

LASER SPECKLE CONTRAST ANALYSIS (LASCA): A NONSCANNING, FULL-FIELD TECHNIQUE FOR MONITORING CAPILLARY BLOOD FLOW

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ABSTRACT

A new noninvasive technique for monitoring capillary blood flow has been developed. Based on the phenomenon of time-varying laser speckle, it is a digital version of single-exposure speckle photography. It provides a velocity map of the area of interest in real time without the need for scanning. The results of some initial experiments on volunteers are presented.

Keywords laser speckle; time-varying speckle; time-averaged speckle photography; laser Doppler velocimetry; blood flow monitoring.

1 INTRODUCTION

Most optical (laser) techniques for monitoring blood flow use either the Doppler effect¹ or the temporal statistics of time-varying laser speckle.² These techniques have been developed separately, though it is easy to show that, at least so far as line-of-sight velocities are concerned, they are identical.³ Both essentially measure the blood velocity at a point. If a map of blood velocity distribution is required, some form of scanning must be introduced. This can either be mechanical scanning or the successive analysis of the intensity fluctuations at the different pixels in a CCD array, or a combination of the two. Although such scanning has been used,^{4–6} and commercial instruments have been introduced, the disadvantages include the presence of moving parts and/or the handling of large amounts of data. The consequence is either a significant escalation of the cost or a time delay that requires the patient to remain still for several minutes and may preclude genuine real-time operation. (A possible exception is a recent development by Tamaki et al.,⁷ who use a converted fundus camera to investigate retinal blood flow by means of time-varying speckle. By restricting the field of view to 0.42×0.42 mm, using an array of only 100×100 pixels, adopting a simplified algorithm to measure the first-order temporal statistics of the intensity fluctuations in each pixel, and using 98 scans at the fast scan-rate of 540 frames per second, they have developed a technique that can produce a false-color blood-flow map in just 15 s.)

2 SINGLE-EXPOSURE SPECKLE PHOTOGRAPHY

Some years ago, a technique was announced that removed the need for scanning and offered a true full-field technique. Single-exposure speckle photography⁸ consisted of taking a photograph of the laser-illuminated area under investigation and using an exposure time that was long enough to allow the faster fluctuating speckles to blur out. Models were proposed^{8,9} that related the spatial statistics (essentially the contrast) of the time-integrated speckle pattern to the velocity of the scatterers. The technique was developed for the measurement of retinal blood flow.¹⁰

Although this technique showed promise, it suffered from the serious disadvantage of being a two-stage process that precluded real-time operation. The film had first to be chemically processed and then the resulting negative optically processed (by spatial filtering) in order to convert the contrast variations to more visible intensity variations.¹¹ As a clinical technique, this was not viable.

3 DIGITAL VERSION: LASER SPECKLE CONTRAST ANALYSIS (LASCA)

The route to real-time operation was to remove the photographic stage and develop a digital version of the method. The first attempt involved the digital processing of the photographs.¹² Although this removed the optical filtering stage and showed the

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promise of a digital technique, it was still necessary to take and process a photograph. Thus the method was still not real-time.

A fully digital technique that totally eliminates the photographic stage has recently been reported.¹³⁻¹⁵ This uses a CCD camera and a frame grabber, and specially developed software to compute the local contrast and convert it to a false-color map of contrast (and hence of velocity). The image is a time-integrated exposure, but at the velocities involved in blood flow, the exposure is short enough (typically 20 ms) to make the technique effectively real-time. (At present, the data processing can take up to 4 min, but this will be improved as development of the technique proceeds.)

Since the method is no longer photographic, the term *single-exposure speckle photography* is inappropriate. We propose to call the new technique *laser speckle contrast analysis* (LASCA). It is worth noting, however, that as far as the hardware is concerned, it is really a version of time-averaged electronic speckle-pattern interferometry (ESPI) as described, for example, by Høgmøen and Løkberg.¹⁶

4 EXPERIMENTAL ARRANGEMENT FOR LASCA

In the current version of LASCA, light from a 40-mW He-Ne laser (wavelength 633 nm) is diverged and illuminates the object of interest. The maximum exposure used in the experiments was just over 5 Wm^{-2} , which is much less than the maximum permissible exposure (MPE) for human skin of 2000 Wm^{-2} for long-term exposure. However, normal safety precautions should be taken against the undiverged laser beam and against exposure of the eye to the laser light.

