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Measuring Peripheral Signal Complexity Values by Applying Non-linear Method to Medical Laser Contrast Images

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Abstract
The physiological signals are considered as a sensitive measure for describing human state. The evaluation of such signals could be accomplished by monitoring peripheral blood flow in the skin. Laser speckle contrast imaging (LSCI) is an optical-based imaging device produces high quality images of microvascular blood flow. In this article, a research study is presented to measure signal complexity values of leg microvascular blood flow into two age healthy groups. Microvascular blood flow of leg skin was acquired using LSCI. The research sample consisted of 18 healthy individuals, divided into two groups according to the age: young group (20 to 30 years old, n=10) and aged group (50 to 70 years old, n=10). Signal complexity values of microvascular blood flow were computed by applying nonlinear algorithm to LSCI data of leg. The use of nonlinear methods to compute leg signal complexity values by processing LSCI data revealed higher entropy values obtained from young group than the ones obtained from aged group. However, the differences on signal complexity values between young and aged groups were not significant (p=0.65). Furthermore, applying nonlinear methods to LSCI data of leg could be used to estimate the deterioration of blood flow in peripheral vessels. Further studies with more subjects are needed to confirm the results presented in this paper. In addition, a comparative study with another body part may give new insight on the peripheral vessels dysfunction associated with aging.
Keywords: *ALaser contrast images, Image processing, Information theory, Entropy, Microcirculation.*

I. Introduction

The introduction of laser-based tools in medical area has provided an exciting opportunity to obtain information from tissue. Over the past few years, many of these tools have been improved to monitor blood vessels function [1, 2]. The majority of these techniques use a random pattern - called as speckle pattern - which is formed due to the diffused light to provide information about the tissue. Laser speckle contrast imaging (LSCI) is a laser-based imaging tool produces high quality images of microcirculation at low-cost [3]. LSCI is widely used in medical domain because of its high performance and no need for surgical intervention.

LSCI devices comprise from a source of laser light to illuminate the zone of interest and a camera to collect the images (Figure 1 shows a LSCI diagram). When a laser source illuminates a zone of interest (such as the skin), the reflected light forms a random pattern (speckle pattern) on the detector which is a camera. This technique exploits the variations inside the speckle pattern (causing by the movement with in the area of interest; such as movement of red blood cells) to get blood flow information in surface tissue [2]. The exposure time of the camera (T) causes a variation in the contrast of the collected speckle images. Thus, a reduction in the speckle contrast is occurred. Speckle contrast (K) value is calculated to quantify the amount of blurring as shown in Eq. (1) [4].

$$k=\sigma/\langle I\rangle \quad (1)$$

In this equation, the standard deviation σ and the mean density ⟨I⟩ are calculated inside N area around the pixels P (X, Y). Investigation of random phenomenon such as laser speckle could only be characterized statistically. Therefore, the use of statistical analyses in the spatial or temporal domain to compute the speckle contrast could provide essential information on the particles behavior within the area of interest [5].

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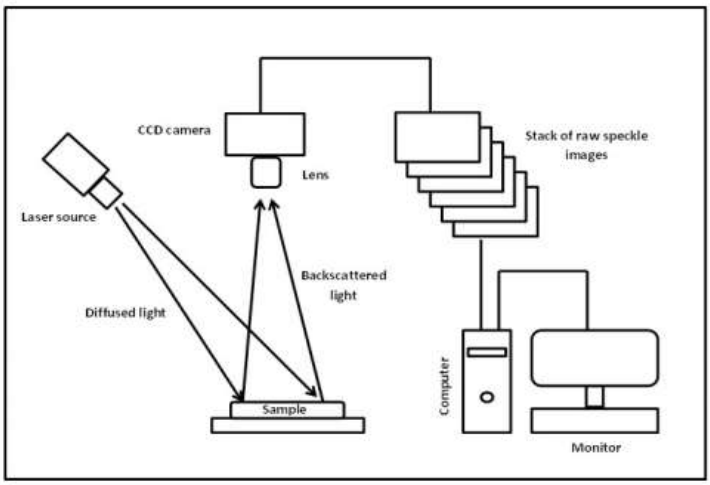

Fig. 1 LSCI setup demonstration

Assuming that the moving particles follow Lorentzian distribution, perfusion images could be obtained from the value of speckle contrast as provided in Eq. (2). Figure 2 shows an experimental image of perfusion.

