Evaluation of Cutaneous Microcirculation Patterns by Laser Speckle Imaging

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***Abstract* - Atherosclerosis is a chronic systemic process affecting distal circulation, a condition known as Peripheral Artery Disease (PAD). Epidemiological and clinical studies indicate a strong association between PAD and death due to cardiovascular diseases, thus the early detection of DAP by measuring perfusion levels of distal body regions is critical to prevent ischemic events. This work proposes a new methodology for the evaluation of local cutaneous perfusion through laser speckle video processing. The speckle pattern generated by a laser beam projected onto the skin surface after being expanded by an optical setup is captured by a CCD video camera. To evaluate the particular characteristics of the speckle pattern, a video processing algorithm based on an adaptive Local Binary Pattern approach, highlighted by a local Gaussian filtering scheme, the LBPg, was developed. In order to test this new method of video speckle analysis, different patterns of microcirculation were evaluated in skin regions with different textures. The experimental results were compared with others obtained in two clinical conditions associated with PAD (i.e., Deep Vein Thrombosis and Diabetic foot). The results show that the proposed approach is sensitive to the change in perfusion levels (even in cases with reduced perfusion variations), thus indicating that the use of laser speckle technology, jointly with LBPg, is a promising noninvasive, low cost and sensitive method for the early detection of PAD-related diseases.**

Keywords – Laser Speckle; Video Processing; Local Binary Patterns; Skin Microcirculation;

I. INTRODUCTION

Atherosclerosis is a complex chronic and inflammatory systemic process affecting the inner layers of large and medium-sized arteries, (e.g. aorta, carotid, coronaries and peripheral arteries). According to the most recent consensus, the disease physiopathology is the result of a complex interaction between environmental risk factors, genetic component, immune system, hematological and endothelial cells, coagulation factors and inflammatory mediators [1], [2]. Peripheral Artery Disease (PAD) is one of the clinical manifestations of generalized atherosclerosis, whose symptoms range from asymptomatic lower blood pressure in the ankles to intermittent claudication, in which patients need to stop the movement for a few moments until circulation is restored. Although the risk of amputation in PAD patients is low, the correlation of PAD with death of cardiovascular cause is high. Hence, detection of early signs of reduced peripheral perfusion is a key prognostic factor for the early treatment of PAD.

Symptoms related to decreased perfusion are subtle in the initial stages of the disease (e.g., distal pulse reduction, changes in local temperature, …), therefore a quantitative perfusion measurement, sensitive to minor changes in perfusion, is of clinical interest. Currently and according to the guidelines of PAD management, besides the classical Ankle-Brachial Pressure Index (ABPI) defined by the quotient between the systolic pressure measured at ankle and arm, the use of ultrasound imaging techniques may also be useful to characterize the disease. Other imaging modalities (e.g. MRI and CT) are also available to study perfusion in distal arteries, however their use is only requested in advanced stages to establish a PAD treatment (e.g. endovascular therapy). These imaging modalities have some important limitations, such as the cost, time of acquisition and availability in primary care hospital, in the case of CT/MRI, and the user proficiency in the case of ultrasound imaging.

Once the symptomatology appears in advanced phases of the disease, and the clinical signs are difficult to assess in the early stage of the condition, the ability to perform a non-invasive, low cost and high sensitivity evaluation is seen as a challenge of central importance for the diagnosis. Moreover, the aforementioned imaging modalities are mostly used to assess perfusion levels within the vascular system.

In this paper, a new method to evaluate local microcirculation profile is proposed, based on an adaptive Local Binary Pattern methodology highlighted by a Gaussian filtering scheme, performed after Laser Speckle video acquisition. The proposed methodology was tested against controlled perfusion experiments and also tested in patients with PAD relate diseases (e.g. Deep Venous Thrombosis and Type 2 Diabetes).

In the remainder of this paper, in Section II the methodology is presented and in Section III the obtained results are shown. Section IV is dedicated to discussion and finally, in Section V, the conclusions are presented.

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II. METHODOLOGY

A. Laser Speckle Imaging Acquisition

Speckle is a physical interference phenomenon obtained by diffused reflections, produced when a rough surface is illuminated by a coherent light source. This multiple reflection of randomly distributed waves with the same frequency, but different phases and amplitudes, thus resulting in varying pattern with specific characteristics. Such patterns can be used to characterize either static (mostly using texture features) or dynamic conditions by using video processing techniques applied on the acquired speckle frame.

For the purpose of this work, an acquisition setup was built, composed by a class III laser beam (633×10^{-9} m wavelength and $5\,mW$ Power), apposite to skin interactions and suitable to access the upper layers of the skin. A beam expander and a CCD Camera (Sony, nxcam AVCHD, 50 fps) were also integrated in the setup, as illustrated in Figure 1.

