

# **Research Article**

**Open Access, Volume 3** 

# Role of infrared thermography in soft tissue tumors: Diagnostic efficacy and value of distinguishing between benign and malignant lesions

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Received: Oct 18, 2023 Accepted: Nov 17, 2023 Published: Nov 24, 2023 Archived: www.jclinmedimages.org Copyright: © Domínguez González JJ (2023).

"Novelty and impact": The processes of angiogenesis and tumor growth in malignant tumors causes an increase in skin temperature. A skin temperature difference  $\geq 0.85$  °C compared to the unaffected side can help differentiate between benign and malignant tumors. Infrared thermography can be used to suspect the benignity or malignancy of tumor and propose a biopsy with a shorter delay time, as well as avoid the possibility of performing unplanned surgeries without prior diagnosis specially in small tumors.

## Abstract

We evaluate the role of infrared thermography in the study of soft tissue tumors and their ability to distinguish between benign lesions and potentially malignant lesions.

**Methods:** 140 adults patients with a soft tissue tumors in limbs have been studied by thermographic images of the affected side and the contralateral healthy side. All patients underwent triple assessment that consisted of clinical, radiological, and histopathological examination, according to usual protocol.

**Results:** 79 tumors (56.4%) were soft tissue sarcomas, 61(43.6%) were benign lesions. Temperature difference between the tumor zone and the healthy zone in malignant tumors was 2,638°C +/- 0.082 p<0.05, statistically significant, in benign tumors temperature difference between the tumor zone and the healthy zone was 0.180°C +/- 0.057 no significant. Temperature difference shows a high discriminant capacity, ROC curve 0.996, sensitivity 98.7%, specificity 96.7%. Optimal cut-off point of temperature was 0.85°C. With Likelihood positive ratio of 29.61.

**Conclusion:** We have observed statistically significant hyperthermia in all malignant tumors, unlike benign tumors in which there is no statistically significant hyperthermia, thermography is a contactless diagnostic method which allows us to perform the test without pain, without radiation emission, as many times as necessary, riskfree and comfortable for the patient. Infrared thermography can assess benignity or malignancy of a soft tissue tumor and propose a biopsy with less delay time, as well as avoiding the possibility of performing unplanned surgeries, specially in small malignant tumors.

**Abbreviations:** CT: Computed Tomography; IRT: Infrared thermography; LCD: Liquid-Crystal Display; MRI: Magnetic Resonance Imaging; ROC curve: Receiver Operating Characteristic; ROI: Region of interest; NDT: Non-destructive testing. **Citation:** Domínguez González JJ, Ortiz Cruz EJ, Rodríguez CV. Role of infrared thermography in soft tissue tumors: Diagnostic efficacy and value of distinguishing between benign and malignant lesions. Open J Clin Med Images. 2023; 3(2): 1149.

#### Introduction

Soft tissue sarcomas (SPB) constitute a heterogeneous group of neoplasms of mesenchymal origin, with the exception of peripheral nerve sheath tumors that are of ectodermal origin. They have an incidence of about 5-6 cases per 100,000 inhabitants and represent 1% of all cancers [1].

There is no imaging test that can completely assure us that a tumor is malignant. Magnetic Resonance Imaging (MR) can help us in this regard, but as we see in normal practice, there are benign tumors that can induce us to considere them as sarcomas when they are not and vice versa [2,5]. Previous studies have reported that malignant neoplasm, such as breast cancer tumors and melanoma, present with skin temperature higher than surrounding healthy tissue [6]. However, benign skin lesions, such as synovial cysts, dermatofibromas, granulomas, are iso- or hypothermic compared with the surrounding healthy skin [6]. Differences in heat generation between malignant and healthy tissues have been attributed to differences in metabolic rate, blood supply, and the presence of angiogenesis [7]. Studies on the relationship between soft-tissue neoplasm and thermography are scarce [8].

Infrared thermography (IRT) is an imaging technique that allows the detection of electromagnetic heat radiation emitted by an object (the body in medical practice). Changes in the temperature of the human body can be caused by disease, physical activity, mechanical or chemical stress and other factors [3]. The behavior of diseased tissue and tumors differs from that of healthy tissue in terms of heat generation and blood supply, because of processes such as increase in metabolic rate, angiogenesis, inflammation, changes in blood vessel morphology, interstitial hypertension and impaired response to homeostatic signals [4]. These physiological changes can be imaged by means of infrared thermography camera in clinical diagnostic applications [9]. The first modern infrared detector of leadsulfide photodetector, was originally developed for military applications, around World War II. Later the technology was released for civilian uses and thereafter IRT has been used in medical sciences as well as in the field of non-destructive testing (NDT). The advantage of IRT imaging in medical diagnostics is that is non-invasive, it does not require the irradiation of the body by an external source of radiation (such as, X-ray, or the administration of contrast substances, as well, it does not implies neither heavy nor expensive equipment. The most numerous studies on the use of infrared thermography in tumors have been developed in breast cancer [15,16,17,25]. In earlier decades, IRT was typically used qualitatively, with visual information captured by the detector converted to a color-coded or grayscale image, and visual patterns interpreted by the naked eye only, without quantifying temperature differences. The qualitative use of infrared information gave the method the reputation of being an imprecise technique and unsuitable for precision quantitative measurements and diagnostic applications, which added to the great advance and development of imaging techniques such as magnetic resonance and computed tomography during the 1980s and 1990s caused thermography to fall into disuse, due to its slower technological development. This has radically changed today with quantitative and dynamic measurements. Advances in IRT detectors, camera technology, computers, image processing techniques and software led to