perfusion ~1/K-1 (2)

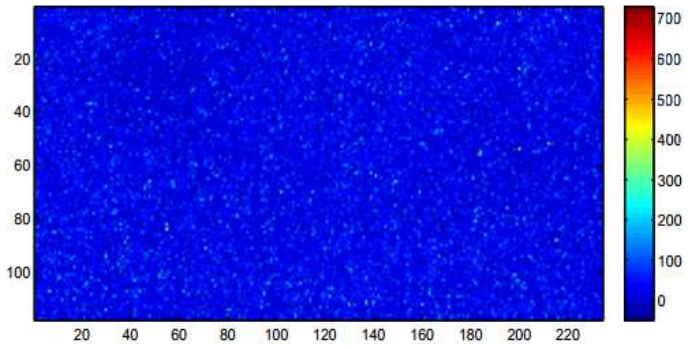

Fig. 2 An experimental perfusion image acquired at rest by using LSCI (234×118 pixels)

The difficult task in the assessment of microvascular vessels is how to obtain physiological information from the medical images. For that reason, several methods to process the medical images were proposed to allow for better comprehension of fundamental physiological features. Among these methods, the use of information theory, especially entropy measure has gained a broad and considerable attention in the medical field. For example, sample entropy (SampEn) is used widely to estimate the physiological signal complexity [6]. However, SampEn computations provide one level of information while the cardiovascular network manifests in various time scales to improve its adaptability in a sophisticated environment. For this reason, single-scale sample entropy analyzes do not provide multiple levels of information about complex condition activity knowledge such as cardiovascular network. Multiscale Entropy (MSE) was therefore introduced as a robust method for processing physiological data over multiple time level, using the same statistical principles as SampEn [7]. Nowadays, MSE is extensively used to study and diagnose different types of macro-vascular diseases, but it also could be used to study the function and structure of microvascular vessels [8, 9].

The MSE algorithm was considered previously to process LSCI data of microcirculation [8, 10]. In these studies, the authors have made effort to better understand the data series provided by LSCI. Another research study explored the effect of aging over micro- and macro-circulation parameters [9]. In contrast, peripheral blood flow complexity values were measured by applying MSE to LSCI data [11]. However, in all these previous studies, the data were obtained from the arm skin. To the best of our knowledge, another part of body has not been examined yet by applying MSE method to LSCI data of microcirculation. Such studies may provide an accurate

insight on the structure and function of microvascular blood vessels in different body part. Therefore, this paper presents a research study to evaluate the function of skin blood vessels by computing perepheal signal complexity values. For this purpose, a group of laser contrast images were acquired from leg skin. MSE algorithm was applied to laser contrast images to compute signal complexity values of peripheral blood flow. The study was conducted into two age groups free of diseases.

II. Material and methods

2.1 Subjects

20 healthy subjects were participated in this study without any known disease history. The research group was subdivided into two groups: a young and elderly group. The young group consists from 10 participants between the ages of 20 and 30. The older group consists from 10 participants between the ages of 50 and 70. Prior to participating in this research study, written permission was requested from all the subject. The research was performed in agreement with Helsinki declaration.

2.2 Experimental protocol

To apply MSE to the LSCI data, all blood flow images of the leg were obtained using PeriCam PSI System (Perimed, Sweden). In this device, a 1388 x 1038 pixel CCD camera is used to collect the images of speckle from the area of interest. The wavelength of laser light was 785 nm with 6 milliseconds of exposure time (T) of camera. The speckle contrast (K) is calculated spatially. Perfusion is calculated from the contrast values as shown above in Eq. (2). Perfusion images are then processed offline in this study. Laser imaging technology is very movement-sensitive. So participants were asked to lie down without movement while getting the data. In this study, 19000 images (approximately 20 minutes) were processed for each participant.

2.3 Image processing procedure

The following image processing procedure was performed to quantify and evaluate the signal complexity of LSCI data acquired from peripheral blood flow in the leg:

1. One pixel was chosen randomly from the first perfusion image and followed with time for all the 19000 perfusion images.
2. In order to minimize the spatial variability in blood flow and get a consistent signal, the mean perfusion value was calculated within a square area around the pixel chosen in step 1. Therefore, a square area of 31×31 pixels was chosen for this purpose.
3. The MSE values for each time series was computed and displayed as a function of the τ (1-267) measurement scale.