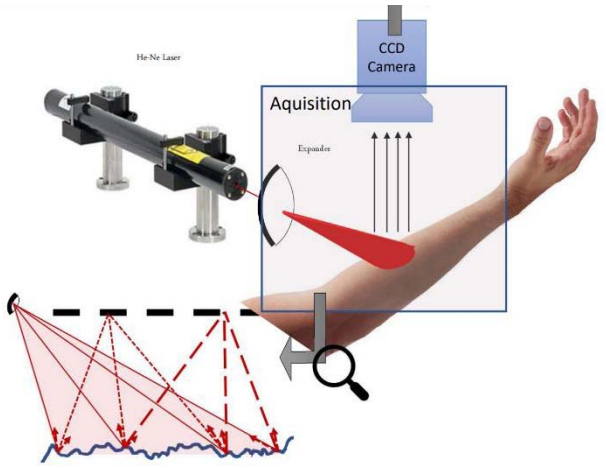

Figure 1: Acquisition Setup.

B. Image Processing Algorithm

When a sequence of speckle video frames is observed, not only the inward spatial, but also the temporal intensity variation across pixels (ranging from white to black) reveal a possible generation of repeating patterns at some underlying frequency [3], [4]. Hence, this characteristics points the LBP as an algorithm having potential to describe speckle activity.

Proposed by Ojala in [5], the LBP methodology was developed to extract 2D surface descriptors, acting as a texture operator, to locally evaluate the variation of intensities of the neighboring pixels (considering a number of points P, and a radius R to the central pixel) [6]. The LBP algorithm labels the pixels of an image by thresholding the neighborhood of each pixel and considering the result as a binary number. Each element of the binary sequence is then multiplied by a power of 2, thus obtaining a grayscale image whose histogram can be used as a texture descriptor. The LBP methodology has being used in several research areas, in particular related to object detection [7], face recognition [8] and image retrrieval [9].

Given the above-described characteristics of the speckle (i.e. spatio-temporal changing patterns, high-frequency content) the local comparison using LBP does not prove to be effective, mostly due to the high variability in the changing patterns and to the uncertainty introduced by the speckle noise. Thus, in the scope of this work, a new methodology to capture high-frequency and local variations is proposed using an algorithm based on LBP, jointly with Gaussian spatial filtering, the LBPg.

The LBP_g code of a given pixel (x_C, y_C) is defined in (1),

$$LBP_g(x_C, y_C) = \sum_{P=0}^{7} s(g[I_P - I_C])2^P , \qquad (1)$$

where I_P and I_C are, respectively, the intensity of the peripheral and central pixels, s is a step function defined in (2) and g the Gaussian function, as defined in (3) by;

$$s(x) = \begin{cases} 1 & if x \in FWHM_{g_{(\mu,\sigma)}} \\ 0, & otherwise \end{cases} \qquad (2)$$

$$g_{(\mu,\sigma)}(x) = e^{-\frac{1}{2}\left(\frac{x-\mu_{\bar{X}}}{\sigma_{\bar{X}}}\right)^2} , \qquad (3)$$

where $\mu_{\bar{X}}$ and $\sigma_{\bar{X}}$ are respectively, the average and standard deviation of the absolute differences to the central pixel in a 3×3 neighborhood, obtained in a reference sequence of frames. The $FWHM_{g_{(\mu,\sigma)}}$ is the full width at half maximum interval of the gaussian function (3).

Next, two measures of speckle activity are proposed. One is defined as a Spatial Index of activity, in which an LBP_g thresholding scheme is settled to determine the level of sensitivity of the method. This dynamic threshold is applied to the LBP_g output using the 1st, 2nd and 3rd Quartil (Q_1, Q_2, and Q_3), thus stablishing a three-level sensitivity Spatial Index, defined in (4)

$$\bar{P}_{Q_j} = \sum_{\substack{i=1 \\ j=\{1,2,3\}}}^{N} P_{i,Q_j} , \qquad (4)$$

where $P_{i,Q_j}\{j = 1, 2, 3\}$ is the probalility of one pixel in the LBP_g matrix being greater than Q_j. The other method is an evolutive measure of activity, defined as a Temporal Index, which is obtained by selecting two video sequences (basal and in study) and then comparing the normalized histograms of these two LBP_g sequences. For histogram comparison purposes, the chi-squared metric χ^2 defined in (5) was applied,

$$\chi^2 = \frac{(\widehat{H}_B - \widehat{H}_S)^2}{\widehat{H}_B + \widehat{H}_S} , \qquad (5)$$

where $\widehat{H}_B$ is the normalized histogram of the basal sequence and $\widehat{H}_S$ the corresponding histogram for the video sequence under study.