the resurgence of interest in infrared thermography in biomedical applications [3,4,7,9,10].

This work aimed to assess the difference in skin temperature between the healthy side and the pathological side in soft tissue tumors and to evaluate the role of infrared thermography in the study of soft tissue tumors and its ability to distinguish between benign and malignant neoplasm.

#### **Materials and methods**

This is a prospective cohort observational study that was approved by the Institutional Review Board (2020-395). Informed consent requirement was waived. The study follows the guide-lines of the Declaration of Helsinki of 1964 with its later revisions. The work included 140 adult patients with a soft tissue tumor in limbs cared for in our hospital, MD Anderson Cancer Center Madrid, from janvier 2020 to june 2021, who gave their informed consent to participate in the study.

The study is descriptive, taking thermographic images of the tumor side and the healthy side, these images are free of risk for the patient and no change was made up to the usual diagnostic protocol in this type of tumor [1]. The thermographic images of the affected side of the patients were obtained using a digital infrared camera FLIR Systems. It is a compact light weight focal plane array-based system with a temperature resolution of 45 mK, <0.045°C. The image matrix size was 640x480 pixel. A highresolution real time image was provided on the Liquid-Crystal Display (LCD). The emissivity setting on the thermal imaging camera was 0.98. It is advisable that the subjects should refrain from exposure to direct sunlight and uses of cosmetics, antiperspirants or deodorants immediately before the thermography examinations. A thermal acclimation time is required for the subjects to achieve thermal equilibrium (9,10). Before the recording, patients were acclimatized in a room with a mean temperature of 21°C (range, 20.5°C-22.5°C) and a relative humidity of 50% (range, 45%-55%) for 15 min. After acclimatization of the patient in the room, the thermographic study was carried out, the shots were made 50-80 cm from the patient and always trying to capture the images at an angle of 90 grades. The region of interest (ROI) was defined as the area encompassing the entire tumor on the affected side and the area symmetrical to the affected side on the unaffected side. As every participant had a different tumor location, the area of the selected ROIs could not be equal. However, the ROI on the affected and unaffected sides of an individual could be the same. The areas under study were delimited, the palpable tumor zone (region of interest) and the contralateral healthy zone (intraindividual control).

On the affected side, the temperature of the skin just above the tumor was measured over the entire tumor area on the recorded thermogram, and the average of all temperatures was calculated. The same measurements were made on the unaffected side. The recorded thermograms were analyzed using the corresponding software of the cameras (Flir Tools +) R.

At least three shots of each projection, frontal, medial and lateral, were captured according to the location of the tumor, which were later studied using the thermal camera software. Temperature measurements of the tumor area and its equivalent on the contralateral side were performed, as well as a study of isothermal regions and temperature gradient. Skin temperature difference was defined as the difference between the mean skin temperature in the affected and unaffected regions.

The software supplied with the camera, FLIR ToolsR, was used to find areas of the tumor having different temperature gradients by generating a color-coded, processed image of the tumor showing suspicious foci. All patients underwent imaging, MRI and/or Computed Tomography (CT) studies and a biopsy study with tru-cut guide biopsy, according to usual protocols [1]. We can see examples of various cases in Figures 1-5.

#### Statistical analysis

The statistical program Statistical Package for the Social Sciences (SPSS) was used, and the Kruskal-wallis and U-Mann-Withney tests were applied to compare the means of the distributions of the quantitative variables in the different groups established by the categorical variable. The study of the discriminant capacity of temperature in tumoral area and the ideal cut-off point of temperature was carried out to assess the probability of risk of tumor lesion being malignant by means of the area under ROC curve (Receiver Operating Characteristic), We compared differences in skin temperature values between benign lesions and malignant tumors. (ROC) curve analyses were conducted to determine the skin temperature difference thresholds between affected and unaffected tissues to differentiate between benign lesions and malignant tumors.

