

Theoretical basis for a new approach of studying Emery-Dreifuss muscular dystrophy by means of thermography

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ABSTRACT

Introduction: Emery-Dreifuss muscular dystrophy (EDMD) is a clinical condition characterized by neuro-skeletal and cardiac impairments. By means of thermography, an image acquisition technique that allows the recording of the heat emitted by objects or bodies, new insight can be obtained about the evaluation and follow-up of this disease. Actually, musculoskeletal disorders are a major cause of counseling and access to rehabilitation services and are some of the most important problems that affect the quality of life of many people. There are urgent both clinical and research needs for the assessment and follow-up of patients with Emery-Dreifuss muscular dystrophy and the thermography is a rapid, non-invasive, easy to use and objective technique that analyzes the temperature of the examined tissue.

Hypothesis: The main aim is to offer a new possible hypothesis of validating the thermography techniques that support the evaluation and clinical follow-up of the Emery-Dreifuss dystrophy. To carry out this work we rely on the evidence of the existing bibliography. To perform this work and to evaluate the current situation on this topic, a systematic review was carried out after the application of an automatic and manual filter, inclusion and exclusion criteria, a total of 0 articles was obtained. Unfortunately, there is a lack of articles that relate the use of thermography in the Emery-Dreifuss muscular dystrophy. Due to the absence of information, we have expanded the search to articles concerning the use of thermography in relation to alterations of the musculoskeletal system compatible with those of Emery-Dreifuss, genetic diseases related to the X chromosome and more generally muscular atrophy. Based on other studies and results carried out in diseases that show signs and symptoms similar to Emery-Dreifuss Muscular Dystrophy, we believe that a new line of translational research could be opened with novel findings and we think that thermography could be an optimal tool for the clinical monitoring of this pathology. We believe that it would be of a great importance to carry out an observational study, to lay the foundations for future works, that relate thermography to the Emery-Dreifuss muscular dystrophies.

Introduction

Emery-Dreifuss muscular dystrophy (EDMD; MIM 310300) is a chronic and degenerative clinical condition characterized by:

- Contractures and muscular stiffness of the tibialis, elbows and rachis, which begin in childhood.
- Initial loss in a correct Humero-peroneal articular distribution.
- Cardiac involvement as palpitations, poor exercise tolerance, heart failure, pre-syncope and syncope. [1,2].

With the term “thermography”, we define an image capture technique that allows us, by means of recorded heat, to interpret and understand different physiological and/or pathological states [3,4] (Fig. 1).

Considering that many of the muscular or articular alterations are related to changes in density, volume and temperature in the affected anatomical areas, and consequently mainly in the tegument of those areas, it is easy to deduce the reason for investigating the integumentary system throughout the use of thermography [5,6].

Despite the musculoskeletal system is fundamental for the

Abbreviations: BAT, brown adipose tissue; BVS, biblioteca virtual en salud; EDMD, emery-dreifuss muscular dystrophy; MIM, mendelian inheritance in man; MR, magnetic resonance; PET-CT, positron emission tomography/computed tomography; PRISMA, preferred reporting items for systematic reviews and meta-analyses; SSR, sympathetic skin response; XHED, hypohidrotic dysplasia

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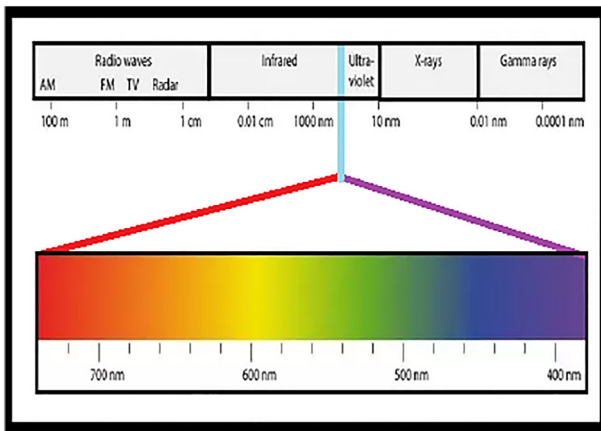


Fig. 1. The radiation recorded by the thermographic camera consists of the capture of long-wave radiation. This waves are represented in this electromagnetic spectrum image. Figure from Tipler & Mosca, "Physics for Scientists and Engineers", 6th edition, p. 1041.

functionality of everyday life activities, it has not been the subject of thermography in-depth studies and, indeed, the few publications available on the muscular system all relate to sport and physical activities [7–9].