The global conceptual framework is illustrated in Figure 2.

C. Experimental Protocols

As mentioned before, the main objective of this work is to obtain quantitative markers of reduced distal perfusion to act as a measure of awareness to PAD, in the early stage of the disease. Accordingly, to test the ability of the above-proposed methodology detecting changes in cutaneous microcirculation levels, experimental tests were performed involving a partially block of the circulation in the upper limb vessels, simulating occlusion and perfusion conditions (occlusion-hyperemia test – OHT).

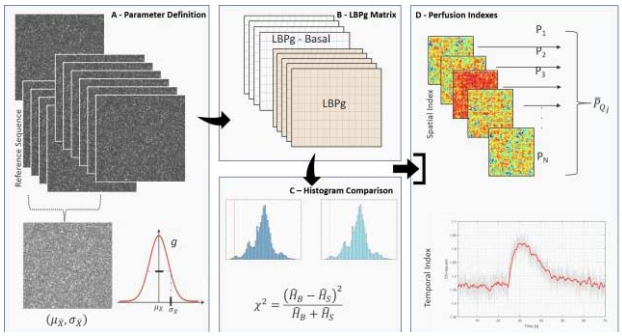

Figure 2: LBPg conceptual framework and derived dynamic indexes.

These experimental tests create distinct profiles of perfusion at the distal level in the arm and were conducted in healthy subjects after a resting period of 5 minutes in a seating position in a controlled temperature room. A distal ROI was selected and a basal speckle video was initially recorded using the acquisition setup shown in Figure 1. Afterwards, a cuff pressure attached to the arm was inflated (pressure level 180 mmHg) and a period of occlusion was accomplished. This occlusion period was followed by a rapid release of cuff pressure to simulate hyperemia, and thus restoring the circulation.

In addition to these experimental pressure-dependent perfusion procedures, two additional tests were also conducted in PAD disease related patients, to confront the results and to assess the sensitivity of the proposed methodology in real word situations. Accordingly, two peripheral regions of two patients diagnosed with Deep Vein Thrombosis (DVP) and type 2 diabetes (DM2) were selected to obtain the temporal and spatial indexes as a measure of microcirculation.

III. Results

The perfusion level as a function of time is shown in Figure 3 for one sample of the OHT test. According to the experimental protocol an inverse relationship between the pressure in the arm-cuff and the tissue perfusion is expected to be observed when the proposed Temporal Index (5) is calculated. In fact, during the acquisition period, this temporal measure of microcirculation shows variations which are correlated with specific time intervals during the test, as observed in Figure 3.

During the occlusion period (**E**$_3$ in Figure 3) an initial decrease in the Temporal Index is observed, followed by a constant trend in microcirculation levels (after the physiological adaptation to the acute occlusion). After releasing the pressure in the arm-cuff, a hyperemia period is clearly observed (**E**$_4$ in Figure 3), which is followed by a decreasing trend in the perfusion index, achieving the basal level values of the experiment (**E**$_5$ in Figure 3).

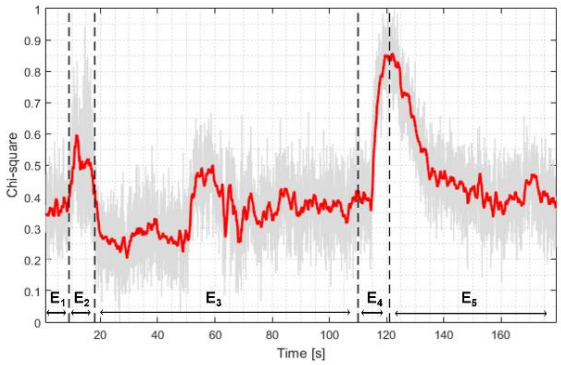

Figure 3: Temporal Index of microcirculation during the occlusion-hyperemia test.

Regarding the Spatial Index, a small interval (i.e. 5 seconds) was selected during three periods associated with changes in the perfusion levels identified in Figure 3 (**E**$_3$ during the occlusion, **E**$_4$ during hyperemia and **E**$_5$ returning to basal conditions). According to the definition in (4), three threshold levels were implemented, being the results of $\bar{P}_{Q_j}$ index for the OHT presented in Table 1.

TABLE I. Spatial Index of Microcirculation in OHT

	$\bar{P}_{Q_1}$	$\bar{P}_{Q_2}$	$\bar{P}_{Q_3}$
E$_3$	0.9473	0.7260	0.1690
E$_4$	0.9933	0.9471	0.5258
E$_5$	0.9639	0.7900	0.2102
Total	**0.9667**	**0.8138**	**0.2891**

The Spatial Index was also used to assess microcirculation profiles in two distal regions (**A** at ankle and **B** shank) in two DVP and DM2 patients. The values of the Spatial Index regarding the two conditions for regions A and B (in each patient) are presented in Table II.