#### Results

140 adult patients with soft tissue tumors were studied, 79 (56.4%) were diagnosed as soft tissue sarcomas after the biopsy study, and 61(43.6%) turned out to be benign lesions. The median age of the cohort population was 48 +/- 1.8 years old. 72 male (55.71%) and 68 female (48.57%). The mean temperature of the healthy area, contralateral side of tumor zone, in malignant tumors group was  $31,924^{\circ}$ C +/- 0.160, the average temperature of the pathological area in malignant tumors group was  $34,562^{\circ}$ C +/- 0.146. In benign tumors group the average temperature on the healthy zone, contralateral side of tumor zone, was  $32,484^{\circ}$ C +/- 0.208 and the average temperature in the area of the tumor was  $32,664^{\circ}$ C +/- 0.218.

The mean temperature of the healthy area of patients with malignant tumor confirmed diagnosis was  $31,924^{\circ}C$  +/- 0,160 while the average temperature in the pathological zone was  $34,562^{\circ}C$  +/- 0,146. This diference (2,638°C +/- 0,082) was statistically significant (p<0,05). As for patients with a confirmed diagnosis of benign tumor, the average temperature on the healthy side was  $32,484^{\circ}C$  +/- 0,208 and the average temperature in the area of the tumor was  $32,664^{\circ}C$  +/- 0,218, the diference of temperature (0,180°C +/- 0,057) showed no statistically significance. There are statistically significant differences in the mean value of the temperature difference between benign and malignant tumors (Graphic 1).

There were no statistically significant differences in the mean temperature value between the different groups of TNM in malignant tumors (p>0.05), although the greatest temperature difference occurred in the largest tumors (Table 1).

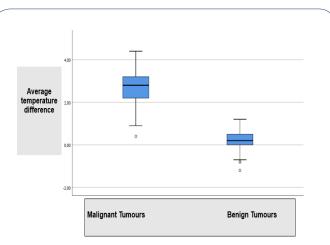
However there is a statistically significant difference in the mean value of the pathological side temperature between the different degrees of tumor in malignant tumors (p<0.05), a greater temperature gradient in high-grade tumors (Table 2).

The temperature difference (Temperature gradient) between

the healthy side and the tumor side in malignant tumors shows a high discriminant capacity with an area under the ROC curve of 0.996 (95% CI 0.988 to 1,000) (Graphic 2).

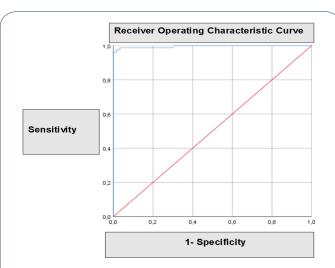
An optimal cut-off point of temperature can be identified at 0.85°C, with a sensitivity of 0.987 and a specificity of 0.967. If the temperature difference between the area of the tumor and the healthy side is greater, the odds of the tumor being malignant are very high (Likelihood positive ratio: 29.61) (Table 3).

Graphic 1: Skin temperature differences.

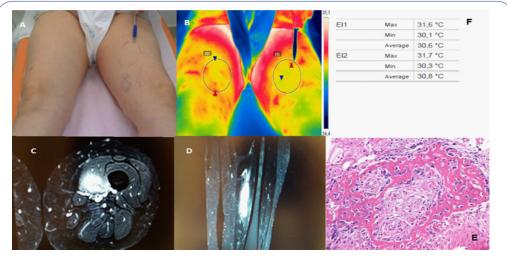


**Graphic 1:** A comparison of skin temperature differences between benign lesions and malignant tumors. The average  $\pm$  standard deviation skin temperature difference in benign lesions (32,664°C +/- 0,2189). In malignant tumors the average  $\pm$  standard deviation skin temperature difference was (34,562°C +/- 0,146) (p<0.05). The skin temperature difference in malignant tumors was found to be statistically significantly higher than that of benign lesions (p<0.05). The vertical axis shows the value of the difference in skin temperature.

**Graphic 2:** Receiver-operating characteristic curve (ROC Curve): temperature differences between benign and malignant tumors.



**Graphic 2:** Diagnostic performance area of the temperature gradient in the identification of a malignant tumor. Receiver-operating characteristic curve (ROC Curve): analysis of skin temperature differences between benign and malignant tumors. The cut-off value for the difference in skin temperature was 0.85°C. The area under the curve was 0.996, and, sensitivity, and specificity were, 98.7, and 96.7, respectively.



**Figure 1: A.** Patient with palpable tumor in the anterior region of the left thigh of several months of evolution.

**B.** The thermographic study in the palette color mode did not detect differences of temperature in the area of the tumor (average temperature  $30,6^{\circ}$ C), with respect to the contralateral healthy zone (average temperature  $30,8^{\circ}$ C).

**C,D.** Upon arrival at the consultation, the patient provides an MRI report from another center with a diagnosis of possible sarcomatous tumor.

- E. The biopsy study confirmed that it was an ossifying myositis.
- F. Maximum, minimum and average temperatures of each area.