Treatments received for musculoskeletal disorders during hospitalization services and subsequently in rehabilitation centers, normally vary from an urgent check by a physician in order to exclude possible injuries throughout physical and instrumental examinations, up to a scheduled or continuous follow-up to evaluate the general conditions of the culprit lesion [9,10].

From a research by N Carboni et al. [11] having as its object a family with 5 patients affected by the recessive form of the muscular dystrophy linked to the X Emery-Dreifuss (mutation of the *STA* gene), it has been shown through magnetic resonance (MR) the muscular involvement of the soleus, the medial portion of the gastrocnemius, and the muscles of the thigh in the onset and progression of the EDMD, which until then had never been registered [11].

Since thermography, appears a very useful method in the early stages of medical diagnosis, it allows a simple, rapid and non-invasive evaluation [12] and EDMD is a pathology directly associated to changes in the muscular and articular system [1,2], we believe that the realization of this research is justified in order to better clarify other aspects of this pathology.

The objective of this work is to offer a new idea that supports the hypothesis of validation of thermography techniques in the evaluation and clinical follow-up of Emery-Dreifuss dystrophy.

To carry out this work, first, a systematic bibliographic review was conducted between September 2017 and February 2018, in which the PRISMA recommendations were followed [13] (Table 1).

In order to guarantee a depth investigation and the highest number of the gathered records, several searches were made in all databases combining different logical descriptors.

After the first search, a total of 213,968 articles were obtained. Filters, inclusion and exclusion criteria have been applied to all research examples.

The inclusion criteria (automatic) were: presence in the title/abstract of the terms thermography and/or Emery-Dreifuss and no restrictions of gender and ethnic group.

The exclusion criteria (manual) established were: articles at the preliminary stage, without conclusion and/or interpretation of the results and Pedro scale lower than 6 and Jadad less than 3 [14].

Automatic filters were: randomized clinical trials, systematic reviews, meta-analysis, human, language, last 10 years.

After the application of automatic and manual filter, inclusion and exclusion criteria, a total of 0 articles were obtained.

Due to the lack of information, we have expanded the search to articles concerning the use of thermography with alterations of the musculoskeletal system compatible with those of Emery-Dreifuss, genetic diseases related to the X chromosome and muscle atrophy more generally.

Proposal and justification of the hypothesis

In regards to the musculoskeletal system, we will define it as previously proposed as the whole of the osteoarticular and muscular system. As regard to the osteoarticular system, we refer to bones, joints and ligaments, while pertaining the muscular system, we refer to the muscles and tendons. [15–17].

According to a meta-analysis published in 2013 on the use of thermography for the diagnosis of injuries of the osseous, muscular and joint system, the use of this technique has not proved to be useful for the diagnosis of stress fractures [18].

Nevertheless, it should be emphasized that the sample of the analyzed articles (3 articles) was very small and so far stress fractures do not present themselves as a typical clinical condition of the diseases related to the emerins (protein complex involved in Emery-Dreifuss diseases).

In fact, according to the current bibliography, the issues of the osteoarticular system in patients with EMDM, do not depend on the bone structure itself, but on the specific deformations of the articular segments typical of this pathology [1,2,11].

The most evident cases of articular deformations recorded, all involve vertebral column, with scoliosis and/or rectifications that affect the whole vertebral spine. G Kwok et al. (2017) used thermography in patients with idiopathic scoliosis and showed differences in temperature between the concave and convex sides of the regions of interest. These differences according to the authors could be due to a greater emission of infrared radiations of the convex side of the observed area [19].

However, we must stress that: A) a relatively small sample of patients is used and; B) the spinal alterations of patients with EMDM are directly related to the genetic alterations present on the X chromosome and are therefore not of an idiopathic nature.

The use of thermography in X-linked genetic disorders such as hypodriotic dysplasia (MIM 305100; XHED causative gene) showed an abnormal distribution of cutaneous temperature derived from the altered peripheral vascular perfusion (RP Clark et al. in 1990) [20].

Although the genes involved in this pathology are different from those of the EMDM, both are linked to the X chromosome and present peculiar syndromic features.

In fact, on the one hand the hypohidrotic dysplasia (XHED) presents dysmorphic signatures at the level of teeth, forehead, lips, nose, skin and sweat glands and on the other hand the Emery-Dreifuss (EDMD) shows them in the rachis, elbows and muscles of the distal part of the lower limbs the internal neuromuscular system being compromised [11,20].