2.4 Statistical analysis

In this study, statistical variation of both young and aged groups was measured using t-test. Interval scale between 1 to 267 was used in order to compute MSE values for both groups (young and elderly groups). The mean MSE values were used to evaluate the complexity behavior between the two age groups. The value of $p<0.05$ has been considered as a significant value for all statistical analyzes.

2.5 Entropy theory

Entropy is a core concept of information theory. Entropy is a measure of disorder relates to a random variable. The term was first introduced by Shannon in 1948 which determines the average information contained in a message.

For the variable X, entropy is defined as follows

$$H(x)=\sum_{i=1}^{n} p_i \log p_i \quad (3)$$

where pi is the probability of output xi.

Entropy has the following characteristics:

$H(x) \geq 0$

$H(x) = 0$ If and only if the "random" variable X has only one result (certain event)

The highest value of entropy can be obtained when the random variable has equal probability of all results.

2.6 MSE method

MSE method measures the dynamic system complexity over multilevel time intervals (see Figure 5). For a vector of one-dimension, {x1, ..., xi, xN ....}, sets of successive points are grouped together to create coarse grained time series , $\{y^{(\tau)}\}$. So, the original vector is subdivided into non-overlapping points-sets of length τ. Average data points is calculated within each data set. The following equation is used to create non-overlapping time sets [7].

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$$y_j^{(\tau)} = \frac{1}{\tau} \sum_{i=(j-1)\tau+1}^{j\tau} x_i \qquad 1 \le j \le N/\tau \qquad (4)$$

Finally, SampEn is used to measure the complexity for each coarse-grained time set. The complexity values are then presented as a function of scale factors τ.

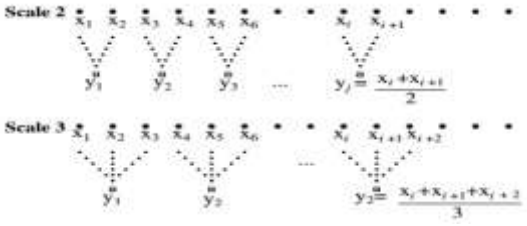

Fig 3. coarse-grain procedure [7].

SampEn algorithm is the concept of conditional probability: if there are two sub-groups that are close to each other for successive points m, within a specified sensitivity r, so these two groups will also remain close together if another new point is included in each subgroup.

For N series data, SampEn is calculated as follows

$$SampEn(m,r) = \lim_{N\to+\infty}\left\{-\ln\left[\frac{B^{m+1}(r)}{B^{m}(r)}\right]\right\}. \qquad (5)$$

The SampEn calculation for a specific set of data is done by the following equation [6]

$$SampEn(m,r,N) = -\ln\left[\frac{B^{m+1}(r)}{B^{m}(r)}\right]. \qquad (6)$$

Thus MSE is calculated for each generated time series as in Eq. (7).

$$MSE(x,\tau\tau,m,r) = -\ln\left[\frac{n_\tau^{m+1}}{n_\tau^{m}}\right], \qquad (7)$$

where n_τ^m is the total number of pairs of identical vectors (time series) at the scale factor τ.

The computed values of entropy could be used to evaluate the intrinsic dynamic of physiological time series. The gradual or study increase complexity values against the increases of the τ parameter demonstrate that the original data is very complex and contains multi-level information. On the other hand, the reduction of the complexity values against the increase in the values of the τ factor indicates that the original data contains information only at the small τ (Costa 2002).

III. Results and discussion

Figure 4 shows the average entropy values of leg obtained by applying MSE to the leg LSCI data sequence of the tested groups (young and old groups). From this figure, a continuous regression of the entropy values can be observed for both groups at the interval time scales between τT =0 and τT = 1. Then, the entropy values return to rise again and stabilize at a constant frequency along the time scales measured. The decline in entropy values is due to the systematic heart function observed in the previous studies at this interval [12, 13]. The processes operating on this interval are considered as having high regularity. It is found that the time interval of 0.9s represents the heart beat period [12]. Therefore, the regularity of cardiac beats could be the cause of low complexity values obtained from MSE.