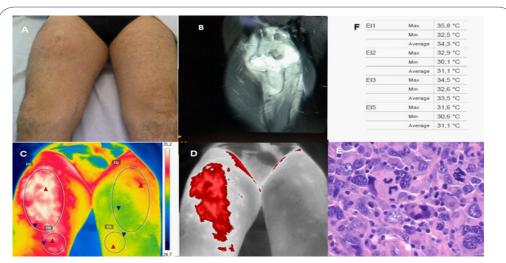


Figure 2: A. Patient with a large tumor in the anterior region of the right thigh.

B. MRI heterogeneus large mass suggesting soft tissue sarcoma.

**C.** Significant hyperthermia was observed in the thermographic study in the palette color mode (average temperature  $34,3^{\circ}$ C),(white color represents the hottest zone), respect to the same area of the contralateral side (average temperature  $31,1^{\circ}$ C).

**D.** Significant hyperthermia in the isothermal analysis mode, of the tumoral side respect to the same area of the contralateral normal side.

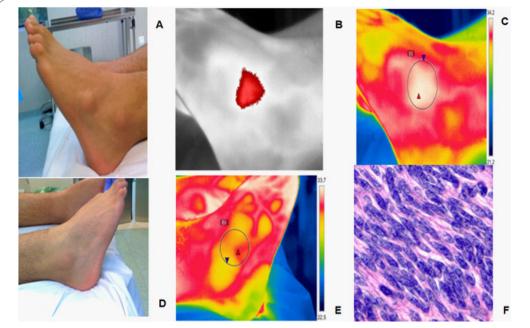
E. The diagnosis of pathological anatomy was high-grade pleomophic sarcoma.

F. Maximum, minimum and average temperatures of each area.

#### Discussion

Malignant tumors are often hypervascular, resulting in temperature elevation. More specifically, an abnormally elevated temperature in the breast cancer can indicate vascular issues or malignancy. A temperature difference that ranges between 1 and 2.5°C has been suggested to be a suspicious clinical finding [8,25,26]. In this study, we found that skin temperature differences in malignant soft-tissue tumors were often higher than those of benign lesions. ROC curve analysis indicated that the cut-off value for skin temperature differences between benign lesions and malignant tumors was 0.85°C although a difference in skin temperature of 0.4°C between the healthy side and the pathological side can help us to suspect the possible existence of malignant tumors, the sensitivity and specificity of the test, is very high, sensitivity 0.987 and specificty 0.967, and that alows us to detect the chances of malignancy or benignity of a tumor in a patient who comes to our consult and to begin treatment faster, using a rapid, risk-free and comfortable test for the patient.

Neoplasm generally have an increased blood supply and an increased metabolic rate which leads to localized high temperature spots over such areas, rendering them to be visualized by IRT. Blood vessels, produced by cancerous tumors are simple endothelial tubes devoid of a muscular layer. Such blood vessels show a hyperthermic pattern due to vasodilatation [18]. Metabolic activity and vascular network in cancerous lesions and



**Figure 3: A.** Patient with a tumor in the lateral region of the left foot of less than 5 cm who initially came to our consultation with a diagnosis of synovial cyst.

B. Significant hyperthermia in the isothermal analysis mode.

**C.** Significant hyperthermia was observed in the thermographic study in the palette color mode (average temperature 33,6°C), white color represents the hottest zone.

D. Contralateral healthy foot.

- E. Thermographic study of the contralateral healthy side (average temperature 31,2°C).
- F. After biopsy, intermediate grade synovial sarcoma was confirmed.

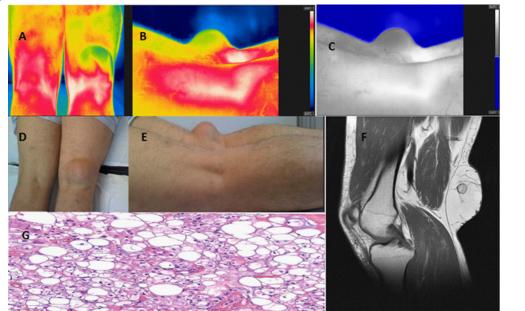


Figure 4: A, B. Color palette thermography of a tumor in the right popliteal fossa, there is no increase in temperature between the area of the tumor and the healthy contralateral area.

C. Thermography in isothermal mode showing the absence of hyperthermia in the tumor.

D,E. Photograph of the tumor in the right popliteal fossa.

F. MRI image T1-weighted sequence, sagittal plane with a tumor with a lipomatous appearance.

**G.** After an anatomopathological study, a soft tissue tumor compatible with a mature lipomatous tumor was confirmed.

in the surroundings of a growing tumor are always more pronounced than in the normal tissue. The processes of angiogenesis and tumor growth in malignant tumors causes an increase in temperature. Intertumoral blood supply influenced elevated skin temperature in malignant soft-tissue tumors.