TABLE II. Spatial Index of Microcirculation in DAP Patients

	Region	$\bar{P}_{Q_1}$	$\bar{P}_{Q_2}$	$\bar{P}_{Q_3}$
DVP	**A**	0.8041	0.5647	0.2882
	B	0.8432	0.7581	0.6511
DM2	**A**	0.7989	0.5312	0.2525
	B	0.5252	0.1773	0.0168

To illustrate the output of this methodology in a joint example, one region in the DVP patient is shown in Figure 4, in which it is possible to observe both indexes (temporal variation at left and LBPg matrices before the thresholding at right).

IV. DISCUSSION

The methodology presented in this work to access cutaneous microcirculation profiles was based on two microcirculation indices (Temporal and Spatial), by the identification of the underlying perfusion patterns (simulated by experimental protocols or obtained in patients with known reduced perfusion levels).

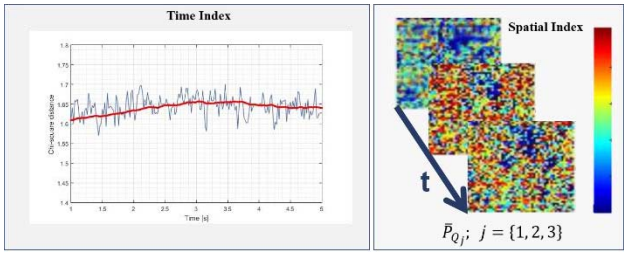

Figure 4: Temporal and Spatial indexes (3) and (4) in one distal region in a DVP patient.

The temporal analysis of the microcirculation profile allows correlating the increase in the pressure levels imposed by the external pressure, with the decrease in microcirculation as measured according to (4). This type of temporal analysis allows us to identify the physiological adaptations of the tissue to hypoxia response, such as the profile change occurring in the E3 period, where after 30 seconds of occlusion there is a muscular contraction response.

The results obtained by the experimental tests also reveal the ability of the temporal index to capture flow variations, thus allowing its use as a dynamic marker. In the cases of DVP, reperfusion time can be measured, so the Temporal Index may be used to quantify the degree of disease by calculating the time to return at baseline levels, or by comparing perfusion time with other regions.

In cases where the degree of cutaneous microcirculation is reduced, the existence of a spatial perfusion marker allows perceiving the flow geometry and its subcutaneous distribution. This index may be of special interest for diabetic foot risk analysis, and for this reason, the definition of three sensitivity levels for the Spatial Index proves to be particularly useful. By analyzing the results in Table 1, is possible to conclude that, for the three levels of sensitivity $(\bar{P}_{Q_i}, i = 1,2,3)$, the highest value presented is that of the E4 region (where de highest variation perfusion levels occur). In cases where the change in perfusion is subtle, it is possible to increase the index sensitivity, by changing the threshold level to $(\bar{P}_{Q_3})$.

Particularly, patients diagnosed with PAD not only have low perfusion levels at distal regions, but they also present a reduced variation of perfusion within these regions. As can be seen from the data in Table 2, by the analysis of $(\bar{P}_{Q_3})$ index, the greatest variation is noted at this level in the DVP patient, who is at an advanced stage of the disease). In the case of the patient with T2DM, who is classified as low level risk of diabetic foot, there is a low perfusion variability between regions A and B (for any of the cut-off levels), whereby the definition of threshold can be in these cases less demanding in terms of sensitivity.

V. CONCLUSION

This work presents a video speckle pattern analysis method to evaluate cutaneous microcirculation profiles. This is an LBP derived image processing methodology, adapted to video speckle characteristics and based on a local filtering scheme using a Gaussian threshold, the LBP_g . Based on the LBP_g output, two metrics were proposed to evaluate the microcirculation profile (a Temporal and a Spatial Index).

The methodology was applied to different perfusion conditions, both in experimental perfusion-occlusion situations and in patients with PAD. The results obtained point to the usefulness of these measures in cases where the diagnosis of PAD is established, with potential practical application in the context of PAD surveillance in primary health care. Additionally, the technique is innocuous, portable and inexpensive imaging modality, that can be easily used for clinical surveillance purposes.

Although based on experimental studies where distinct perfusion profiles were simulated, these results should be analyzed with caution, due to the reduced number of clinical experiments. In the near future, a clinical study will be conducted to reinforce the findings reported in this work, requiring a study enrolling more patients to achieve a greater level of detail in the analysis. Nevertheless, the results are encouraging and promising for potential use of this technique - speckle video analysis - based on the LBPg patterns and the respective Temporal and Spatial Indexes in the surveillance of PAD patients.

VI. REFERENCES

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