

Is infrared thermography (IRT) a possible tool for the evaluation and follow up of Emery-Dreifuss muscular dystrophy? A preliminary study



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ABSTRACT

Hypothesis: The hypothesis of this work is that infrared thermography could become a valid tool for the diagnosis and follow-up of the Emery-Dreifuss disease due to putative temperature changes produced by a constant degenerative evolution of this muscular dystrophy.

Testing the hypothesis: To justify this hypothesis we proposed a pilot study with 2 brothers affected of Emery-Dreifuss who present a very different age, with the principal objective to evidence a possible evolution of this pathology. Acquisition and comparison of images of computerized axial tomography (CT) and thermography (IRT) of the distal limbs in 2 affected brothers.

Data and discussion: Important image correlations in the region of the thighs and the posterior region of the legs have been highlighted. The comparison between the CT and the thermography showed how the first results are encouraged and promising and open a possible new line of research on the evaluation and follow-up of this disease. Despite this, a larger number of studies are needed to validate the thermography as a diagnostic technique and follow-up of this pathology.

Background

Emery-Dreifuss muscular dystrophy (EDMD MIM 310300) is a degenerative pathology of the skeletal neuro-muscular system with an incidence of 1 in 100.000 patients creating articular deformations and cardiac changes [1–3]. According to the description made by Emery in 1966, the disease is characterized by the triad of contractures and stiffness in the tibialis, elbows and rachis, loss of the humeral-peroneal distribution and finally alterations of the heart muscle that, if not treated, can lead to death sudden [1–3].

To try to clarify the clinical evolution and the pathophysiology of this disease, in the bibliography there are some studies that included family groups, incorporating the functional magnetic resonance (MRI) and computerized axial tomography (CT) to find the muscular alterations of the lower limb which had not been registered previously [4–6].

Magnetic resonance imaging (MRI) is defined by the National Institute of Bioengineering and Biomedical Images, based in the USA, as a non-invasive diagnostic imaging technique that use an electromagnetic field to detect lesions and alterations in non-bone or soft parts

[7]. The CT is defined as an imaging technique based on the use of X-rays, which, producing ionizing radiations, can generate changes or biochemical effects in the human body [8].

Although magnetic resonance imaging is a very important diagnostic tool for precision and efficiency in diagnostic imaging, it is a very expensive technique and also generating an electromagnetic field, cannot be used in some types of diseases that lead to defibrillator implantation or a monitoring systems subcutaneous as the cardiac Reveal LINQ, due to electrical interference that may occur. These types of systems are common in patients suffering from cardiac abnormalities, as happens in our patients with EDMD.

On the other hand, as mentioned in the in the previous section, the CT is an examination that, even if few, presents risks of radioactive contamination, and this is why according to a very recent study published in 2018 the thermography could be a good evaluation technique and follow-up for this pathology [9].

In fact, thermography is defined as a rapid, economic and non-invasive diagnostic imaging technique that allows the infrared radiation emitted by a particular body or surface to be encoded and to provide a

Abbreviations: CT, Computed axial tomography; EDMD, Emery Dreifuss muscular dystrophy; IRT, Infrared thermography; MRI, Magnetic resonance

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clear and direct image based on the recorded temperature [10,11].

The authors try to justify the use of infrared thermography in patient with Emery Dreifuss, taking into account that the changes produced in the vascularization of muscle by avascular scar tissue, typical of this disease, could be reflected in the analysis of thermograms [9].

According to literature data, thermography sees recent applications above all in the field of sports and ocular medicine, but also the musculoskeletal system is starting to be the subject of important research work [12,13].

The need for a rapid, objective and non-invasive diagnostic technique should be a priority for the evaluation of this disease and for this reason, to justify the hypothesis that thermography could be a valid tool for evaluation and monitoring this disease, we propose a pilot study with 2 brothers affected of Emery-Dreifuss who present a very different age, with the objectives on the one hand, to describe, in this pathology, a possible correlation between TC and IRT in the muscular lesions of the lower limbs and on the other hand to evidence a possible evolution of this illness.

Hypothesis

The hypothesis of this work is that inferred thermography, due to the possible temperature changes produced by the constant degenerative evolution of muscular dystrophy of Emery-Dreifuss, could be a valid tool for the diagnosis and follow-up of the disease.