A CCD camera images the illuminated area and the image is observed on a monitor. In response to an instruction from a personal computer, a frame grabber captures an image and immediately processes it by built-in software to produce a false-color contrast map indicating velocity variations. The operator has several options at his disposal, including the number of pixels over which the local contrast is computed, the scaling of the contrast map, and the choice of contour colors.

5 BASIC THEORY OF LASCA

The basic concept of LASCA is very simple. Coherent light scattered from a collection of randomly distributed particles produces a characteristic random interference pattern known as a speckle pattern. If an optical system is used to image the field of scattering particles, and if the individual particles are too small for the imaging system used to resolve, the image observed consists of such a speckle pattern. The intensity observed at any point in such an image is not deterministic and can only be described statistically. These speckle statistics

have been studied in detail and are well understood. One property of a "fully developed" (ideal) speckle pattern is that the standard deviation of the spatial intensity variations is equal to the mean intensity. For speckle patterns that are not fully developed, the ratio of the standard deviation to the mean intensity can be used as a measure of the contrast of the pattern. This definition of speckle contrast is used in this paper:

$$\text{Speckle contrast } K = \sigma_s / \langle I \rangle. \quad (1)$$

In Eq. (1), σ_s is the standard deviation of the spatial intensity variations in the speckle pattern. $\langle I \rangle$ is, strictly speaking, the ensemble average of the intensity, but can be taken for present purposes to be the spatial average.

If the scattering particles producing the speckle pattern are in relative motion, the optical path differences in light traveling from the various particles to the image plane will be constantly changing. This results in a constantly changing speckle pattern. Such randomly fluctuating speckle patterns have been studied extensively as "time-varying speckle." If such a speckle pattern is captured by an imaging device that has a finite integration time, it is clear that some of the fluctuations will be averaged out and the speckle pattern will display a lower contrast. Mathematically, the standard deviation σ_s is reduced, whereas the mean intensity $\langle I \rangle$ is unchanged. If the integration time of the detector is much longer than the cycle time of the speckle fluctuations, all intensity variations will be averaged out and σ_s will be zero. The speckle contrast, defined as the ratio $\sigma_s / \langle I \rangle$, therefore depends on the integration time of the detector and on the velocity of the scatterers, and lies between the values of 0 and 1.

The exact relationship between the velocity and the speckle contrast in the time-integrated speckle pattern is very complex. Multiple scattering and scattering from tissues other than blood complicate the matter, as does the non-Newtonian flow patterns of the red blood cells through capillaries. However, this problem is shared with all time-varying speckle techniques, as well as with laser Doppler, and with all these techniques it is necessary to resort to models and to make a number of simplifying assumptions. If the problem can be solved for any of these techniques, it is immediately solved for LASCA. This can be seen from a result of Goodman¹⁷ that links the spatial statistics of a time-integrated speckle pattern to the temporal statistics of the speckle fluctuations. He showed that the variance of the spatial intensity variations is equal to the time average of the autocovariance of the intensity fluctuations:

$$\sigma_s^2(T) = \frac{1}{T} \int_0^T C_t(\tau) d\tau, \quad (2)$$

where T is the integration time and $C_t(\tau)$ is the autocovariance of the intensity fluctuations (the subscript t indicating that this is a temporal statistic). $C_t(\tau)$ is defined in the usual way, as follows:

$$C_t(\tau) = \langle \{I(t) - \langle I \rangle\} \{I(t + \tau) - \langle I \rangle\} \rangle_t. \quad (3)$$

Methods that analyze the temporal statistics of speckle fluctuations, including laser Doppler, essentially measure the quantity on the right-hand side of Eq. (2). LASCA measures the quantity on the left-hand side.

