Extraction of Quantitative Indices from Infrared Imaging in patients with Type 2 Diabetes Mellitus: A Case Study

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Abstract

This case study is a proof of concept for using radiometric asymmetry, pictured in biomedical infrared images, as an aiding tool for the early diagnosis of diabetic neuropathy and diabetic foot disease. The purpose is to discern when peripheral damage is predominantly neuropathic. The results are extracted from comparing the so-called asymmetrical thermal response index (ATR) with the statistical thermal response index (TRI). The core inclusion criteria for controls and patients are age and demographic characteristics. The clinical evaluation shows 100% agreement with the data extracted from this image analysis.

1. Introduction

Type 2 Diabetes Mellitus (DM2) is a chronic disorder that develops when the body is unable to produce sufficient insulin or effectively utilize the insulin it produces, leading to elevated blood glucose concentrations. Long-term uncontrolled hyperglycemia is associated with progressive micro vascular and macro vascular damage, contributing to complications including cardiovascular disease, nephropathy, diabetic retinopathy, and Diabetic Foot Disease (DFD) a leading cause lower-limb amputation [1]. DFD represents a spectrum of anatomical and functional abnormalities affecting the feet of individuals with diabetes, primarily driven by the evolution of diabetic peripheral neuropathy (DPN) and peripheral artery disease (PAD). The risk of developing PAD is 1.5 to 4 times higher in people with type 2 diabetes mellitus [2]. Furthermore, DPN can mask the characteristic symptoms of PAD, resulting in a higher prevalence of asymptomatic cases of these conditions. PAD and DPN are responsible for a dramatically increased risk of foot ulcerations that can spread or worsen to the point of amputation of the toe, foot, or leg. Moreover, between 30% and 50% of diabetic patients who have undergone an amputation are at high risk of undergoing a second amputation within 5 years of the first. Furthermore, the long-term survival ratio at 3 years after having suffered a major amputation is 59% and at 5 years it is 27% [3]. The prevalence of this complication is very high, as around 15% of diabetic patients may have an ulcerous lesion on the foot during their lifetime [4], also, if the ulcer heals, there is a high risk of developing a new ulcer [5] and can also increase the risk of cardiovascular disease [6]. Studies suggest that proper foot care practices, patient education, and early intervention for foot lesions may prevent approximately 40–50% of amputations in patients with diabetes [7, 8]. Therefore, it is essential to develop tools that allow for the early detection of these abnormalities. There are different imaging techniques that are useful in timely clinical diagnosis [9, 10]. Although all of these techniques provide relevant information related to the patient's vascular status, some of them are often expensive, and others have certain drawbacks whose application is restricted due to the risks posed by contrast media and ionizing radiation, limiting the number of studies that can be performed with these techniques or even not being an alternative in the presence of kidney damage. Considering the foregoing, the importance of validating new safe imaging methods that can aid in the early diagnosis and ongoing monitoring of patients with peripheral impairment who pose a significant risk of developing a diabetic foot is evident. Infrared (IR) imaging has significant advantages: it is a non-contact, non-ionizing, relatively inexpensive, and safe modality, that allows for the evaluation of skin temperature distribution over large regions of the body. The recorded thermal patterns are linked to peripheral blood flow dynamics, which are regulated in part by the autonomic nervous system [11, 12, 13, 14, 15, 16]. These characteristics make it well suited for the early detection of peripheral damage. In addition, the use of appropriate thermal indices may facilitate the discrimination between damage arising predominantly from DPN, or the combined effects of DPN and PAD, we refer to this case as mixed peripheral damage (MPD).

2. Case History

This research presents the results of evaluating a study group comprised six subjects: two volunteers serving as controls and four patients with a clinical diagnosis of DM2, with more than 15 years of disease progression. Two of them have medical evaluation reports varying levels of peripheral damage related to DPN; the clinical evaluation of the other two patients shows different levels of peripheral damage related to MPD. All participants were volunteers and agreed to the guidelines of clinical protocol DI/10/301/4/115 of the General Hospital of Mexico. The objective of this protocol is to be able to study the characteristics of altered heat distribution in the lower extremities using infrared imaging. As part of this protocol, all participants were fully informed about the study and had all their questions answered before signing the required informed consent form. Subsequently, all participants underwent a blood test, a physical examination performed by a specialist physician who is an expert in DFD diagnosis, and imaging studies to complete the clinical evaluation. More information about the participants can be found in Table 1. In addition, a series of infrared images was acquired and radiometric information extracted from the thermograms was compared with the results of the clinical evaluation. This comparison revealed a 100% agreement between the diagnosis of clinical evaluation and infrared image analysis.