Testing the hypothesis

Given that one of the patients has an internal defibrillator that is not compatible with MRI, the study will be carried out with analysis of CT and IRT. For the recording of thermographic images, we followed the TISEM (Thermographic imaging in sports and medical exercise) recommendations, that ensure an adequate methodological precision of the work [14], whereas for the acquisition of the CT data of the lower limbs we followed a normal protocol, already used in other studies [15,16].

Patients

The patients were recruited from the neurology service, underwent a medical check-up (Table 1), a thermographic record, and as a last test the analysis of tomography. Once at the hospital center all patients were allowed to acclimatize to the environment during a period of 15/20 min in a room of 14 m², at a temperature between 23° and 24°, humidity 40 (± 0.8) %, free of electronic devices and with sunlight that passed through a large window far from the point of measurement [14,17]. During this period, the patients underwent a body temperature check (with a digital thermometer) to discard alterations of the basal temperature, and being in both cases less than 37° the researchers continued with the recording of the data of each patient in Table 1.

Before proceeding with the registration of the distal limbs, the patient was placed only with intimate clothing on a 1 centimeters (cm) thick cotton pad to avoid direct contact with the floor and thus generate temperature changes. When the thermographic recording period was over, 2 different radiologists in a blind form analyzed the tomographic and thermographic images. The CT images were reported by. In the thermographic evaluation of the lower limbs, as observed in previous works, 4 images were recorded, one in the front and in the back of the thighs, one in the front and in the back of the legs. The region of interest (ROIs) in the body segment have been defined using conventional anatomical references: in the anterior vision of the thigh at the proximal level, the ROI begins 15 cm below the anterosuperior iliac spine and extends up to 2 cm above the upper border of the patella (cuadricipital region), whereas in the posterior view it begins immediately below the gluteal fold and extends to the upper edge of the ditch Popliteus (is-quotibial region) [18].

Table 1

Patient,s data.

	Patient 01	Patient 02
Time	15:30	16:10
Sex	M	M
Age	22	38
Surgery	NO	INTERNAL CARDIA DEFIBRILLATOR
Eva	0	0
Weight	51.2 Kg	66.5 Kg
Height	170 Cm	173 Cm
IMC	17,72	22,22
Alcohol	NO	NO
Coffee	NO	NO
Drug	NO	NO
Smoke	NO	NO
Food	5 HOURS BEFORE THE VISIT	5 HOURS BEFORE THE VISIT
Cosmetics	NO	NO
Shower	5 HOURS BEFORE THE VISIT	5 HOURS BEFORE THE VISIT
Sun rays	NO	NO
Sport	NO	NO
Frequency	NO	NO
Duration	NO	NO
Intensity	NO	NO
Physical therapy	NO	NO

BMI: Body Mass Index, EVA: Visual analogic scale; KG: Kilograms.

In the anterior view of the leg the ROIs starts 2 cm below the inferior border of the patella up to 2 cm higher than the tibialis malleolus (tibialis region), while in the posterior view it identified from the inferior border of the Popliteus ditch up to 8 cm higher than the inferior border of the heel (gastrocnemius region) [18]. Regions of interest (ROI) were analyzed with the Flir research IR program.

Thermograph

The thermograph used for the realization of this work is the Flir E60 model. This thermograph has a thermal image quality of: 20 × 240 pixels, thermal sensitivity: < 0.05 °C, and records from −20 °C to +650 °C. The thermograph also offers the possibility to record up to 3 different points inside a narrow anatomic segment, giving information on the maximum and minimum temperature and the average variation with respect to the reference temperature.

To allow the correct configuration of the machine to the room, the main researcher turned on the machine an hour before the first registration made, placing it in a tripod at 1 m away from the patient registration point with an inclination of 10°/15°. The emissivity was 0.98 as suggested by the manufacturer and this figure was corroborated in other studies [19,20].

The analysis of the images was carried out with the Flir research IR program [19]. This study has been approved by the ethical committee dated 16/10/2018 acceptance number: 110/2018/CE.

Data of the test

The Fig. 1, A1 shows the cross section made in the middle section of the thigh of the young subject. Fig. 1A2 shows the cross section in the middle third of the leg of the young subject. In both images the distribution of the muscular groups is observed as well as the existing atrophy based on the gray scale analysis. Muscle groups with a lower gray scale index reflect greater muscular atrophy. Fig. 1B1 and B2 show the same cut of images in the elderly patient.