In this study we can objectify how malignant soft tissue tumors have a very significant temperature difference between the tumor area and the contralateral healthy area, as well as between benign tumors, which do not show significant temperature differences between the tumor area and the healthy contralateral area. We have already mentioned how the processes of angiogenesis and tumor growth in malignant tumors causes an increase in temperature, this has already been seen in different works on breast cancer, melanoma and malignant urinary bladder tumors, making the termographic test a meth-

| 35,5 °C<br>34,5 °C |
|--------------------|
|                    |
|                    |
| 35,0 °C            |
| 32,5 °C            |
| 31,6 °C            |
| 32,1 °C            |
| 33,4 °C            |
| 32,8 °C            |
| 33,1 °C            |
|                    |

**Figure 5: A.** patient with a papular and reddish lesion on the forearm of several weeks' evolution and with a history of chronic lymphedema in the left arm due to breast cancer.

**B.** In the thermographic study, significant hyperthermia of the lesion was observed, in the color palette mode (average temperature 35°C), the white color represents the hottest area. There is no temperature increase in the surrounding area of the forearm.

**C.** Significant hyperthermia, in the isothermal analysis mode, of the tumoral region respect to the surrounding area of the forearm.

grade.

**D.** After biopsy, an angiosarcoma was confirmed in the context of Stewart Treves syndrome.

E. Maximum, minimum and average temperatures of each area.

|       | TNM        | Tª healthy<br>side | Tª<br>pathological<br>side area of<br>interest | Temperature<br>Difference |
|-------|------------|--------------------|--|---------------------------|
|       | Average    | 31,16              | 33,76  | 2.60°C                    |
| T1A   | N          | 13                 | 13   |                           |
|       | Desviation | 1,0850             | 1,2546   |                           |
| T1B   | Average    | 32,07              | 34,53  | 2.46°C                    |
|       | N          | 13                 | 13   |                           |
|       | Desviation | 1,4532             | 1,0988   |                           |
| T2A   | Average    | 32,34              | 34,89  | 2.55°C                    |
|       | N          | 15                 | 15   |                           |
|       | Desviation | 1,2783             | 1,3761   |                           |
| T2B   | Average    | 31,96              | 34,71  | 2.75°C                    |
|       | N          | 38                 | 38   |                           |
|       | Desviation | 1,5145             | 1,2874   |                           |
| Total | Average    | 31,92              | 34,56  | 2.64°C                    |
|       | N          | 79                 | 79   |                           |
|       | Desviation | 1,4217             | 1,3004   |                           |

 Table 1: Relationship between the temperatures and the TNM tumor staging.

Relationship between the temperatures of the healthy side and the affected side and the TNM tumor staging in patients with a diagnosis of soft tissue sarcoma. There were no statistically significant differences in the mean temperature value between the different groups of TNM in malignant tumors (p>0.05), although the greatest temperature difference occurred in the largest tumors.

| Tumor G      | rade            | Tª<br>healthy<br>side | Tª<br>pathological side<br>area of interest | Temperature<br>Difference |
|--------------|-----------------|-----------------------|---|---------------------------|
|              | Average         | 31,85                 | 34,05                                       | 2.20°C                    |
| Low          | N               | 17                    | 17  |                           |
|              | Desvia-<br>tion | 1,5456                | 1,4984                                      |                           |
| Intermediate | Average         | 31,77                 | 34,27                                       | 2.50°C                    |
|              | N               | 26                    | 26  |                           |
|              | Desvia-<br>tion | 1,1782                | 0,9263                                      |                           |
| High         | Average         | 32,06                 | 35,01                                       | 2.95°C                    |
|              | N               | 36                    | 36  |                           |
|              | Desvia-<br>tion | 1,5435                | 1,3169                                      |                           |
| Total        | Average         | 31,92                 | 34,56                                       | 2.64°C                    |
|              | N               | 79                    | 79  |                           |
|              | Desvia-<br>tion | 1,4217                | 1,3004                                      |                           |

Table 2: Relationship between temperatures and the tumor

Relationship between the temperatures of the healthy side and the affected side and the tumor grade in patients with a diagnosis of soft tissue sarcoma. There is a statistically significant difference in the mean value of the pathological side temperature between the different degrees of tumor in malignant tumors (p<0.05), a greater temperature gradient was confirmed in high-grade tumors.

