

Relationship between infrared skin radiation and functional tests in patients affected by Emery-Dreifuss muscular dystrophy: Part 2

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ARTICLE INFO

Keywords:

Thermography
Emery-Dreifuss
Muscular dystrophy

ABSTRACT

Hypothesis: This study represents a second part of a recently published study about a new form of evaluation and development of rare genetic neurodegenerative diseases. The objective is to provide a more global vision of thermography with respect to the Emery-Dreifuss pathology, through the analysis of the data collection carried out for one year. The basic hypothesis is that thermography could become a valid tool for the diagnosis and follow-up of this pathology because is a very specific tool for registering temperature changes produced by a constant degenerative evolution of this muscular dystrophy.

Background and hypothesis

Emery-Dreifuss muscular dystrophy (EDMD MIM 310300) is a rare neurodegenerative disease of a genetic nature [1–3]. The aetiology and epidemiology of this disease have changed over time since it was first described by AE Emery and FE Dreifuss in the mid-1960s [4–6]. Regarding pathophysiology, research on this disease has shown the presence of limitations in the range of the joints, muscle wasting and weakness, and cardiac abnormalities that can lead to death if not treated correctly [1–6]. Since all patients suffer cardiac alterations that in many cases lead to the implantation of an internal defibrillator, quantifying the progress of the disease by means of the most used diagnostic techniques (CT, MRI and ultrasound) is a long and complicated process in some cases. MRI seems to be the most successful technique to show muscle injuries, but not all defibrillators are compatible with the electromagnetic field generated by this technique, thus posing a significant risk for patients [7,8]. CT and ultrasound seem to be the most successful options. However, high radiation emissions, the impossibility of analysing large muscle regions simultaneously, the high cost of these two techniques and the long time they require to perform them, make them not very functional elements to quantify this disease quickly, economically and objectively. To this end, there is already growing scientific information regarding the use of thermography in these types

of patients. According to these studies, it is possible to quantify the neurodegenerative nature of the disease based on the analysis of infrared radiation emitted by the regions analysed in these patients [7–9]. Considering that infrared radiations are electromagnetic elements common to all bodies that have a temperature above 0°Kelvin and that the higher the temperature of an object, the more infrared radiation it is possible to record [9–12], there is no doubt that the trophic nature of the disease could be quantifiable since vascular scar tissue increases compared to normally vascularized muscle tissue. In order to confirm this hypothesis, very recent studies have been carried out regarding the relationships between CT and thermography and thermography with stress tests in these types of patients. Even though these very recent observational studies use a small sample of patients, they are undoubtedly laying the foundations for a new line of research, so that a longitudinal study could represent a further advance in this regard [13,14]. Accordingly, we have carried out a study of one-year evolution of this disease using thermography in a family of 4 siblings affected by Emery-Dreifuss muscular dystrophy in order to clarify and better explain the possible pre-established correlation between the neurodegenerative nature of the disease concerning the emission of infrared waves. This study represents a second part of a study recently published by Cabizosu et al. entitled: “Relationship between infrared skin radiation and functional tests in patients affected by Emery-Dreifuss

Abbreviations: BMI, Body Mass Index; EDMD, Emery Dreifuss muscular dystrophy; TAC, Computed Axial Tomography; IRT, Infrared thermography; TISEM, Thermographic Imaging in Sports and Medical Exercise

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<https://doi.org/10.1016/j.mehy.2020.110348>

Received 26 August 2020; Received in revised form 5 October 2020; Accepted 14 October 2020