Table 1. *Clinicodemographic information of the participant group, divided according to the study group. TDP: Time of disease progression; BMI: Body Mass index; HbA1c: glycated haemoglobin; blood glucose level (BGL).*

Group	Sex	Age [years]	TDP [years]	BMI $[kg/m^2]$	BGL $[mg/dL]$	HbA1c [%]
Neuropathy Status						
	Male	74	15	26.54	210	9.95
	Male	60	15	27.02	138	7.13
MPD Status						
	Male	49	15	28.08	348	12.05
	Female	63	20	32	228	8.74
Control group						
	Male	58	NA	24.69	97	5.38
	Female	60	NA	28.19	92	5.78

3. Methods

The image acquisition methodology consists of obtaining infrared images of the lower extremities of the participants. For that, we use a rigorous IR-images acquisition protocol. The person under test is graphically guided to achieve specific positions for their feet such that anterior and posterior views are achieved in a reproducible and standardized manner. The IR-camera is positioned at a distance of 100 cm, at 40 cm above floor-level, with viewing axis matching the middle distance between the legs position. See Fig. (2.a) as guidance for the description.

Infrared images of the lower extremities were detected both in the passive state (passive mode) and in the subsequent states after the lower extremities had been subjected to an external thermal stimulus (active mode). The external thermal stimulus was introduced after moistening the legs with a towel and from that moment on each image was detected every 15 seconds for a period of 4.5 minutes. This process is detailed in the diagram in Fig. 1b).

Two thermal quantifiers previously introduced by our research group are employed to evaluate the metabolic performance of each subject. First, the asymmetry and thermal response index (ATR) reported in ref. [17] and the thermal response index (TRI) reported in ref. [18] are obtained independently. Each of these indices contributes essential information for the neuropathic and vascular responses associated with the performance of each limb in the participants. The integration of these indices provides enhanced information content and surpass calculations performed independently. This integration was proposed in [19], where authors use a framework of polar coordinates to display the results and suggest that each of the quadrants represents different complications of peripheral damage. In [20], this framework is used for the first time as an auxiliary tool in the diagnosis of peripheral damage related to MPD, where the quadrant corresponding to MPD is also determined. In this work, the integration of ATR an TRI in this framework is used for the first time as a diagnostic tool to validate its ability to differentiate damage predominantly attributable to DPN.

4. Results and Discussion

In addition to the infrared imaging protocol, all volunteers underwent a clinical evaluation by an expert angiologist in the diagnosis and treatment of patients with diabetic foot disease, the physical examination included an objective evaluation of the complication of the lower limb. The clinical diagnosis reveals that two of the four patients presented different degrees of DPN and the other two presented MPD.

One of the manifestations of DPN is a decreased ability of the body to respond to external thermal stimuli [21, 22]. On the other hand, PAD alters the structure and function of the vascular network, consequently modifying the thermal distribution associated with metabolic activity [23]. To identify these alterations, thermographic indices are designed to evaluate both heat conservation and dissipation in the lower extremities by comparing the right and left legs using the ATR and TRI indices calculated in specific regions of interest (ROIs). To this end, the thermal map of the legs was recorded at different times, allowing for the calculation of ATR and TRI values and the characterization of the thermal response of each