| Positive if temperatura, in °C is greater<br>than or equal to | Sensitivity | 1 - Specificity |
|---|-------------|-----------------|
| 0,4000  | 0,987       | 0,295           |
| 0,4500  | 0,987       | 0,262           |
| 0,5500  | 0,987       | 0,197           |
| 0,6500  | 0,987       | 0,131           |
| 0,7000  | 0,987       | 0,098           |
| 0,7500  | 0,987       | 0,082           |
| 0,8000  | 0,987       | 0,066           |
| 0,8500  | 0,987       | 0,033           |
| 0,9500  | 0,975       | 0,033           |
| 1,1000  | 0,975       | 0,016           |
| 1,2000  | 0,962       | 0,016           |
| 1,3500  | 0,962       | 0,000           |
| 1,5500  | 0,949       | 0,000           |
| 1,6500  | 0,924       | 0,000           |
| 1,7000  | 0,911       | 0,000           |
| 1,7500  | 0,886       | 0,000           |
| 1,8500  | 0,861       | 0,000           |
| 1,9000  | 0,835       | 0,000           |
| 1,9500  | 0,823       | 0,000           |
| 2,0500  | 0,797       | 0,000           |
| 2,1500  | 0,759       | 0,000           |
| 2,2000  | 0,722       | 0,000           |
| 2,2000  | 0,709       | 0,000           |
| 2,2500  | 0,684       | 0,000           |
| 2,3000  | 0,633       | 0,000           |
| 2,3500  | 0,620       | 0,000           |
| 2,4000  | 0,582       | 0,000           |
| 2,4500  | 0,570       | 0,000           |
| 2,5500  | 0,557       | 0,000           |
| 2,6500  | 0,544       | 0,000           |

 
 Table 3: Curve Co-ordinates: Test result variables: Temperature difference.

An optimal cut-off point of temperature can be identified at 0.85°C, if the temperature difference between the area of the tumor and the healthy side is greater, the odds of the tumor being malignant are very high (Likelihood positive ratio: 29.61).

od to consider for detection and monitoring [6,7,11-13,15-17]. These results allow us to assess the suitability of the use of this technique as a method of diagnostic approach in soft tissue tumors, allowing us with a high sensitivity and probability to assess whether a tumor can be potentially malignant.

It should be noted that the thermography is a contactless diagnostic method based on the recording of the radiation heat emitted from the human body using a infrared camera which allows us to perform the test without pain, without radiation emission, as many times as necessary and it allows us to expedite decision-making, especially in small tumors where imaging tests such as MRI can lead to diagnostic and interpretation errors. We have seen that high-grade tumors show a significant increase in temperature (Table 2), but with regard to size this is not the case, observing how small malignant tumors have high temperature differences, (Table 1) which it is very important not to neglect the malignant potential of small tumors, especially in acral regions.

There are very few studies on thermography and soft tissue

sarcomas, in 1987 Sanchez Estella R, et al. studied using infrared thermography 8 patients with soft tissue tumors, 6 sarcomas and 2 lipomas, hyperthermia of 2.83 +/- 0.39°C was confirmed in sarcomas and in an area greater than that seen in clinical examination and hypothermia in patients with lipomas. They describe a sensitivity of 80% and a specificity of 100%, with a positive predictive value of 100% and a negative predictive value of 66.6%. In that work the study was about a very small sample [19].

In another work by Gardani et al. 1983, the authors study the thermographic behavior of bone and soft tissue tumors (168 malignant), submitted for examination from 1971 to 1981, they had been retrospectively analyzed and statistically evaluated. In the group of malignant neoplasms, thermography reached a good sensitivity (81.5%), a little better (but not significantly) in soft tissue tumors. Mainly three pathological features have been analyzed: histological type, size and site of neoplastic masses. None of them appears to be related with the result of thermographic examination [20]. Another study by Farrell et al. in 1968 indicate that thermography is useful in evaluating patients with osteosarcoma. It may be employed to determine local extent and vascularity of the primary tumor, recurrence, and metastases. Nineteen patients with osteosarcoma have been evaluated. The primary tumor was accurately outlined in the 14 patients who presented with a primary lesion and the thermogram were correlated with roentgenography. Metastatic lesions and recurrent tumor were detected often, and frequently the thermogram was the first evidence of disease [21]. Shimatani et al. in a recent study ussing infrared thermography report statistically significant difference found in tumor-related temperature differences in the healthy and affected sides of benign lesions and malignant tumors in 118 soft-tissue tumors, excluding adipose tumors. Using a ROC curve, a cut-off value of 0.2°C was considered a meaningful index for the skin temperature difference. They found that the area under de curve vas 0.75, and the odds ratio, sensitivity and specificity were 6.71, 0.67 and 0.77 respectively. According this autors the factors contributing to the skin temperature differences were unrelated to the size and depth of the tumor [26]. In our study, the thermographic test showed a temperature difference of more than 2.5°C on average in all malignant tumors, regardless of tumor size, compared to the healthy side, which did not occur with benign tumors, only in some non-sarcomatous tumor types, such as villonodular synovitis, and desmoid fibromatosis, a temperature difference values of 0.5°C were found compared to the healthy side.

