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LETTER TO THE EDITOR

Application of temporal correlation algorithm to interpret laser Doppler perfusion imaging

M. Z. Ansari[1] · A. Mujeeb[1]

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Introduction

Laser Doppler perfusion imaging (LDPI) is a full-field imaging technique that generates a two-dimensional map of blood flow [1]. Using LDPI approach, skin perfusion is obtained by measuring the Doppler shift introduced by coherent light reflected by both static tissue and the moving scattering centers (such as red blood cells, RBC) [2]. LDPI can provide perfusion maps over a surface of up to 50×50 cm^2 [3]. Depending on the laser wavelength and properties of the tissue, the sampling depth is typically from 1 to 2 mm [4].

LDPI has widely been utilized for many biomedical applications, for instance in the diagnosis of burns [5–12], the study of cerebral blood flow in small animals [13], drug uptake studies [14], the measurement of microvascular dysfunction in Raynaud's phenomenon and diabetes [15, 16], and the assessment of microvascular perfusion in the skin [17], and for many other applications including chronic pain [18], cancer and angiogenesis [19, 20], and brain [21].

In clinical and research applications, an average perfusion value is often computed over a given ROI and serially over time by using the LDPI [22]. This, however, breaks the bidimensional nature of the LDPI maps and undermines the advantages of the technique.

To aid in performing this task, efficient and consistent processing algorithms are required that can predict the perfusion changes over time without computing a mean value. Recently, Ansari et al. have reported a view-based qualitative method called the motion history image (MHI) that was successfully implemented on laser speckle contrast imaging (LSCI) and laser fluorescent imaging [23, 24]. MHI had provided information on time evolution of the perfusion variations without computing a mean value.

In order to improve the perfusion variation measurements using the LDPI data, we propose a quantitative image processing algorithm, the temporal correlation analysis for which no mean value is computed and a perfusion evolution in time can be monitored without computing the mean value over a stack. The method has been shown to be of utility to monitor fluctuations in the perfusion level in healthy subjects. The fast changing perfusion levels and the perfusion variations in a longer continuous LDPI measurement were monitored using the temporal correlation function. The algorithm is fast (typical run time between 5 and 10 s), and so, the analysis can be used to interpret the LDPI data to follow the perfusion variations for a clinical application.

Materials and methods

Two independent experiments were reported, consisting of LDPI measurements, the monitoring of fast changing perfusion levels in the dorsal side of the hand of a subject (female, 23 years) in rest and following the perfusion variations in the longer continuous LDPI measurement in the wrist of a healthy subject (male, 27 years), by Draijer et al. [22]. All the measurements in the reported experiments were performed using a Twente Optical Perfusion camera (TOPCam), a laser Doppler Perfusion Imager based on CMOS imaging array [22]. TOPCam imager provides a fast imaging speed to image perfusion and has been used both in online mode and in offline mode of imaging [22].

The first measurement reports a continuous LDPI recording following the fast changing perfusion levels (e.g., the heartbeat) in the dorsal side of the hand of the subject (female, 23 years) in rest [22]. Perfusion imaging was acquired for 3.8 s with an image size of 128×128 pixels [22].

The second measurement reported was performed to follow the perfusion variations in a longer continuous LDPI

✉ M. Z. Ansari
mohamedzaheer1@gmail.com; mdzaheer@cusat.ac.in

[1] International School of Photonics, Cochin University of Science and Technology, Kochi 682022, Kerala, India

measurement; an occlusion was applied by inflating a blood pressure cuff around the upper arm of a healthy subject (male, 27 years) [22]. LDPI imaging on the wrist of the subject was performed 3 min after the occlusion was applied. The occlusion was released around 3 s after the onset of the measurement. LDPI perfusion images were grabbed for about 15.5 s. The entire details of the experiments and LDPI measurements can be studied from the work of Draijer et al. [22].