In neuromuscular diseases, thermography is used as a diagnostic and monitoring tool for patients with nervous system disorders. Sudek syndrome and cerebrovascular accidents are the areas where thermography has more room in this medical specialty, however, EB Neves et al. (2015) argue that this tool has great potential for diagnosis in many other neurological diseases [21] (Fig. 2).

These facts are supported in another very recent study, by B Hegedus (2018) who described that the totality of patients with stroke had a microcirculation and function in the area affected, presenting differences in temperature between the healthy side and the pathological side [22].

This temperature difference has changed after a physiotherapy program highlighting a strong correlation between the improvement of the joint function and the change in temperature [22].

Although we are aware of the different nature between the

Table 1
Summary of the research strategy.

Editorial platform	Research
PubMed	thermography[Mesh] AND “Emery-Dreifuss”[Mesh] thermography[Mesh] AND “Emery-dreifuss”[Mesh] AND laminopathies “Infrared Rays”[Mesh] AND “Emery-dreifuss”[Mesh] “infrared Rays”[Mesh] AND “Emery-dreifuss”[Mesh] AND laminopathies (thermography[Mesh] OR thermometry[Mesh] OR “infrared rays”[Mesh] OR “body temperature”[Mesh]) AND “Emery-Dreifuss”[Mesh]) thermography[Mesh] OR thermometry[Mesh] OR “infrared rays”[Mesh] OR “thermal imaging” OR “body temperature” [Mesh] OR “thermographic evaluation”) AND(“Emery-dreifuss”[Mesh] OR laminopathies OR DMED) (thermography OR “thermograph” OR “infrared thermography” OR “infrared rays” OR “infrared images” OR “infrared thermal imaging” OR “thermal imaging” OR “thermographic evaluation” OR “ir thermography” OR “temperature mapping” OR “temperature mappings” OR “mapping, temperature” OR “mappings, temperature” OR “diti” OR “infrared thermogram” OR thermometry OR “body temperature”) AND Emery-dreifuss
Ebsco, Web of science, Science direct	(thermography OR thermometry OR “infrared rays” OR “thermal imaging” OR “body temperature” OR “thermographic evaluation”) AND (“Emery-dreifuss” OR laminopathies OR DMED) (thermography OR “thermograph” OR “infrared thermography” OR “infrared rays” OR “infrared images” OR “infrared thermal imaging” OR “thermal imaging” OR “thermographic evaluation” OR “ir thermography”) AND (“Emery-dreifuss” OR laminopathies OR DMED)
Biblioteca virtual en salud, Ovid, PEDro, Teseo	(thermography OR thermometry OR infrared rays OR thermal imaging OR body temperature OR thermographic evaluation) AND (“Emery-dreifuss” OR laminopathies OR DMED) (thermography OR thermograph OR infrared thermography OR infrared rays OR infrared images OR infrared thermal imaging OR thermal imaging OR thermographic evaluation OR ir thermography) AND (“Emery-dreifuss” OR laminopathies OR DMED”)

DMED: Muscular dystrophy Emery-Dreifuss; DITI: Digital infrared thermal imaging (DITI); IR THERMOGRAPHIC: Infrared thermography.

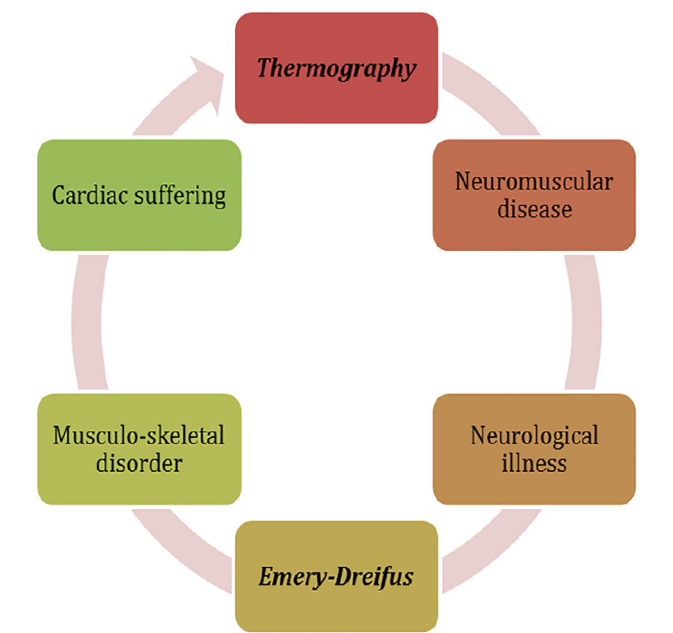


Fig. 2. Schematic view of thermography applications and clinical pathology of Emery-Dreifuss.

biomolecular mechanisms of stroke patients and the biological condition of the patients with Emery-Dreifuss, we believe that the presence of neurological contractures, muscle shortening, and decreased elastic response, in both cases, are all related to the microcirculation.