In our work we have observed significant hyperthermia in all malignant tumors, which is greater in high-grade sarcomas, using a ROC curve, a cut-off value of 0.85°C was considered a meaningful index for the skin temperature difference from which we can say with high probabilities that a soft tissue tumor could be malignant. On this point we differ from the Shimatani study, which set a cut-off temperature of 0.2°C. We think that temperature differences below 0.5°C could not be attributed to a malignant process, but rather to a benign tumor with possible local aggressiveness. All the neoplasms in this work were palpable tumors. We find that the area under de curve was 0.996 (95% CI 0.988 to 1,000). with a sensitivity of 0.987 and a specificity of 0.967. This makes this test one more aid in the management of these tumors than sometimes because of their great variability and heterogenicity in imaging tests can induce diagnostic errors, catalog sarcomas as benign lesions and vice versa especially in small lesions which could lead unplanned excision ("whoops" procedure) [22,23].

This technique can also be useful for preoperatively evaluating the local extent of sarcomas since it can be used to know the infiltration associated with them, as well as the study of recurrences after unplanned surgeries, where MRI type imaging tests may not be resolutive to allow us to plan a surgery with a sufficient safety margin, which we are currently studying.

IRT real role in clinical practice could only be evaluated through a large multicenter trial that would estimate the accuracy of digital thermography in soft tissue sarcoma evaluation. We must work in developments in infrared imaging and supportive technologies that meet the needs and challenges for developing sensitive, reliable, and inexpensive quantitative diagnostic tools for early detection of soft tissue sarcomas and potentially staging of the disease in vivo.

We acknowledge a few limitations of this study. First, thermography is not useful for the definitive diagnosis of malignancy, biopsy is always necessary. Second, all patients in this study had palpable tumors, so very deep non-palpable tumors may have attenuation of measured surface temperature, which could lead to an inconclusive result.

#### Conclusions

IRT imaging is a non-contact, non-invasive, inexpensive and accessible imaging modality method, and this feature offers advantages in terms of ease of application and the ability to image larger surface areas and multiple lesions.

Infrared thermography can be used to suspect the benignity or malignancy of a soft tissue tumor and propose a biopsy with a shorter delay time, as well as avoid the possibility of performing unplanned surgeries, specially in small tumors, which can cause temptation to perform a excision without prior diagnosis [22,23].

Skin temperature differences measured with IRT may help in diagnosing malignant soft-tissue tumors. A skin temperature difference  $\geq 0.85^{\circ}$ C compared to the unaffected side can help differentiate between benign and malignant tumors.

The rapid development of advanced infrared detectors and the reduction in costs are very promising, and their integration in a smartphone-like device is now a reality, which would allow, for example, the use of infrared thermography in primary care and this could avoid false benign diagnoses in small malignant tumors and delays in their referral to a specialized center, which would facilitate the possibilities of early treatment of a possible sarcoma. This makes this test one more aid in the management of these tumors than sometimes because of their great variability and heterogenicity in imaging tests can induce diagnostic errors, catalog sarcomas as benign lesions and vice versa especially in small lesions which could lead unplanned excision.

The importance of making a diagnostic approach in terms of benignity or malignancy in the first consultation would be of great importance when it comes to the peace of mind of the patients and thear family.

#### Declarations

**Disclosure statement:** All the authors formally declared no conflict of interest with ongoing research. This work has not been supported by any company or organization.

**Conflicts of interests:** We have no conflicts of interest to disclose.

Author contributions: Conception and design of the study: José Javier Domínguez González. Development of methodology: José Javier Domínguez González and Eduardo José Ortiz Cruz. Acquisition of data: José Javier Domínguez González and Eduardo José Ortiz Cruz. Analysis and interpretation of data: José Javier Domínguez González and Carolina Varela Rodriguez. Writing of the manuscript: José Javier Domínguez González and Carolina Varela Rodriguez. Review, and/or revision: all authors. The study reported in the paper has been performed by the authors, unless clearly specified in the text.