Temporal correlation analysis

Continuous LDPI signals acquired in healthy subjects (human hand) were analyzed using a temporal correlation approach. The details of the experimental data acquired from the two healthy subjects can be studied [22]. The correlation analysis has been applied to extract information from the speckle temporal variations [25, 26]. In our case, fluctuations in perfusion level of the LDPI signal were considered analogous to speckle temporal variations, and that allowed the method to be implemented on the perfusion data. A stack containing LDPI perfusion images in temporal sequence was chosen for the analysis. The images having a resolution of 100 × 100 pixels were selected and submitted for the correlation analysis. The analysis yielded results as accurate as ones obtained with the images of higher resolution. The images were temporally analyzed using a cross-correlation analysis of the first perfusion image $P_I(t_0, x_0, y_0)$ with the kth perfusion image $P_I(t, x, y)$ of the temporal sequence:

$$\xi(t,x,y) = \frac{\langle P_I(t_0,x_0,y_0)P_I(t,x,y)\rangle - \langle P_I(t_0,x_0,y_0)\rangle\langle P_I(t,x,y)\rangle}{\sqrt{\left[\left(\langle {P_I}^2(t_0,x_0,y_0)\rangle - \langle P_I(t_0,x_0,y_0)\rangle^2\right)\left(\langle {P_I}^2(t,x,y)\rangle - \langle P_I(t,x,y)\rangle^2\right)\right]}} \quad (1)$$

where $t = k \times \Delta t$ is the time, k is the frame number ($k = 1....N$), Δt is the time step, and $(x, y) = (m \Delta r, n \Delta r)$. m and n are the pixel positions ($m = 1, ..., 100$, *and* $n = 1, ..., 100$) in the perfusion image, and Δr is the pixel size [25, 26].

The temporal correlation was obtained by summing $\sum_{m,n} \xi(t, x, y)$ and varying the time offset and thereby $\xi(t)$ evolution with time. It shows the comparison between two perfusion images and gives a quantitative analysis of the perfusion variations between these two states.

Results and discussion

Monitoring fast changing perfusion levels in the dorsal side of the hand of the subject in rest

A continuous LDPI signal was recorded following the fast changing perfusion levels (e.g., the heartbeat) in the dorsal side of the hand of the subject (female, 23 years) in rest [22]. Perfusion imaging was acquired for 3.8 s with an image size of 128 × 128 pixels [22].

Figure 1 shows the values of the correlation coefficient of each LDPI perfusion image (400 × 400 pixels) as a function of time.

To perform the correlation analysis, the LDPI signal (26 frames/s, 650 × 571 pixels) was converted to a stack containing 100 frames with a dimension of 650 × 571 pixels using the ImageJ software. The extracted frames were then submitted for the correlation analysis using a custom code written in MATLAB 7.6.0 (R2008a). A perfusion area of 400 × 400 pixels was selected in the original LDPI signal, and the correlation analysis was performed over a stack of 100 images.

It should be noted that the proposed algorithm of the correlation analysis is not computational time consuming. The average run time needed to process a stack of 100 frames (a resolution of 400 × 400 pixels) was about 5 s using the usual functions of the software package MATLAB 7.6.0 (R2008a) with a 1.48-GHz AMD E1-1500 APU laptop. Due to a less computational time, the algorithm can be useful for the assessment of the fast changing perfusion levels, e.g., the heartbeat.

The average time between the correlation peaks of the LDPI signal (Fig. 1) is 750 ms, which results in the normal regular heartbeat frequency of around 80 beats per minute and as was reported previously [22]. A slighter variation between the heartbeats is caused by tissue motion due to the pressure waves in the larger arteries [22].

Figure 2 presents decorrelation function computed using Fig. 1. Using Fig. 2, one can easily monitor fluctuations in the perfusion level in the hand of a healthy subject and this is in agreement with what was previously reported [22]. The peaks corresponding to a high perfusion level can now be compared around the time points A, B, C, D, E, and F, respectively.

Monitoring the perfusion variations in the longer continuous LDPI measurement in the wrist of a healthy subject

To follow the perfusion variations in a longer continuous LDPI measurement, an occlusion was applied by inflating a blood pressure cuff around the upper arm of a healthy subject (male, 27 years) [22].