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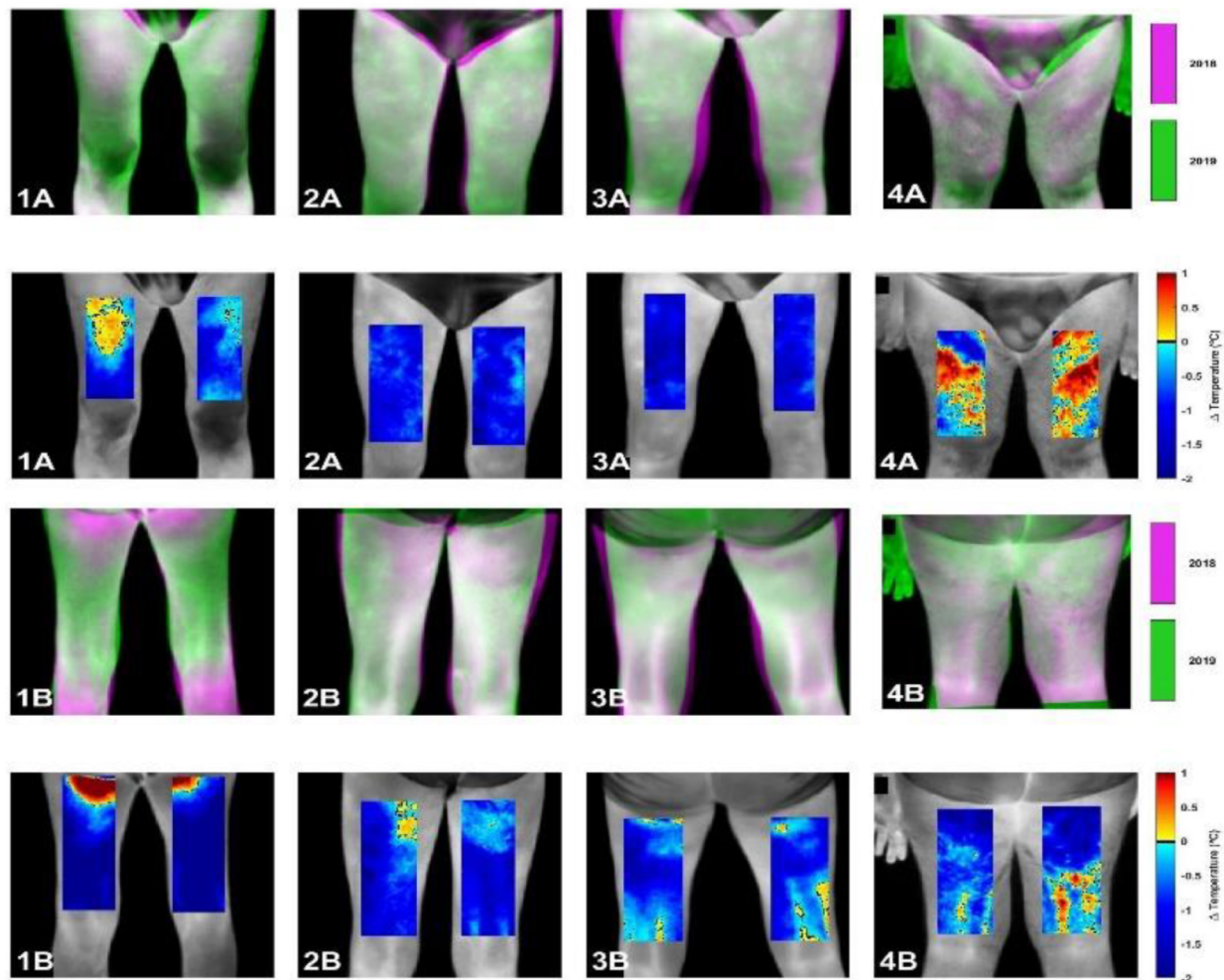


Fig. 1. 2018 (Violet) and 2019 (Green) thermographic images of the anterior and posterior thigh of the 4 patients. The images show the overlap of the thermographic patterns of the patients for the years 2018 (violet) and 2019 (green). The “A” images show the anterior thigh region, while the “B” images show the posterior thigh region. The images marked with ROI show the differences between the 2 years. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

muscular dystrophy” [14]. The objective of this work is to provide a more global vision of this technique regarding this disease through the analysis of the data collection carried out for one year.