In addition, a loss of complexity level can be observed with age when applying MSE to leg LSCI data (see Fig. 4). It is obvious from this figure that the complexity values of younger group (blue) are higher than the those of older group (red). In fact, it is well known that the organism system is a very complex system. This complexity derives from a broad range of adaptive responses in the surrounding environment, with specific physiological conditions. The physiological complex nature of the living organism demonstrates its adaptability to constantly changing conditions required to incorporate multi-band processes. In contrast, under baseline condition, the ongoing reduction in organism complexity level represents a weak physiological responses of the organism to external environmental factors.

The deterioration in complexity level observed within the microvascular blood flow signal may be due to dysfunction in the cardiovascular structure and function associated with aging. It has been shown that macro- and micro-circulation systems are interconnected [9]. Previous studies reported that the cardiac rhythms of healthy young people are extremely complex. However, this level of complexity decreases as a result of aging [14, 15].

Degradation of microvascular activities has been observed with age in many previous studies [16, 17]. As age progresses, a decrease in the amount of oxygen that reaches tissue, and inconsistency in important

metabolic processes may occur in the construction and demolition process [18]. Moreover, it has been shown that with aging, a reduction in the number of active capillaries, defects in their primary functions due to phenomena such as loss of regularity, destruction and sluggish blood vessels occurs [16]. Aging is also related to impairment of endothelial vascular function, cytochemical processes, and degradation of the nervous system [19]. Collagen and elastic fibers could also be affected as a result of aging [20]. In fact, one could conclude that the decreased complexity with aging may be due to age-related structural changes in the skin. A number of physiological characteristics are modified gradually with age such as connective tissue structure, water absorption, and skin density itself (see Waller and Maibach [21] for review).

The MSE algorithm on leg LSCI data shows ability to separate young group from aged group when measuring peripheral blood flow complexity. The fluctuations of young group demonstrate greater complexity level than the ones of aged group. The deterioration in complexity of leg blood flow signal of the elderly group can be explained by changes within the heart and blood vessels associated with age. However, the difference between the young and elderly group on the entropy values obtained from MSE applied to leg LSCI data was no statistically significant ($p = 0.65$, see Fig. 4).

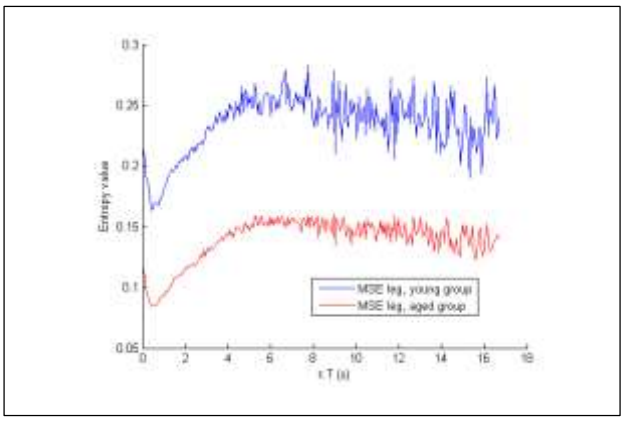

Fig. 4 Average complexity level obtained from leg LSCI data of two healthy groups of people. Young group (blue) and old group (red). Each group contains 10 subjects. MSE was applied to leg LSCI data for both groups. The measurement interval was ($\tau = 1$ to $\tau = 267$).

IV. Conclusion

The conclusion drawn is that the fluctuations in the physiological signal of microvascular vessels in healthy young people are very complex but this complexity declines as a result of aging. Furthermore, it has been concluded previously that there is a close relationship between the large and micro circulation and the two systems are interconnected [9]. Therefore, the results presented in this study give an indication of the possibility to predict diseases that may affect the heart through the study of micro-blood vessels. In addition, this research has shown the possibility of using nonlinear algorithms to study microvascular network by processing microvascular LSCI data.

One of the most important determinants of this research is the size of the relatively small sample. Therefore, we recommend that the same study be applied to a larger sample after confirming the normal distribution of this sample. In addition, we recommend applying new nonlinear methods to laser images and comparing them with the results presented in this paper. Furthermore, comparing the results presented in this paper with results obtained from another part in the body may give new insight on the peripheral vessels dysfunction associated with aging. Finally, the application of new nonlinear algorithms to microvascular diseases data such as diabetes may give an accurate picture of early treatment and prevention.

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VI. References

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