The Fig. 2 shows a thermographic image of the anterior and posterior view of the thigh in both subjects. Fig. 3 shows the thermographic image of the anterior and posterior view of the shank in both subjects. In both results the existing injury is observed based on the color

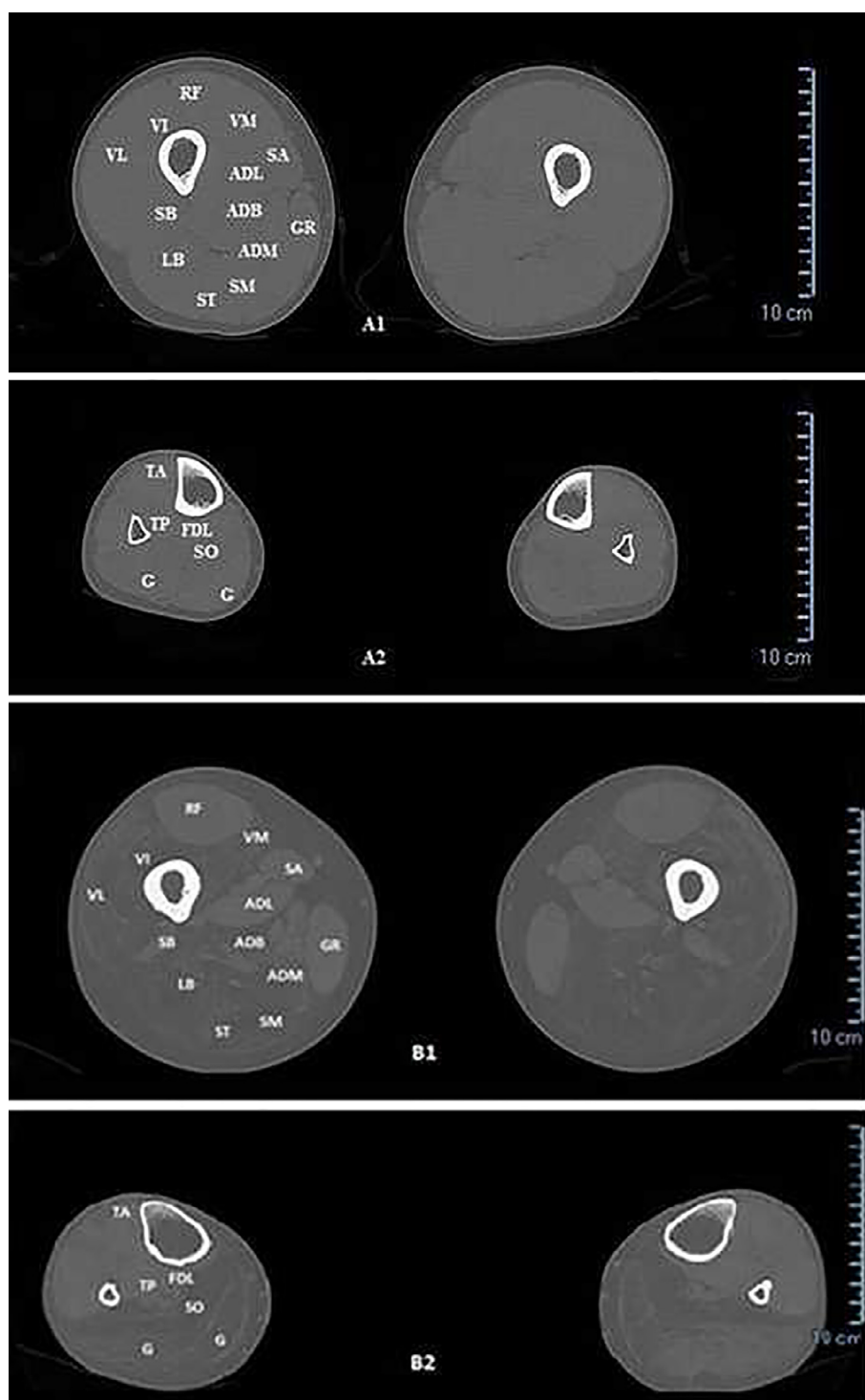


Fig. 1. TC images of the patients. A1: Thigh muscle of young patient A2: Shank muscle of young patient, B1: Thigh muscle of older patient. B2: Shank muscle of older patient. ADB: Adductor brevis, ADL: Adductor longus, ADM: Adductor maioris, FDL: Flexor longus digitorum, G: Gastrocnemius, GR: Gracilis, LB: Large hand biceps femoris, RF: Rectus femoris, SA: Sartorius, SB: Short hand biceps femoris, SM: Semimembranosus, SO: Soleus, ST: Semitendinosus, TA: Tibialis anterior, TP: tibialis posterior, VI: Vastus intermedius, VL: Vastus lateralis, VM: Vastus medialis.

analysis. Muscle groups with a lighter color index, reflect a lower injury on the darker color index.