Testing de hypothesis

In order to be as reliable and precise as possible, we have carefully followed the same work protocol as previous studies, since this is a one-year longitudinal study of evolution [13–15]. As with previous works, with regard to the sample, equipment, imaging protocol, organisation of the patients, and the tests carried out, we have based ourselves on the TISEM (Thermographic Imaging in Sports and Medical Exercise) and the existing bibliography [14,15].

Patients, room, thermographer and functional test

The study sample and the room used on this occasion were the same as the one provided for the study by Cabizosu et al. [14]. The only differences registered with the previous study were age since in this case all patients are one year older (median age 31 years) and the BMI variable in patient number 2 who recorded an increase in weight of 10.4 kg, which changes the BMI of the previous study from 34.37 to 38.27 currently [14]. In order to eliminate all those aspects that could influence the collection of thermographic data, the same protocol was

followed regarding acclimatisation of the patients and the environment, performing an interview before imaging for 20 min at a constant temperature between 23° and 24°, with a room humidity of 40%, (± 0.8) and an atmospheric pressure of 0.98. The thermograph used, Flir E60 model, and the image analysis program, “Flir researchIR” were the same as in the work aforementioned [13,14]. In addition to the “Flir researchIR” program, our group created an application for the elaboration and overlapping of images from both years and was also used. The ROIs used were also the same as those used in the study by Cabizosu et al. [13,14] in which 3 different shots of 4 images of the lower limbs were recorded at thigh level (quadriceps and hamstring region) and leg level (tibial and calf region) [13,14]. A researcher specialised in thermography and a doctor specialised in radiological techniques oversaw the realisation and analysis of the images using a blinded approach. Regarding the Chair Stand Test 30-S, the recommendations given, the material, the room and its distribution were the same as in the previous study [13,14].

Images analysis

This work analyses the evolution of temperature at each point in the patient’s muscles. It is important to note that the pairs of images have been taken over the interval of one year, hence the exact position of the patients as well as other camera parameters can vary in the data