The continuous LDPI data reported using the TOPCam optical system [22] was utilized for the temporal correlation analysis. LDPI imaging on the wrist of the subject was started 3 min after the occlusion was applied. The occlusion was released around 3 s after the onset of the measurement. Perfusion images were acquired for about 15.5 s.

To perform the correlation analysis, the LDPI signal (26 frames/s, 993 × 280 pixels) was converted to a stack of 408 frames with a dimension of 993 × 280 pixels using the ImageJ software. The correlation analysis was performed over the

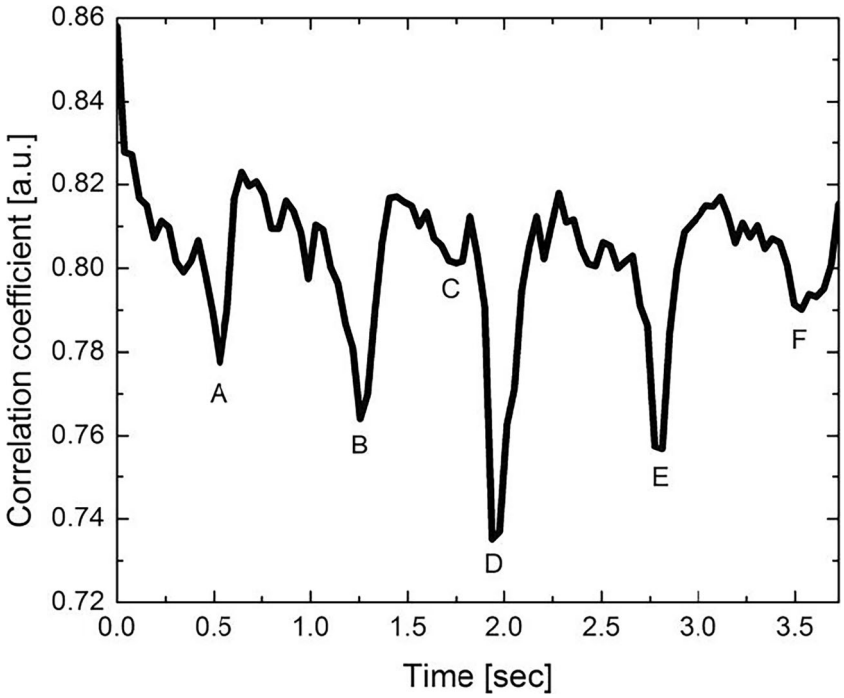

Fig. 1 The correlation functions of a continuous LDPI perfusion signal as function of time. Original LDPI data of [22] was collected *with permission from The Optical Society of America, USA (Copyright 2009)*

stack using a custom code written in MATLAB 7.6.0 (R2008a). A perfusion area of 100 × 100 pixels was then selected from the original LDPI signal, and the correlation analysis was performed over a stack of 408 images. The average run time needed to process a stack of 408 frames (resolution of 100 × 100 pixels) was about 10 s using the usual functions of the software package MATLAB 7.6.0 (R2008a) with a 1.48-GHz AMD E1-1500 APU laptop.

Figure 3 shows the results of the correlation analysis as a function of time of the continuous LDPI signal. As can be observed from Fig. 3, the average time between the correlation peaks of the LDPI signal is 829 ms, which results in the normal regular heartbeat frequency of around 73 beats per minute as was reported earlier [22].

The perfusion variations can easily be followed from the decorrelation measurements of the correlation curve (shown in Fig. 3). Figure 4 shows a plot of the decorrelation function computed using Fig. 3. The perfusion around the time points B, C, D, and E, respectively, can be monitored easily. The position C (corresponds to just after the release of the occlusion) relatively shows an increased perfusion. The point D corresponds to a maximum increase in perfusion level after the release of the occlusion. After 14 s (position E) of the release of the occlusion, the decorrelation value is still more

