16 | 0.07 |
| **Fat Infiltration** | | | | | | |
| Present | 29.48 (2.54) | 29.34 (1.71) | 26.46 (2.81) | 29.62 (2.24) | 29.35 (1.21) | 27.82 (1.07) |
| Absent | 28.08 (3.87) | 29.89 (1.52) | 27.83 (2.31) | 29.59 (2.53) | 30.32 (1.42) | 29.01 (2.07) |
| *P* value | .39 | .49 | .24 | .92 | .12 | .13 |
| Hedges' *g* | -0.23 | 0.19 | 0.31 | 0.03 | 0.46 | 0.44 |
| **Dermoepidermal Layer Thickness** | | | | | | |
| Present | 28.69 (2.67) | 29.34 (1.59) | 27.21 (2.41) | 30.15 (2.28) | 29.94 (1.68) | 28.49 (1.86) |
| Absent | 28.04 (4.04) | 29.98 (1.50) | 27.87 (2.33) | 29.48 (2.54) | 30.35 (1.36) | 28.49 (2.08) |
| *P* value | .62 | .23 | .28 | .40 | .58 | .27 |
| Hedges' *g* | -0.08 | 0.19 | 0.17 | -0.14 | 0.09 | 0.18 |
| **Loss of Differentiation** | | | | | | |
| Present | 29.12 (2.43) | 29.28 (1.24) | 26.82 (2.63) | 31.53 (2.97) | 30.76 (1.19) | 28.66 (2.16) |
| Absent | 28.08 (3.91) | 29.91 (1.55) | 27.83 (2.32) | 29.52 (2.47) | 30.26 (1.43) | 28.97 (2.06) |
| *P* value | .50 | .31 | .31 | .15 | .49 | .83 |
| Hedges' *g* | -0.15 | 0.23 | 0.23 | -0.49 | -0.24 | 0.07 |

TA: forearm assessment point; TB: arm assessment point; Tmax: maximum temperature; Tmin: minimum temperature; Tmean: mean temperature; SD: standard deviation.

## 4. DISCUSSION

The ultrasound findings for the upper limb with lymphedema revealed a higher prevalence of dermoepidermal layer thickening (57.9%) and fibrosis (47.4%). The lymphedema group demonstrated the highest risk for fat infiltration in the forearm (18.6) and dermoepidermal thickening in the arm (23.9). However, these results were not statistically significant (*P*> .05) for fat infiltration at TA and TB, with only dermoepidermal thickening at TB showing significance.

Early identification of lymphedema is crucial to minimize its impact on quality of life and daily functioning. Studies suggest that initial symptoms tend to decrease and stabilize 18 months post-surgery, while volume and circumference changes continue to increase up to 36 months post-surgery—key indicators of established lymphedema (Armer, 2019). In the present study, 29 women reported a sensation of heaviness in the limb, exceeding the number of women diagnosed with lymphedema (19). This finding suggests the potential for an early stage of lymphedema in the symptomatic sample, as heaviness and paresthesia are predictive indicators for early lymphedema intervention, as outlined in post-breast cancer treatment surveillance programs (Wong, 2024).

Some studies have reported that volumetry, a commonly used clinical method to assess lymphedema, is less effective because it cannot differentiate between tissue changes and fluid accumulation. This distinction is critical for determining the stage of lymphedema (Park et al., 2024; Rezende et al., 2023). Imaging methods, particularly ultrasound, have therefore gained prominence due to their ability to distinguish between tissue layers and identify the most affected areas of the upper limb. Literature shows that the anterior forearm (TA) is the region most frequently presenting tissue alterations, consistent with the findings of this study (Suehiro, 2016).

Another significant result of this study is the high prevalence of dermoepidermal layer thickening in both regions of interest. This aligns with evidence that, across all stages of lymphedema involving volume changes, dermal edema emerges as the first and most characteristic alteration associated with the pathology (Ricci et al., 2022).

Ultrasound evaluation in this study also identified a greater number of women with fibrosis in the affected limb. Literature suggests that subcutaneous and skin changes in lymphedema are caused by extracellular alterations, such as connective tissue hypertrophy (Carvalho et al., 2020). Fibrosis is more common from stage 2 of lymphedema, while fat accumulation typically arises in stage 3 (Bowman & Rockson, 2024). This indicates that most participants in the current study had moderate lymphedema, as only a small number of individuals exhibited fat infiltration, while a larger proportion presented with fibrosis and dermoepidermal thickening.

Thermography has been increasingly utilized for the diagnosis of lymphedema, showing promise as a non-invasive and complementary tool. Recent studies have demonstrated its reproducibility and accuracy in aiding lymphedema diagnosis, particularly in breast cancer survivors (Dębiec-Bąk et al., 2020; Gomes, 2024a, 2024b). Thermography has been shown to detect initial temperature elevations in the limb that reflect ongoing inflammatory processes, with evidence supporting its good-to-excellent reproducibility across various postures and regions of interest. However, in the present study, no significant association was observed between thermographic findings and tissue alterations. This suggests that thermography may lack the sensitivity required to differentiate between clinical stages of lymphedema and their associated tissue changes. Further studies with larger and more diverse samples are needed to validate these findings and to explore thermography's potential role in clinical staging and monitoring of lymphedema.

However, this study concluded that thermography has limitations in sensitivity for detecting tissue alterations, as no significant correlation was found with ultrasound findings. It is important to note that the sample was heterogeneous, with regions of interest often showing multiple tissue alterations, complicating the precise correlation of temperature with individual findings. The lack of statistical significance in the correlated data is primarily attributed to the small sample size, despite the presence of effect size (Hedges' *g*), which was small in some analyses.

## 4. CONCLUSION

Thermography and ultrasound are used techniques for detecting secondary lymphedema following breast cancer treatment. However, this study did not find a significant correlation between these two modalities. This highlights the limitations of using these methods independently and underscores the need for future research that integrates thermography and ultrasound. Studies with larger sample sizes and a combined approach may enhance diagnostic precision, offering a more comprehensive understanding of tissue alterations associated with lymphedema and improving patient outcomes.

## CONSENT

All authors declare that ‘written informed consent was obtained from all participants.

## ETHICAL APPROVAL

All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee under protocol no. 5.434.586and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

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