This idea depends on the observation of scar tissue (avascularized) in the gastrocnemi muscles of Emery-Dreifuss patients that has been investigated with magnetic resonance [11].

With regards to the vascular theme and muscle-tendinous changes, S Chaudhry et al. (2016) produced a systematic review with the aim of collecting, evaluating and reviewing all the articles based on tendinopathies. According to studies previously accomplished and then analyzed in this paper vasculature is a vital feature for normal functioning and improvement of the lesion [23].

The authors show that, there is evidence in detecting temperature differences between the healthy side and the affected side by patellar

tendinopathy and in the epicondylitis, identifying areas of higher temperatures.

Therefore, since there are changes in vascularization and/or presence of inflammation in the tendons due to a numerical increase of the inflammatory cells [24] the thermography can capture the infrared radiations emitted by the culprit area and quantify them in the thermogram.

In the rotator cuff tendinopathy, no significant differences were found between injured and healthy areas. According to S Chaudhry et al. (2016), no evidence was found in Achilles’ tendinopathy, on the plantar fascia, on the gluteal tendinitis or on the wrist [23], all areas of direct relationship with the Emery-Dreifuss disease.

In the alterations of the muscular system in fact, the use of thermography has given very different results and the bibliography offers different points of view according to the analyzed areas

In other studies, performed on the human fascia, in patients with trigger points and muscle tension in the trapezius, variations in the temperature between the healthy side and the pathological side were observed. Despite everything, MF Megallahes et al. (2014) concluded that presently, there are a few studies that evaluate the accuracy and reliability of thermographic evaluation in this clinical condition [25].

However, although the researchers do not have a definitive vision on the subject due to the little information, and although no studies have been carried out to analyze the presence and behavior of trigger-points in patients with Emery-Dreifuss, there are recent investigation that examined the progressive restriction of movements in muscular atrophy, a condition reproduced also in patients with Emery-Dreifuss, and the use of thermography [26,28].

SP Niehof et al. (2006), for example, describes how Sudek patients, when they are subjected to changes in temperature from hot to cold, present differences in temperature between the affected area and the healthy zone [26].

The same condition was observed by other authors, who analyzed the predictive value of the cutaneous sympathetic response (SSR) in patients with the same pathology. HJ Kim et al. (2015) observed that five out of six tested patients, they showed a prolonged latency on the sensitive response [27].

An answer to why sensitive and circulatory differences exist in patients with diseases that produce trophism has been proposed by H Monobe et al. (2012), who described from a patient suffering from progressive facial hemi-atrophy, they described that this condition can

lead to atrophy of the subcutaneous adipose tissue, giving evident differences in the thermographic patterns of the two sides of the body [28].

It is important to underline that the sub-cutaneous fat has already been a matter of thermography studies. Currently, the PET-CT (Positron Emission Tomography/Computed Tomography) is the most used method for the detection of brown adipose tissue (BAT) in humans, despite the high cost of the images and the high absorbed radiation. For this reason, C Jang et al. (2014) and subsequently Q Yang et al. (2017), implemented a research by using thermography to quantify the activity of BAT. Both groups stated that the use of thermography is a promising tool to quantify BAT cells activity [29,30].

Given the lack of information on this matter, we can't currently observe and describe the bibliographic relationship between the use of thermography and the acquisition of clinical data in the setting of Emery-Dreifuss.

Despite of this, taking into account other studies carried out in diseases that show signs and symptoms similar to Emery-Dreifuss, we believe that a clinical and/or observational study could open a new line of research to deepen and show possible evidences that support the hypothesis of validation of the thermography techniques in the evaluation and in the clinical follow-up of the Emery-Dreifuss type muscular dystrophy.

In this regard, we note that there aren't studies that exclude the relationship between temperature changes and hereditary diseases related to the X chromosome in patients with scoliosis. We believe that this could be an additional field for future 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.

Disclosure of conflicts of interest

None of the authors has any conflict of interest to disclose.

Conflict of interest

Authors declare no conflict of interest.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <https://doi.org/10.1016/j.mehy.2018.06.027>.

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