#### References

- 1. National Comprehensive Center Network NCCN. Practice guideline in Oncology. Soft tissue sarcoma. NCCN 2-2022. Avaliableat: http://www.nccn.org/professionals/physician-gls/pdf/sarcoma. pdf.
- Alramdan MHA, Kasalak Ö, Been LB et al. MRI after Whoops procedure: diagnostic value for residual sarcoma and predictive value for an incomplete second resection. Skeletal Radiol. 2021; 50(11): 2213-2220. doi: 10.1007/s00256-021-03790-z. Epub 2021 Apr 26. PMID: 33900432; PMCID: PMC8449770.
- Jones BF. A reappraisal of the use of infrared thermal image analysis in medicine. IEEE Trans Med Imaging. 1998; 17(6): 1019-1027.
- 4. Anbar M. Assessment of physiologic and pathologic radiative heat dissipation using dynamic infrared imaging. Ann NY Acad Sci. 2002; 972: 111-118. [PubMed: 12496005].
- Moulton JS, Blebea JS, Dunco DM et al. MR imaging of softtissue masses: diagnostic efficacy and value of distinguishing between benign and malignant lesions. AJR Am J Roentgenol. 1995; 164(5): 1191-9. doi: 10.2214/ajr.164.5.7717231. PMID: 7717231.
- Shada AL, Dengel LT, Petroni GR et al. Infrared thermography of cutaneous melanoma metastases. J Surg Res. 2013; 182(1): 9-e14. doi: 10.1016/j.jss.2012.09.022. Epub 2012 Sep 27. PMID: 23043862; PMCID: PMC4426199.
- Buzug TM, Schumann S, Pfaffmann L et al. Functional infrared imaging for skin-cancer screening. Conf Proc IEEE Eng Med Biol Soc. 2006; 2006: 2766-9. doi: 10.1109/IEMBS.2006.259895. PMID: 17945738.
- Shimatani A, Hoshi M, Oebisu N et al. Clinical significance of thermal detection of soft-tissue tumors. Int J Clin Oncol. 2020; 25(7): 1418-1424. doi: 10.1007/s10147-020-01658-1. Epub 2020 Mar 21. PMID: 32200480.
- Ring E.F.J. The historical development of temperature measurement inmedicine, Infrared Physics & Technology. 2007; (49): 297-301.
- 10. Ring F. Thermal imaging today and its relevance to diabetes, Journal of Diabetes Science and Technology. 2010; 4: 857-862.
- Hakim A, Awale RN. Thermal Imaging An Emerging Modality for Breast Cancer Detection: A Comprehensive Review. J Med Syst. 2020; 44(8): 136. doi: 10.1007/s10916-020-01581-y. PMID: 32613403.
- 12. Aweda M. A., Ketiku K. K., Ajekigbe A. T et al. Potential role of thermography in cancer management, Archives of Applied Science Research. 2010; 2: 300-312.
- Wishart GC, Campisi M, Boswell M et al. The accuracy of digital infrared imaging for breast cancer detection in women undergoing breast biopsy. Eur J Surg Oncol. 2010; 36(6): 535-40. doi: 10.1016/j.ejso.2010.04.003. Epub 2010 May 10. PMID: 20452740.

- 14. Ring E.F.J, Ammer K. The technique of infrared imaging in medicine, Thermology International. 2000; 7: 7-14.
- 15. Kennedy D, LeeT, Seely D. A comparative review of thermography as a breast screening technique, Integrative Cancer Therapies. 2009; 8: 9-16.
- 16. Ng E.Y.K. A review of thermography as promising non-invasive detection modality for breast tumor, International Journal of Thermal Sciences. 2009; 48: 849-859.
- 17. Gamagami P. Atlas of Mammography: New Early Signs in Breast Cancer, Blackwell Science, United Kingdom. 1986.
- Wink DA, Vodovotz Y, Laval J et al. The multifaceted roles of nitric oxide in cancer. Carcinogenesis. 1998; 19(5): 711-21. doi: 10.1093/carcin/19.5.711. PMID: 9635855.
- Sanchez Estella R., Redondo E, .Sanchez Estella J. Termografía en los sarcomas de partes blandas. Cirugia Española. Vol XLII. 1987; (6): 852-856.
- 20. Gardani G, Bergonzi S, Viganotti G, Nessi R et al. Il ruolo della teletermografia nella diagnosi dei tumori primitivi delle parti molli e dello scheletro [Role of teletermography in the diagnosis of primary tumors of soft tissues and bones]. Radiol Med. 1983; 69(6): 433-8. Italian. PMID: 6665242.
- 21. Farrell C, Wallace J D., Edeiken J. Thermography and Osteosarcoma.. Radiology. 1968; 9(4): 792-793.

- 22. Ardakani AHG, Woollard A, Ware H et al. Soft tissue sarcoma: Recognizing a rare disease. Cleve Clin J Med. 2022; 89(2): 73-80. doi: 10.3949/ccjm.89a.21078. PMID: 35105695.
- 23. Tedesco NS, Henshaw RM. Unplanned resection of sarcoma. J Am Acad Orthop Surg. 2016; 24(3): 150-159. doi:10.5435/ JAAOS-D-15-00074.
- 24. Stefanadis C, Chrysochoou C, Markou D et al. Increased temperature of malignant urinary bladder tumors in vivo: the application of a new method based on a catheter technique. J Clin Oncol. 2001; 19(3): 676-81. doi: 10.1200/JCO.2001.19.3.676. PMID: 11157017.
- Mashekova, A., Zhao, Y., Ng, E. Y. K et al. Early detection of the breast cancer using infrared technology – A comprehensive review. Thermal Science and Engineering. 2022; 27: [101142].
- Shimatani A, Hoshi M, Oebisu N et al. An analysis of tumor-related skin temperature differences in malignant soft-tissue tumors. Int J Clin Oncol. 2022; 27(1): 234-243. doi: 10.1007/s10147-021-02044-1. Epub 2021 Oct 10. Erratum in: Int J Clin Oncol. 2021 Oct 17; PMID: 34628566; PMCID: PMC8502238.