Discussion

The thermography data expressed in Table 2 are the average temperature of the analyzed ROI. Based on some studies published previously in healthy patients, the temperature of normalization of the

muscles of the thigh, with the use of thermography, oscillates in anterior and posterior visions between 29° and 30° while the temperature of the anterior and posterior muscles of the legs oscillates between 27° and 32° without registering important changes between one leg and the other in the same subjects [18,21].

However, we consider that these results cannot be used as a comparison in our patients since the period of acclimatization, in these studies, takes place at an average temperature of 21° while the

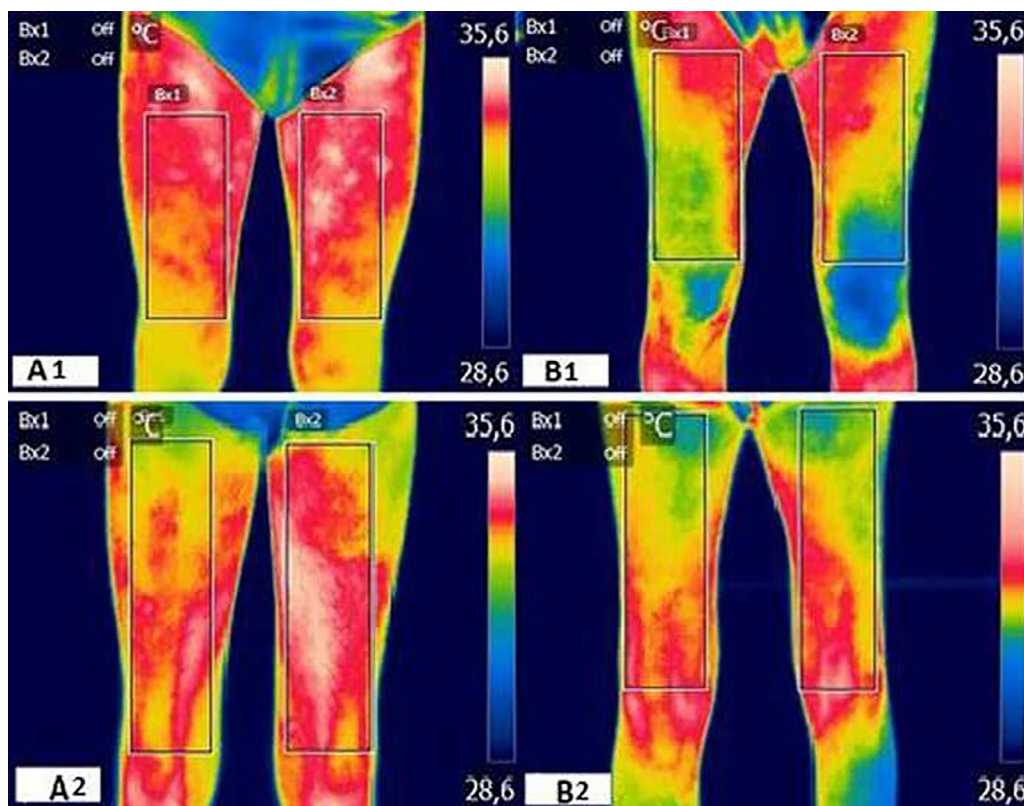


Fig. 2. Front and back view of the thigh muscles. A1: Patient 01 front view, A2: Patient 01 back view; B1: Patient 02 front view, B2: Patient 02 back view.

acclimatization of our patients takes place at an average temperature of 23.5°.