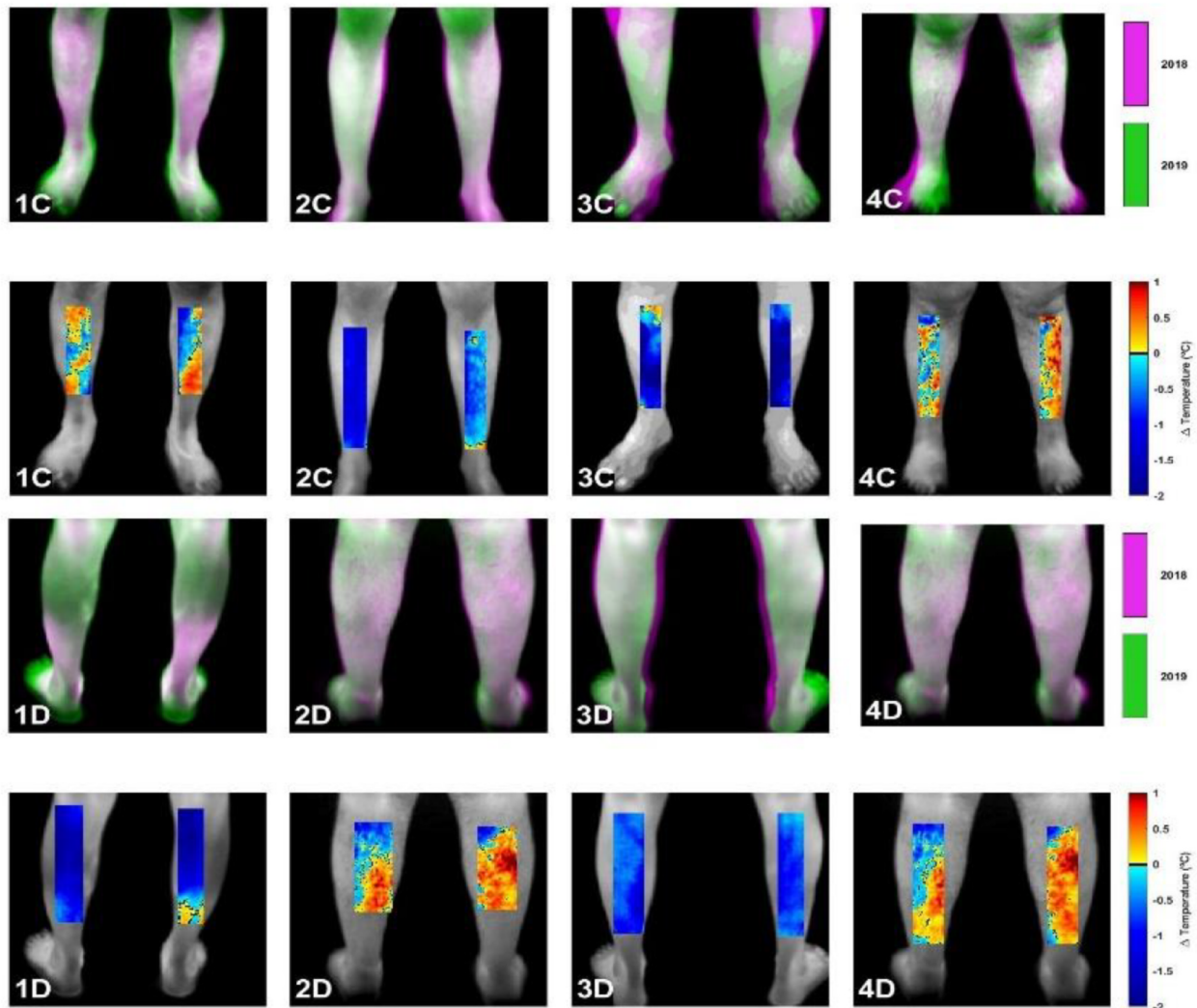


Fig. 2. 2018 (Violet) and 2019 (Green) thermographic images of the anterior and posterior thigh of the 4 patients. The images show the overlap of the thermographic patterns of the patients for the years 2018 (violet) and 2019 (green). The “C” images show the anterior leg region, while the “D” images the posterior thigh region. The images marked with ROI show the differences between the 2 years. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

acquisition process. Therefore, to apply this longitudinal study, some medical image processing techniques need to be applied to infrared images. First, a histogram equalization was applied to the pairs of images to preserve the mapping between pixel values and temperature values [16]. Secondly, an intensity-based image registration was performed to obtain an appropriate similarity between the images acquired in 2018 and 2019 [17,18]. It should be noted that this process applies an affine transformation to the 2019 images to maximise their overlap with the 2018 images. Finally, the difference between the pairs of images was calculated. This allows us to determine the increase in temperature, positive or negative, at each point in the muscle during this period.

Data of the test

The following images show the evolution of the diseases according to the thermographic images. Such images are organised from the youngest age of the first patient to the oldest in the fourth.

Fig. 1. 2018 (Violet) and 2019 (Green) thermographic images of the anterior and posterior thigh of the 4 patients.

Fig. 2. 2018 (Violet) and 2019 (Green) thermographic images of the anterior and posterior leg of the 4 patients.

Table 1. Data corresponding to the evolution of the average temperature ($^{\circ}\text{C}$) measured in the regions of interest selected in Fig. 1 with one year of evolution. 2018 values are described in relation to the more current 2019 values.

Table 2. Data corresponding to the evolution of the average temperature ($^{\circ}\text{C}$) measured in the regions of interest selected in Fig. 2 with one year of evolution. 2018 values are described in relation to the more current 2019 values.

Table 3. Data corresponding to the stress test with one year of evolution. 2018 values are described in relation to the more current 2019 values.