6 IMAGE PROCESSING IN LASCA

The camera used in the current version of LASCA has an active imaging area of 6.4×4.8 mm with approximately 402,000 pixels. The images captured by the frame grabber and processed by LASCA consist of 512×512 pixels. The number of pixels used to compute the local speckle contrast can be selected by the user: lower numbers reduce the validity of the statistics, whereas higher numbers limit the spatial resolution of the technique. For the examples presented in this paper, squares of 7×7 pixels were used. The software computes the speckle contrast ($\sigma_s / \langle I \rangle$) for any given square and assigns this value to the central pixel of the square. The contrast values are then converted to a color according to the false-color scale in use. This scale is currently linear, in equal steps of contrast. In general, the contrast range obtained in an image is much smaller than the theoretically possible 0 to 1. In order to make full use of the false-color scale, the user can apply a scaling factor to "stretch" the contrast range to fill the scale. The process is then repeated for 7×7 squares centered on each pixel in turn. This results in a smoothing of the contrast map, but the resolution of the technique is limited by the necessary use of a finite number of pixels in computing the local contrast. This is the trade off compared with those techniques that use the temporal statistics of the speckle fluctuations (including laser Doppler). The latter have high spatial resolution, sampling a single point in space over a finite time. Because of this, they require some form of scanning to produce a two-dimensional map of velocity. LASCA, on the other hand, samples the spatial velocity distribution at (almost) an instant in time, but loses spatial resolution due to the necessity to compute spatial statistics. For the examples presented in this paper, the field of view was approximately 150×100 mm. The resolution of the image is effectively reduced by the use of 7×7 squares of pixels from 512×512 (pixels) to approximately 73×73 (pixel blocks). Hence the spatial resolution on the object is approximately 2 mm ($150/73$). Using the same imaging system, the resolution of laser Doppler (or other temporal statistics methods) would be a single pixel, or approximately 0.3 mm. This relatively low resolution is currently a disadvan-

tage of the LASCA technique, but it could be improved by the use of more pixels or of a smaller area of view.

7 INTERPRETATION OF LASCA IMAGES

The quantitative interpretation of any of the light-scattering techniques for monitoring capillary blood flow is extremely difficult. This applies equally to LASCA as to all the time-varying speckle and laser Doppler techniques. The system being monitored is very complex. Light is scattered from all the layers of the skin and from the walls of capillaries as well as from the blood cells. Many of these scattering media are also in motion. In addition, the movement of red blood cells through the narrow capillaries is far from Newtonian, with the cells rolling and changing shape as they force their way through. Finally, much of the light will be multiply scattered at several points before reemerging and contributing to the speckle pattern.

Models can be devised, but the simplifying assumptions that must be made drastically reduce the reliability of the interpretation. Even calibration of the various techniques is difficult, because of the lack of a reliable standard method for *in vivo* measurements. What is clear, however, is that the rate of fluctuation of the intensity variations, and hence also the spatial contrast of the time-integrated speckle in LASCA, must be affected by the velocity of the scattering particles, and since much of the scattering takes place at red blood cells, blood velocity must play a role. Hence, even though absolute measurements may be difficult, relative measurements should be possible and reliable. This is the basis on which scanning laser Doppler techniques are currently marketed and it is also the present status of LASCA. (For medical diagnostic use, it is possible that this is all that is needed or is possible, especially if the expected variation among normal patients is taken into account.)