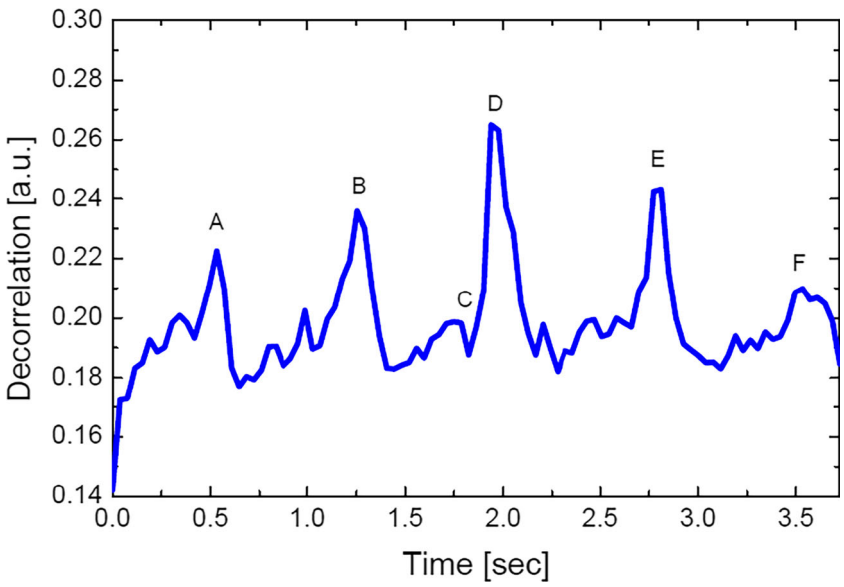

Fig. 2 Decorrelation as a function of time. The values have been computed around the time points corresponding to Fig. 1

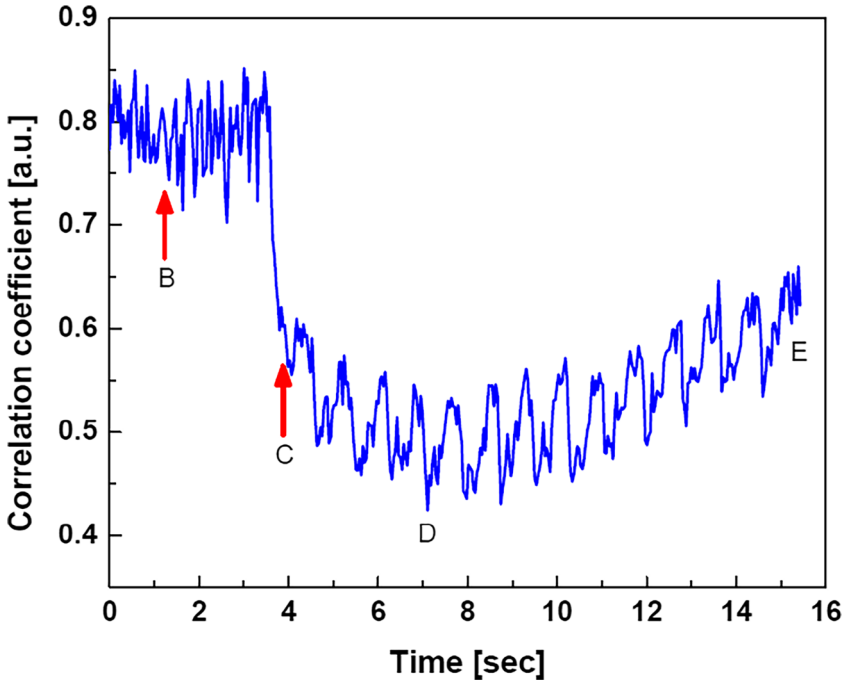

Fig. 3 The correlation functions of each perfusion image (continuous recording of 128 × 16 pixels) as a function of time. Original LDPI data of [22] was collected *with permission from The Optical Society of America, USA (Copyright 2009)*

than the value at B (during occlusion). Thus, the decorrelation measurement has clearly identified the variations in perfusion level during and after the release of the occlusion, and this is in agreement with the previously reported work [22].

Conclusions

We have presented an algorithm, the temporal correlation analysis, to interpret continuous LDPI signal. The method has shown its feasibility to monitor fluctuations in the perfusion level in the healthy subjects. Fast changing perfusion levels (e.g., the heartbeat) were monitored using the correlation analysis of the continuous LDPI recording and the corresponding heartbeat frequency measured. The same analysis was too validated for a longer continuous LDPI measurement. The decorrelation measurement was shown to provide an alternative way to monitor the perfusion variations, for example, during the heartbeat as well as that induced during the occlusion in a hand of the healthy subject.