Discussion

Because our thermograph is capable of measuring a temperature difference of up to 0.5°C , this value has been established as significant in the analysis of the data. Regarding the anterior and posterior portion of the thigh and the leg, when comparing Tables 1 and 2, we find that in almost all cases, there is a significant decrease in temperature after one year of evolution of the disease. If we rely on the existing scientific literature and in particular on the findings of Cabizosu et al. in his studies carried out on this type of patients with CT scan and

Table 1

Data corresponding to the evolution of the average temperature (°C) measured in the regions of interest selected in Fig. 1 with one year of evolution.

Thermography Thigh			
Anterior		Posterior	
2019	2018	2019	2018
01 DX:32.9° SX:32.9°	DX: > 1.3° SX: > 1.4°	DX:32.4° SX:32.8°	DX: > 1.1° SX: > 1.5°
02 DX:32.3° SX:32.5°	DX: < 0.2° SX: < 0.4°	DX:32.4° SX:32.7°	DX: < 0.2° SX: < 0.4°
03 DX:32.6° SX:32.6°	DX: > 0.7° SX: > 0.5°	DX:32.3° SX:32.3°	DX: > 1.4° SX: > 1.4°
04 DX: 31.1° SX:31.0°	DX: > 0.8° SX: > 1.1°	DX:30.8° SX:30.6°	DX: > 2.2° SX: > 2.6°

DX: Right; SX: Left; > :Major; < : Minor.

Table 2

Data corresponding to the evolution of the average temperature (°C) measured in the regions of interest selected in Fig. 2.

Thermography Shank			
Anterior		Posterior	
2019	2018	2019	2018
01 DX:32.3° SX:32.4°	DX: > 1.6° SX: > 1.2°	DX:31.7° SX:32.0°	DX: > 1.6° SX: > 1.7°
02 DX:32.5° SX:32.9°	DX: < 0.1° SX: < 0.4°	DX:32.4° SX:32.6°	DX: < 0.5° SX: < 0.6°
03 DX:33.2° SX:32.7°	DX: > 0.6° SX: > 0.8°	DX:32.1° SX:32.0°	DX: > 0.8° SX: > 0.9°
04 DX:31.9° SX:32.1°	DX: > 0.5° SX: > 0.5°	DX:30.4° SX:30.6°	DX: > 1.9° SX: > 1.7°

DX: Right; SX: Left; > : Major; < : Minor.

Table 3

Data corresponding to the stress test with one year of evolution.

Chair stand test		
	2019	2018
01	11	> 2
02	7	> 3
03	11	> 3
04	4	> 4

< : Minor.

thermography and with thermography and strength tests in the lower limbs, we can understand and justify the results obtained in our study [13,14]. As we can see in images 1 and 2, the patient with the lowest mean temperature is patient number 4, and, as reflected in Table 3, is the one performing the least number of repetitions in the Chair Stand Test. This is probably due, as already mentioned by Cabizosu et al, to the fact that being the eldest patient and Emery-Dreifuss muscular dystrophy being a neurodegenerative disease, it is the patient with the highest degree of muscular atrophy [13,14]. Numerous authors, who have used this test for strength evaluation of the lower limbs, have shown that the higher the number of repetitions, the greater the strength presented by the evaluated, in fact, Jones et al, through this test, were the first to mark a functional correlation in healthy patients between ageing and strength decrease [19–21]. Recent studies carried out using this test and thermography, for the evaluation of Emery-Dreifuss muscular dystrophy, concluded that, the more significant the atrophy, the lower the motor response, that is to say, fewer repetitions