We believe that this difference of more than 2.5° could generate changes in basal temperature of the integumentary system which would

naturally alter the thermographic image, despite this, regardless of the temperature difference between healthy and pathological, we believe it is important to underline that at the bibliographic level no significant difference was observed between the temperature of a right or left limb

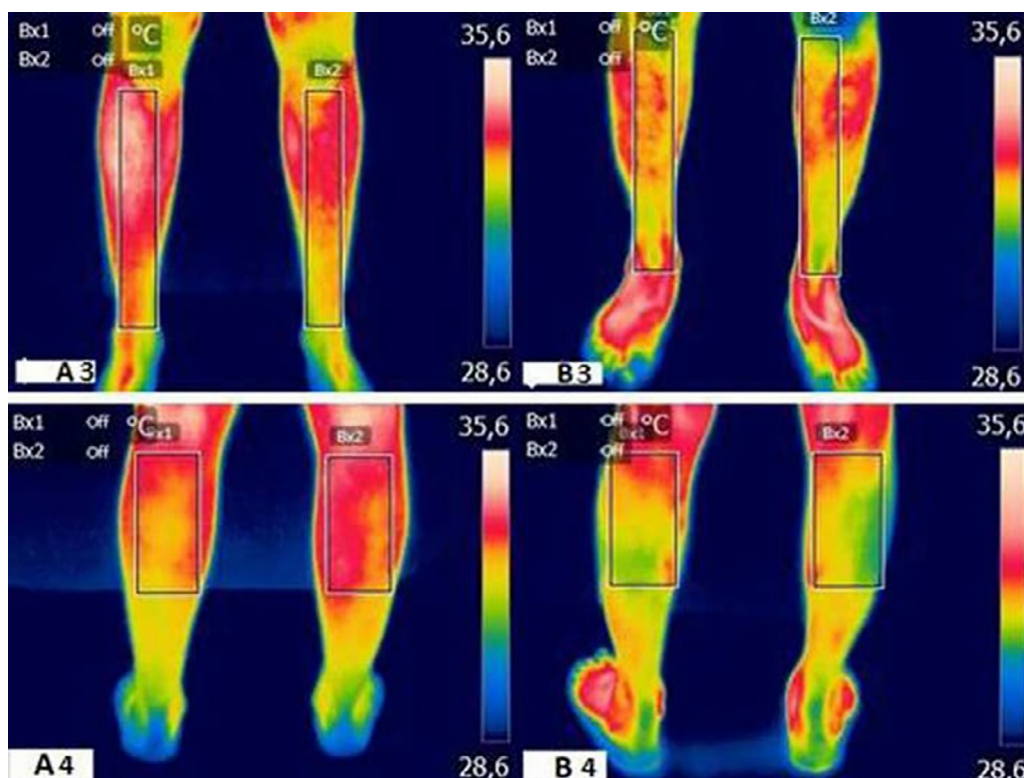


Fig. 3. Front and back view of the shank muscles. A3: Patient 01 front view, A4: Patient 01 back view; B3: Patient 02 front view, B4: Patient 02 back view.

Table 2
Summary of result of thermography and Tomography.

THERMOGRAPHY		SHANK	
THING		ANTERIOR	POSTERIOR
01 DX:34,1°	POSTERIOR DX:33,8° SX:34,2°	DX:33,8°	DX:33,2° SX:33,7°
SX:34,2°		SX:33,3°	
02 DX:32° SX:32°	DX:32,3° SX:32,3°	DX:32,7° SX:32,6°	DX:31,8° SX:32,0°
TOMOGRAPHY COMPUTED AXIAL		INJURY	
MUSCLE		01	02
Rectus femoris		x	+
Vastus intermedius		x	+
Vastus lateralis		x	+
Vastus medialis		x	+
Large hand biceps femoris		x	+
Short hand biceps femoris		x	+
Gastrocnemius		+	+
Soleus		+	+

01: Yung patient; 02: Mayor patient; DX: Right; SX: Left; X: No affected; +: Affected.

with respect to the contralateral in the same patient [22].

The fact of not being able to count on the support of a control group could appear as one of the possible limitations of our study, although we want to underline that the main objective of our work is not to show a difference between the healthy and the pathological but a possible evolution between two pathological patients in different stages.

If we look at the thermographic images, we can see that on the general level there is an important difference in temperature between the younger patient and his older brother. Analyzing them more specifically, we can see how the most important thermographic changes can be appreciated at the level of the thigh muscles in the anterior region (Fig. 2) and in the leg muscles in the posterior region (Fig. 3).

In the first case, we can observe how in the right thigh there is a difference of +2.1 °C and in the left thigh of +2.2 °C of the younger patient compared to the older one, while in the posterior region of the legs the difference is reduced, passing to +1.4 °C in the right leg to +1.7 °C in the left leg (Table 2).

This temperature difference found with the thermography can be explained and justified by analyzing the CT images. In fact, in the muscles of the thigh region in an anterior and posterior view, the older patient shows evident signs of hypodensity, accompanied by a reduction in volume by atrophy with adipose substitution, whereas in the younger patient there are no signs of morphological changes.