Notwithstanding the above caveats, it is possible to make some quantitative estimates from the speckle contrast measured. This would at least show whether the contrasts being measured were consistent with accepted values of capillary blood flow. The subcutaneous capillary network is so convoluted that there is no definite direction to the blood flow and the line-of-sight velocity distribution can be taken to be approximately Lorentzian. With this assumption, and using Eq. (2), it has been shown⁸ that in an ideal system (assuming, among other things, perfect speckle formation and no multiple scattering), the speckle contrast in a speckle pattern integrated over a time T is given by:

$$K = \{(\tau_c/2T)[1 - \exp(-2T/\tau_c)]\}^{1/2}, \quad (4)$$

where τ_c is the decorrelation time of the intensity fluctuations (the time taken for the autocorrelation function of intensity to fall from a value of 1 to $1/e$). The relationship between τ_c and the mean (or

some typical) velocity is also open to speculation. The simplest approach leads to a characteristic "decorrelation velocity" defined as follows:

$$v_c = \lambda / 2\pi\tau_c. \quad (5)$$

For helium-neon laser light ($\lambda=0.633 \mu\text{m}$), this becomes:

$$v_c \approx 0.1 / \tau_c \mu\text{m s}^{-1}. \quad (6)$$

Contrast values obtained from the skin (back of the hand) tend to be between 0.1 and 0.15 for the integration time used (fixed by the camera available at 20 ms). From Eq. (4), it can be calculated that this is equivalent to values of τ_c/T of 0.02 to 0.05 for the Lorentzian model adopted. As $T = 20$ ms, this corresponds to values of τ_c of 0.4 to 1 ms. Equation (6) would then give $v_c \approx 100\text{--}250 \mu\text{m s}^{-1}$. This is in excellent agreement, considering the significant assumptions implicit in the model, with generally accepted values of 200 to 300 $\mu\text{m s}^{-1}$ for the mean velocity of capillary blood flow.

In general, however, it would be unwise to take too much account of the quantitative value of the LASCA technique (or of any time-varying speckle or laser Doppler method used to measure capillary blood flow). The system being monitored is extremely complex and there are many indeterminate factors in play. What is important from a medical diagnostic point of view is the ability to monitor changes and variations, and that all these techniques can do. It will be seen from the examples that follow that when changes are made that might be expected to lead to an increase in perfusion (blood flow), there is always a reduction in the observed speckle contrast. These examples are therefore offered as evidence of the feasibility and viability of the LASCA technique.

8 SOME DEMONSTRATIONS OF LASCA IN MONITORING CAPILLARY BLOOD FLOW

Several experiments have been carried out to demonstrate the validity of the LASCA technique in monitoring changes in capillary blood flow. Some of these are reported below and are presented as a demonstration of the ability of the technique to detect these changes. As mentioned above, caution should be exercised in assigning too much quantitative interpretation to the results, but some semi-quantitative deductions have been made in the first experiment described. The remainder are presented as qualitative demonstrations only.

8.1 APPLIED HEAT

The effect of temperature on blood flow was investigated by asking a group of twelve volunteers to immerse one hand in cold water and the other in warm water. The cold water was at a temperature

between 3 and 10 °C and the hand was immersed for 30 s. The warm water was between 41 and 48 °C and the hand was immersed for 2 min. LASCA was used to calculate the speckle contrast in an area on the back of the hand measuring approximately 40×40 mm. With every subject the contrast measured on the "warm" hand was lower than that measured on the "cold" hand, indicating increased movement of the scatterers. The contrast reduction from cold to warm varied from 5 to 25% among subjects, even for similar temperature differences, thus demonstrating significant differences among subjects, but the change was always in the same (expected) direction. If the Lorentzian model and all its associated assumptions are correct, and if the reduction in speckle contrast is entirely due to increased blood flow (another bold assumption), the changes in speckle contrast convert to blood velocity increases of between 10 and 50% for the various subjects.

Figure 1 shows contrast maps for the hands of one subject, (a) being of the hand that had been immersed in cold water, (b) the hand that had been immersed in hot water. (Note that in these and the succeeding photographs, the color bar below the image shows the contrast scale, with *low* contrast (and hence higher velocity) being toward the right.)

8.2 RUBBING THE SKIN

Stimulation of the skin by rubbing is known to increase local blood flow. Figure 2(a) shows the contrast map of a hand under normal conditions. Figure 2(b) shows the same hand after a small area had been gently rubbed. The area of reduced contrast corresponds exactly with the area rubbed.