in this type of test [13,14]. Such hypothesis is once again corroborated in this study, where after one year of evolution, as expressed in Table 3, we can see that patients tend to experience a decrease in temperature accompanied by a decrease in strength as the disease evolves. However, it should be noted that there is an exception represented by patient number 2 who with a slight increase in temperature, as we can see in Table 3, has a decrease in the functional test of strength in lower extremities equal to his respective older brother. This result has already been previously discussed by Cabizosu et al, who in their 2020 study already evidenced, based on the bibliography, how there is a close relationship between a higher BMI and lower strength performance, even for this type of patient [14,22–24]. The sudden change in BMI by patient number 2 could be a clear sign of how a weight gain of > 10 kg influences strength and motor response. In this respect, because the muscular system, the tendon system and the ligamentous system are the architects of movement and body stability, and weight gain affects these structures, there is no doubt that the relationship between BMI and Emery-Dreifuss should be the basis of the evolutionary follow-up of the patients. Because of, on the one hand, due to the rare nature of the disease, which affects a small number of patients and, on the other, to the different form of expression of Emery-Dreifuss disease, so far it has not been possible to draw an evolutionary line of the disease, however, this study shows some signs that can introduce us to possible evolutionary patterns that must be deepened [13,25]. Accordingly, if we look at Tables 1 and 2, we realise that despite patient number 4 being the one with the lowest temperature and logically the one with the fewest repetitions in the strength test, there is a homogeneous pattern compared to the loss of infrared emission in the lower limbs. The youngest patient, on the anterior part of the thigh and leg, presented a much more abrupt and significant decrease in temperature than his older brother after the one year follow-up. We believe that this data may depend on multiple variables. On the one hand, the fact that the patient is younger may affect the metabolic evolution of the disease, something that has already been observed in other degenerative diseases [26–29], on the other, it is also possible that as there is a more significant presence of muscle tissue, due to the early stage of the disease, there is a higher possibility of it collapsing, which is not possible in a more advanced stage due to the abundant presence of fibroadipose tissue over the healthy muscle. However, it should also be noted that this pattern does not apply to the posterior side, where, as we can see in Tables 1 and 2, there is a significant difference in the decrease in temperature in favour of the older patient in the thigh (right: +1.1°; left: +1.1) but not so significant in the leg (right: +0.3° SX: =0.0°). In this respect, it should be noted that the purely anatomical and physiological composition of the muscles located in the anterior part of the thigh is not the same as in the posterior part, in fact, the tendinous portions of the muscles of the posterior region (ischio-tibio-fibulae) are longer and broader than on the anterior portion (quadriceps) with the quadriceps and patellar tendons [30–32]. Since the prognosis and evolution of this type of patient depends to a great extent on the involvement of myotendinous contractures and cardiac involvement and that in general there is a significant lack of information on the biology and functionality of the mechanisms of development and pathogenesis of the tendon, hypotheses about a possible anteroposterior or posterior-anterior evolution of the disease cannot be ruled out, depending on age and tissue physiology that undoubtedly need to be clearly and conclusively deepened [33–35]. These results are the first bibliographic information, obtained after one year of evolution in this disease through the use of thermography and could show how the disease evolves at the level of the lower limbs in this type of patients, however we are aware that further studies should be carried out, if possible, more extensive in techniques and numbers of patients in order to better demonstrate and quantify the relationship between muscular dystrophy / BMI/strength in the lower limbs. Nevertheless, this work further corroborates the theories that propose thermography as a monitoring and quantification tool for Emery-Dreifuss muscular dystrophy [7,13,14].

Limitations and strengths

This study is the result of an innovative year-long study of the evolution of the disease with diagnostic elements very seldomly used before for this disease. However, some aspects could be improved. Since the aim of the study was both to describe a possible evolution of the disease and to add more accurate aspects about thermography as a valid tool for the follow-up of Emery-Dreifuss muscular dystrophy, a larger sample would be needed, even though, when referring to a rare disease, the samples available in these cases are usually scarce. Despite the good results obtained, and the advances made in this area of study, more research is needed on the subject to better explore this new line of research.

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.

Equal contribution

These authors contributed equally to this work.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.mehy.2020.110348>.

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