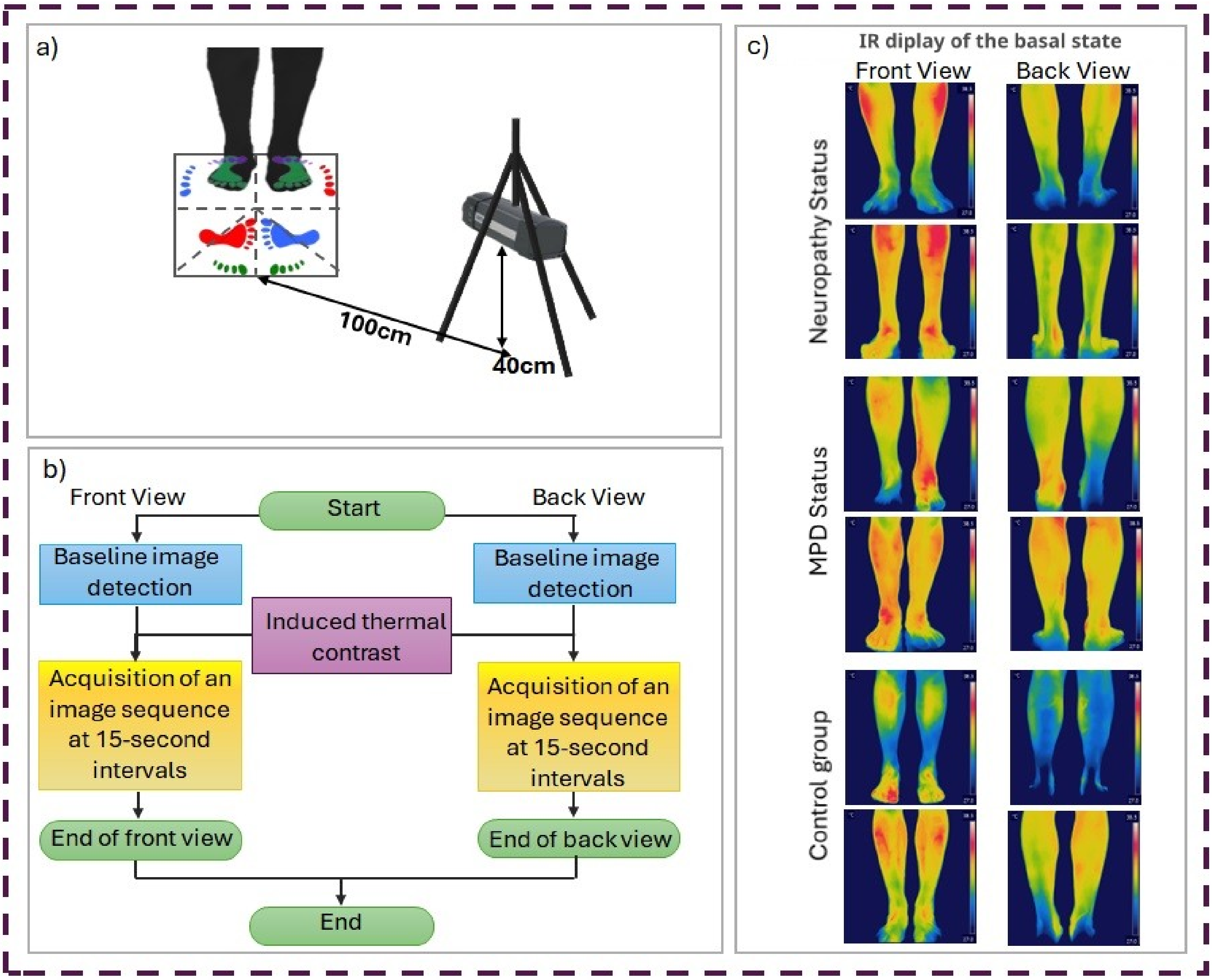

Fig. 1. *General diagram of the infrared image acquisition protocol. a) Schematic of the acquisition of each infrared image. b) Flowchart that explains the process in which for each study subject, two infrared image sequences are obtained from the lower extremities, corresponding to frontal and posterior views in both passive and active modes. c) Infrared images detected in the base state (passive mode), divided according to the study group.*

limb.

Although both indices detect the characteristics of both DPN and PAD, due to their statistical construction, each index provides an assessment that highlights specific aspects of the different peripheral damages. The ATR index is a theoretical representation of how the heat distribution changes based on asymmetry and the thermal response to an external stimulus; despite this, the predominant component of the ATR index is the longitudinal one, which is presented in the numerator of its definition, and this represents the thermal response performance. In the presence of DPN, the response to thermoregulation processes becomes deficient, and it is reflected in the evaluation of the ATR index, so it is expected that as the response to thermoregulation processes becomes more deficient, this index will decrease. This behavior can be observed in Fig. 2 a). On the other hand, the TRI is a nonparametric index expressed through statistical dispersion and average behavior. It represents the temporal evolution of the skin's thermal response as a function of tension and measures the statistical dependence between left-to-right or anteroposterior projections. This makes it more sensitive for assessing temperature differences in metabolic heat maps of the lower extremities, which are altered in the presence of PAD. It is expected that as the severity of peripheral damage increases, the rating between metabolic heat maps decreases and tends to be zero, which translates into a decrease in the evaluation of the TRI index; this can be observed in Fig. 2 b). When evaluating the asymmetry of each of the images, neuropathic patients often appear as false negatives in this test, as is the case of one of the patients in that same figure. Considering the joint visualization of the indices to highlight physiological alterations in [19], the polar representation of the data is proposed, defining the radial and angular coordinates, where the distance is defined by the magnitude constructed by both indices and the angle is defined by the $\arctan$ of the quotient of the indices.