8.3 SCALDED SKIN

One of the areas of application of LASCA is expected to be in the assessment of burns and other localized traumas. The occurrence of an accident (outside the laboratory and unrelated to these experiments) in which a person's arm was scalded by steam created an opportunity to use the technique. Figure 3 shows a portion of the forearm, and the area affected by the scald clearly shows a decrease in speckle contrast.

8.4 OCCLUDED FLOW

Two experiments on occluded blood flow are illustrated. In Figure 4, a rubber band around the base of the second finger has clearly produced an increased contrast (indicating reduced blood flow) in that finger.

In Figure 5, a blood-pressure cuff was used to reduce the blood flow to the entire hand. Figure 5(a) shows the hand under normal conditions, Figure 5(b) the same hand after the cuff was inflated.

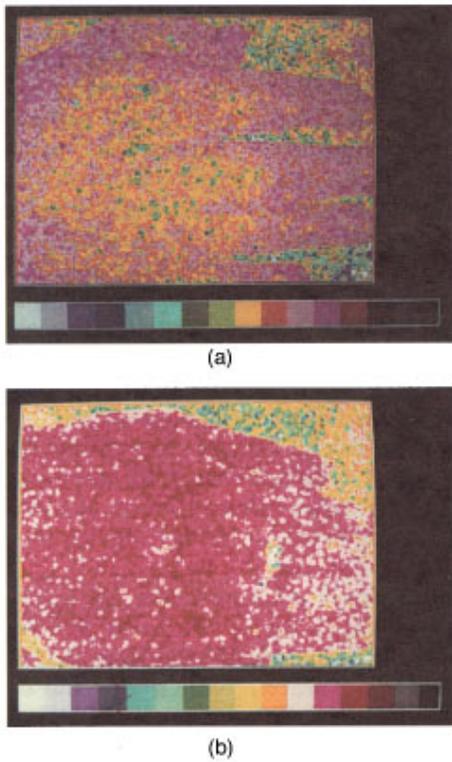


Fig. 1 LASCA images showing the effect of temperature; (a) hand after immersion in cold water, (b) hand after immersion in hot water. (Note: the color bar below the images in the figures shows the contrast scale, with contrast decreasing (and hence velocity increasing) from left to right.)

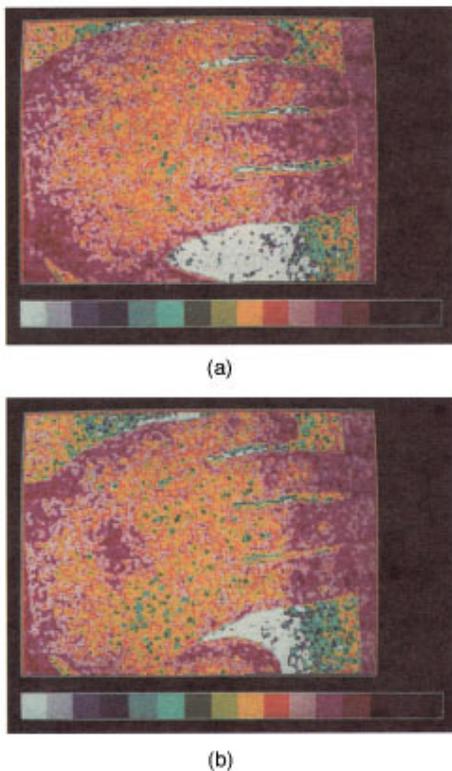


Fig. 2 LASCA images showing the effect of rubbing the skin; (a) hand under normal conditions, (b) same hand after a small area had been gently rubbed (the area rubbed is indicated by the red patch, showing increased perfusion).