The proposed algorithm of correlation analysis is not computational time consuming. The average run time to process the LDPI signal using the correlation analysis was between 5 and 10 s (for a stack containing 100–408 frames). The analysis

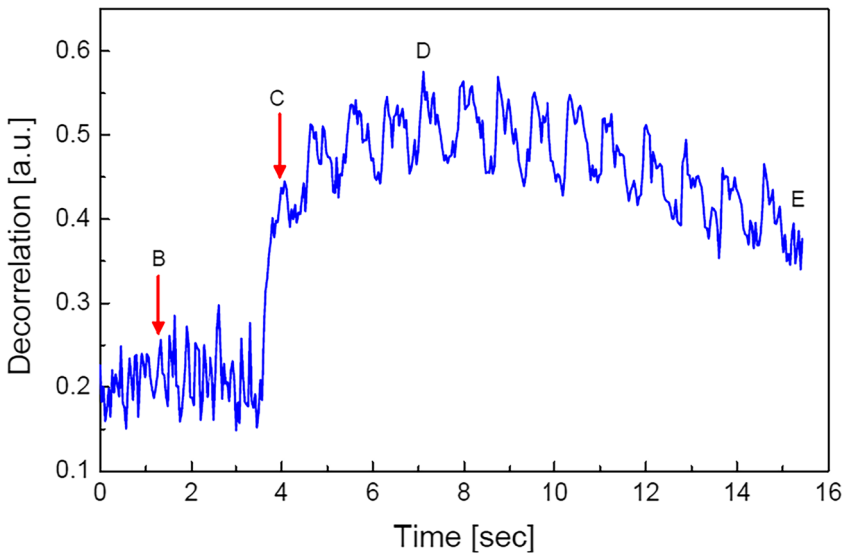

Fig. 4 Decorrelation as a function of time. The values have been computed at the time points corresponding to Fig. 3

can be used to interpret other LDPI data to monitor perfusion variations.

Further, to follow the perfusion variations using a LDPI signal, one has to measure the average value of each perfusion image of the temporal sequence. The correlation analysis allowed monitoring the perfusion variations without computing the average perfusion value of each perfusion image over the stack. Moreover, it also allows ROI monitoring of the LDPI data in the time domain.