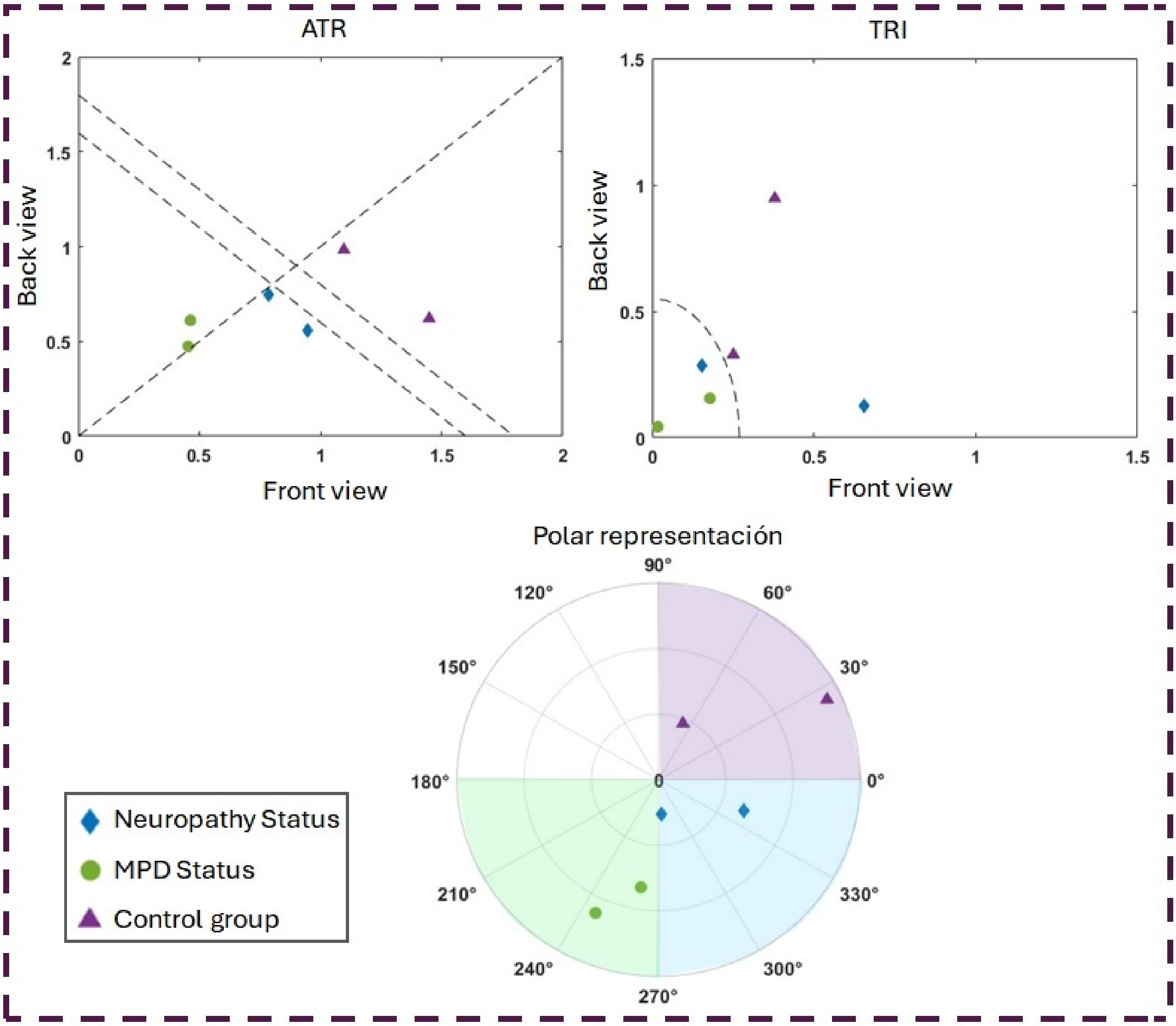

Fig. 2. *Results of the radiometric data analysis using the indices: (a) ATR, (b) TRI, and (c) polar representation. The population is divided into three groups; One corresponds to the control group (purple triangle) and the other two to the patients: subjects diagnosed with DPN (blue rhombus), and subjects diagnosed with MPD (green circle).*