On the other hand, in the posterior region of the leg muscles, in the older patient the same condition can be observed that in the thighs, with great incidence in the soleus and medial and lateral gastrocnemius, whereas in the younger brother the images show signs of hypodensity, with initial adipose substitution. This means that at the proximal level of the lower limbs, the difference in temperature found with the thermography is greater because in the younger patient there is no trace of important muscular lesions, whereas at the lower level, the difference in temperature between the two patients is perceived as minor because, in both cases, we have the presence of muscular involvement, even if in one case it is more advanced than the other.

Regarding the possible mechanisms that could generate thermographic alterations in these type of patients, some authors have analyzed different possibilities, thanks to a bibliographic study on the use of thermography and all the conditions potentially present in this type of patients [9].

In that study, one of the aspects treated and that seems to be the most reliable to the authors, was the lack of vascularization of trophic and scarred muscle tissue compared to healthy muscle tissue found in other types of muscle atrophy [9,23,24]. In this regard, we would like to point out that in addition to the presence of adipose scar tissue that had been previously observed in this type of patients, we observed in

the older patient the presence of calcifications in the bilateral femoral artery and other calcifications in posterior tibialis artery on the left side.

It is important to underline that the arterial calcifications had never been observed in this type of patients before and more specifically had never been reported in this patient. This clinical data evidenced by the CT images could contrast with the thermographic results obtained, in fact, that calcifications at the arterial level, make the arteries harder and less elastic generating a decrease in blood flow that would have repercussion in small vessels at the level more superficial [25–27].

In spite of this we believe that the thermographic results are not compromised because, being a first appearance, the calcifications are not sufficiently important to decrease the blood flow in the arterial level. Given the novelty of the information encountered and the small sample adopted in our work, we are not able to define whether this condition is the result of the evolutionary mechanisms typical of the disease or if it is only an isolated and independent case to the pathology on sidering the small number of patients. In spite of this we believe it would be useful to look into this research work in further depth in adult patients with EDMD with a larger display and blood analysis, to determine the epidemiology and the evolution of arterial calcifications in these patients.

Given the information already known on the topic and the new results obtained, we therefore believe that the presence of adipose scar tissue compared to normal muscle tissue, is the main cause on which to establish the basics of thermographic research in these patients. Since the Emery-Dreifuss is a degenerative disease, we believe that the thermographic picture obtained in these two patients, is in fact a possible evolutionary character of the disease even if we are aware that in order to affirm with certainty this data is necessary a long-term observational study maybe re-evaluating the thermographic data proposed in this study on the same patients each year.

Despite this, the excellent correlation between the CT images and the thermography allows us to affirm that the first results obtained in this type of patients are encouraging and promising and open a possible new line on the evaluation and follow up of this disease through an objective technique and easy to use, which is the thermography.

Limitation

We believe that the proposed study presents aspects that can be improved through future research work and new theories on which to base others. On the one hand we are aware that the number of patients analyzed could be improved in future work, we believe that despite the first results being hopeful, a family of 2 brothers is an inconsistent number to demonstrate the effectiveness of this technique in this disease.

Despite everything, this being a rare disease means it is difficult to find a very large sample of patients, despite a sample of 15–20 patients we believe that it could be an adequate number. Another aspect that could present a limitation in our work could be the fact of not having a control group with which to compare the results obtained. The normal values used cannot be totally compared to our patient sample, although we believe it is important to stress that the goal of our work was not to show a difference between the healthy and the pathological but a possible evolution between two pathological patients in different states.

On the other hand, we believe that one of the strengths of our work lies in the fact that it is the first time that thermography has been used in this type of patient, while also offering positive results that will certainly form the basis of further research studies.

Future research

This preliminary study provided promising results that allow to open a new field of research based on the evaluation of infrared thermography as a tool for the diagnosis and follow-up of the Emery-Dreifuss muscular dystrophy.

Further observational studies should be focused on the analyzes the thermographic evolution of this disease along its different stages. A higher sample size from the different ages will be useful to establish a correlation between the evolution of this disease and temperature variations in the surface of affected areas of the muscle.

Patient involvement could also become a promising line of research in this type of disease. Future studies should address the relationships between stress tests and infrared thermography analysis.

Ethical publication statement

We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

Declarations of interest

None.

Equal contribution

These authors contributed equally to this work.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.mehy.2019.04.011>.

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