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References

1. Essex TJ, Byrne PO (1991) A laser Doppler scanner for imaging blood flow in skin. J Biomed Eng 13(3):189–194
2. Stern MD (1975) In vivo evaluation of microcirculation by coherent light scattering. Nature (London) 254:56–58
3. O'Doherty J, McNamara P, Clancy NT, Enfield JG, Leahy MJ (2009) Comparison of instruments for investigation of microcirculatory blood flow and red blood cell concentration. J Biomed Opt 14(3):034025
4. Briers JD (2001) Laser Doppler, speckle and related techniques for blood perfusion mapping and imaging. Physiol Meas 22(4):R35–R36
5. Stewart CJ, Frank R, Forrester KR, Tulip J, Lindsay R, Bray RC (2005) A comparison of two laser-based methods for determination of burn scar perfusion: laser Doppler versus laser speckle imaging. Burns 31:744–752
6. Niazi ZBM, Essex TJH, Rapini R, Scott D, McLean NR, Black MJM (1993) New laser Doppler scanner, a valuable adjunct in burn depth assessment. Burns 19:485–489
7. Pape SA, Skouras CA, Byrne PO (2001) An audit of the use of laser Doppler imaging (LDI) in the assessmentof burns of intermediate depth. Burns 27(7):233–239
8. Kloppenberg FW, Beerthuizen GI, ten Duis HJ (2001) Perfusion of burn wounds assessed by laser Doppler imaging is related to burn depth and healing time. Burns 27:359–363
9. Droog EJ, Steenbergen W, Sjoberg F (2001) Measurement of depth of burns by laser Doppler perfusion imaging. Burns 27:561–568
10. Bray R, Forrester K, Leonard C, McArthur R, Tulip J, Lindsay R (2003) Laser Doppler imaging of burn scars: a comparison of wavelength and scanning methods. Burns 29:199–206
11. La Hei E, Holland A, Martin H (2006) Laser Doppler imaging of paediatric burns: burn wound outcome can be predicted independent of clinical examination. Burns 32:550–553
12. Monstrey SM, Hoeksema H, Baker RD, Jeng J, Spence RS, Wilson D, Pape SA (2011) Burn wound healing time assessed by laser Doppler imaging. Part 2: validation of a dedicated colour code for image interpretation. Burns 37(2):249–256
13. Dunn AK, Bolay H, Moskowitz MA, Boas DA (2001) Dynamic imaging of cerebral blood flow using laser speckle. J Cereb Blood Flow Metab 21:195–201
14. de Mul FFM, Blaauw J, Aarnoudse JG, Smit AJ, Rakhorst G (2007) Diffusion model for iontophoresis measured by laser-Doppler perfusion flowmetry, applied to normal and preeclamptic pregnancies. J Biomed Opt 12:14,032–1
15. Anderson ME et al (2004) Digital iontophoresis of vasoactive substances as measured by laser Doppler imaging: a non-invasive technique by which to measure microvascular dysfunction in Raynaud's phenomenon. Rheumatology 43(8):986–991
16. Muris DM, Houben AJ, Schram MT, Stehouwer CD (2013) Microvascular dysfunction: an emerging pathway in the pathogenesis of obesity-related insulin resistance. Rev Endocrinol Metab Disord 14(1):29–38
17. Payette JR, Kohlenberg E, Leonardi L, Pabbies A, Kerr P, Liu K, Sowa MG (2005) Assessment of skin flaps using optically based methods for measuring blood flow and oxygenation. Reconstr Surg 115(2):539–546
18. Grothusen JR, Schwartzman RJ (2011) Laser Doppler imaging: usefulness in chronic pain medicine. Pain Physician 14:491–498
19. Kalka C, Masuda H, Takahashi T, Kalka-Moll WM, Silver M, Kearney M, Li T, Isner JM, Asahara T (2000) Transplantation of ex vivo expanded endothelial progenitor cells for therapeutic neovascularization. Proc Natl Acad Sci 97(7):3422–3427
20. Ferraro B, Cruz YL, Baldwin M, Coppola D, Heller R (2010) Increased perfusion and angiogenesis in a hindlimb ischemia model with plasmid FGF-2 delivered by noninvasive electroporation. Gene Ther 17(6):763–769
21. Broderick PA, Kolodny EH (2010) Biosensors for brain trauma and dual laser Doppler flowmetry: enoxaparin simultaneously reduces stroke-induced dopamine and blood flow while enhancing serotonin and blood flow in motor neurons of brain, in vivo. Sensors 11(1):138–161
22. Draijer M, Hondebrink E, van Leeuwen T, Steenbergen W (2009) Twente Optical Perfusion Camera: system overview and performance for video rate laser Doppler perfusion imaging. Opt Express 17(5):3211
23. Ansari MZ, Kang EJ, Manole MD, Dreier JP, Humeau-Heurtier A (2017) Monitoring microvascular perfusion variations with laser speckle contrast imaging using a view-based temporal template method. Microvasc Res 111:49–59
24. Ansari MZ, Mujeeb A (2017) Application of motion history image (MHI) on dynamic fluorescent imaging for monitoring cerebral ischemia induced by occlusion of middle cerebral artery (MCA) in mouse brain. Biomed Spectrosc Imaging 6(3–4):135–142
25. Nassif R, Abou Nader C, Pellen F, Le Brun G, Abboud M, Le Jeune B (2013) Retrieving controlled motion parameters using two speckle pattern analysis techniques: spatiotemporal correlation and the temporal history speckle pattern. Appl Opt 52:7564
26. Abou Nader C, Pellen F, Roquefort P, Aubry T, Le Jeune B, Le Brun G, Abboud M (2016) Evaluation of low viscosity variations in fluids using temporal and spatial analysis of the speckle pattern. Opt Lett 41(11):2521