From the polar representation, shown in Fig. 2 c), one can see that the analyzed population for controls, is grouped in the quadrant defined by the angles of 0° and 90° [19]. Instead the data for the MDP population are placed in the quadrant defined by the angles of 180° and 270° [20]. Finally, the population corresponding to the DPN group lies in the quadrant from 270° and 360° or 0°.

As noted before, the presence of DPN causes limited radiometric response, say body's response, to external stimuli targeting the metabolic heat-response. By way of this test, we notice that the ATR index favors the evaluation or performance of the thermal response. The so far guiding conclusion is that the lower the index value, the greater the degree of evolution of DPN.

In contrast, the TRI index helps assess the asymmetry of metabolic heat in contralateral limbs. Since one of the metabolic characteristics of PAD is a local modification of the metabolic heat map, an expected result is that the greater the asymmetry between the limb heat patterns, the lower the value of the TRI index. As the studied group shows damage due to both DPN and PAD, it is expected that the participant's values of the ATR and TRI indices are in agreement with the clinical evaluation. Since the nature of DM2 involves vasculopathy and neuropathy damage, the current assessment suggests that the TRI-index is related to the former, and the ATR-index is related to the latter. Therefore, a forecast of the evolution of diabetes necessarily requires both of these indices, with the advantage that it would be possible to identify the dominant component. The task then is to find out an appropriate modality of combining the indices, such that one can be able of decoupling both effects and simultaneously avoid affecting the identification of the MPD cases. One of the features we introduce, is the use of polar coordinates to display the ATR and TRI indices. This is an eye-simplification for the data interpretation. In a natural way, each case is placed on the plane. Apparently, the natural placement of the data aligns with the separation between controls and diabetic patients with a MPD or diabetic patients with DPN aiming for the sensitivity of 100%.

The current findings appear to point out that the current IR-imaging methodology can picture alterations in the metabolic performance of the lower extremities of diabetic subjects, without visible damage, and yet with disease of 15 years or more; and connect it with DPN as underpinning damage. Thus the specialists could make quick decisions and address the course of treatment based on hard data, instead of subjective criteria, as is the current case in several geographical regions.

Whilst this case of study is limited to a small sample; it is done so purposely to lay the evidence and foundations on the necessity to expanding the database, to cover clinical cases and disclose the dominant peripheral arterial disease.

5. Conclusions

The case of study covers the six cases shown in the IR images in Fig. (2.c); and correspondingly labeled as: two controls, two subjects diagnosed with diabetic peripheral neuropathy (DPN), and two subjects diagnosed with mixed peripheral damage (MPD); related to both: DPN and peripheral arterial disease (PAD). The core concept to pursue with this methodology is to analyze how feasible it is to relate the radiometric information, obtained through statistical analysis of the radiometric data, and using cross-referencing analysis of the physiological imprint of thermoregulation. and heat dissipation between the contralateral extremities.

Image interpretation involves evaluating the ATR and TRI indices, which assess metabolic damage in the lower extremities of patients with type 2 diabetes mellitus due to the presence of DPN and PAD. However, these indices alone do not distinguish between these two complications of diabetes. However, by combining them, three groups can be differentiated. Namely, the identification with considerable certainty of: controls, subjects with DPN, and subjects with MPD. The identification of the likely cause of peripheral deterioration resulting from these two complications, we believe that is a fundamental milestone.

An average person is unaware that their legs can display fundamental metabolic information. What could be extracted as information about clear signs and symptoms of abnormal metabolic performance, goes unnoticed, for themselves and for the healthcare professionals. The current contribution is in the line of finding out relatively low-cost flexible imaging tools, to support the quick diagnosis of DM2 and related diseases, relying on hard data evidence.

5.1 References

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