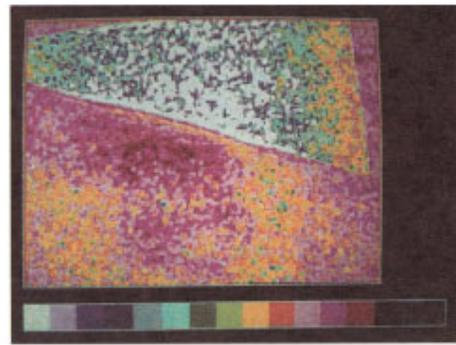


Fig. 3 LASCA image of a forearm, showing an area scalded by steam.

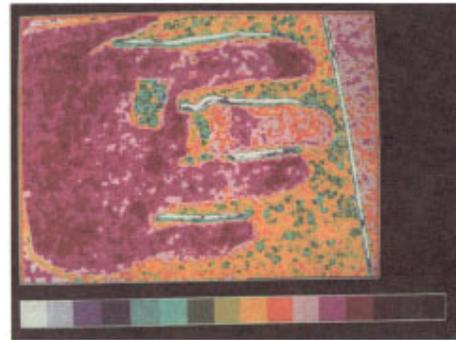


Fig. 4 LASCA image of a hand, showing the effect of occluded blood flow: a rubber band has been placed round the base of the second finger.

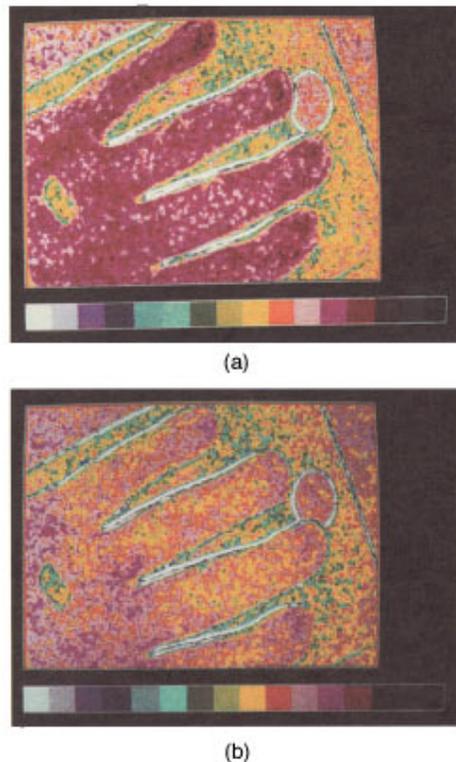


Fig. 5 LASCA images of a hand, showing the effect of occluded blood flow; (a) hand under normal conditions, (b) same hand when a blood-pressure cuff is inflated to reduce blood flow to the hand.

Again the increase in speckle contrast is apparent. (In Figs. 4 and 5, the rectangular patch on the back of the hand is a control patch, consisting of layers of medical adhesive tape and aluminum foil, used to check for gross motion of the hand.)

9 PRELIMINARY PRECLINICAL TRIALS

Preliminary experiments have been performed on some patients at University College Hospital, London. The subjects examined had a variety of hematological diseases, mainly various forms of anemia. Patients were usually examined before and after transfusions, the aim being to see if the differing amounts of red blood cells present would alter the detected contrast. The response of one patient to the application of heat was also investigated. Initial indications from these trials are encouraging, as is the positive response from the clinicians involved.

10 CONCLUSIONS

Laser speckle contrast analysis is a full-field laser speckle technique for measuring flow velocity. We believe it is the only proposed technique that uses the spatial statistics of laser speckle. All other methods that use time-varying speckle, including laser Doppler, use the temporal statistics of the intensity fluctuations.

The advantages of LASCA are that it is a true full-field technique that produces a two-dimensional map of flow velocity at a particular instant in time and that it achieves this without the need for scanning, expensive equipment, or very heavy computing power. Its main disadvantage is the reduced spatial resolution. It shares with the other techniques the problems of producing truly quantitative results, but in a medical diagnostic environment this may not be of significant importance.

LASCA has been shown to be a viable real-time method for detecting variations in blood flow. Preliminary experiments on volunteers and patients have been encouraging. LASCA is still under development and various refinements are being investigated.

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