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Laser speckle contrast imaging for measuring blood flow

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When a diffuse object is illuminated with laser light, a random interference effect known as a speckle pattern is produced. If there is movement in the object, the speckles fluctuate in intensity. These fluctuations can be used to provide information about the movement. A simple way of accessing this information is to image the speckle pattern – the fluctuations cause a blurring of the speckle, leading to a reduction in the local speckle contrast. Thus velocity distributions are coded as speckle contrast variations. The same information can be obtained by using the Doppler effect, but producing a two-dimensional Doppler map requires scanning: speckle imaging provides the same information without the need to scan. This paper reviews the development of laser speckle imaging, starting with the connection established between speckle fluctuations and movement in the nineteen-seventies. In the eighties, a photographic technique for monitoring retinal blood flow was developed, and ten years later a digital version was used to monitor capillary blood flow in the skin. Today, many groups around the world are either using or researching the technique, and the paper will close by presenting some of their recent results.

Keywords: laser speckle, laser Doppler, time-varying speckle, medical imaging, blood flow, perfusion.

1. Introduction

This is a review paper, outlining the history and development over the last thirty years or so of a non-invasive technique for monitoring blood flow. The technique uses the phenomenon of laser speckle. The basic theory of laser speckle was developed in the nineteen-sixties. In the seventies, time-varying speckle, caused by motion, became a subject for research. In particular, a connection was established between the fluctuations of the speckle pattern and the movement of scattering centres in living organisms. One way in which the speckle fluctuations manifested themselves was in a reduction in the normally high contrast of the speckle pattern. In the eighties, this effect was used in a photographic technique known as single-exposure speckle photography, developed to study blood flow in the retina. Although the method worked, the need to process the photographs before the information could be accessed

proved to be a major problem and interest in the technique waned. In the nineties, new digital methods allowed the development of a quasi-real time version of the method, and this has proved to be much more useful. Today, researchers in at least seventeen countries around the world are either using or further developing the technique.

2. Background

2.1. Laser speckle

The arrival of the laser in 1960 brought with it a new phenomenon. When laser light illuminates a diffuse surface, the high coherence of the light produces a random interference effect – a sort of coherent noise. At first, researchers called the effect "granularity" [1], but soon the name "speckle" became more popular. Figure 1 shows a typical "speckle pattern."

Fig. 1. A typical laser speckle pattern.

In the early days of lasers, speckle was regarded purely as a nuisance: it severely affected resolution when laser light was used, for example in holography, and much effort was directed towards reducing speckle in images formed in laser light [2]. However, it was not long before researchers started to study speckle for its own sake and to develop practical applications of the phenomenon [3].

Laser speckle is an interference pattern produced by light reflected or scattered from different parts of the illuminated surface. If the surface is rough (surface height variations larger than the wavelength of the laser light used), light from different parts of the surface within a resolution cell (the area just resolved by the optical system imaging the surface) traverses different optical path lengths to reach the image plane. (In the case of an observer looking at a laser-illuminated surface, the resolution cell is the resolution limit of the eye and the image plane is the retina.) The resulting intensity at a given point on the image is determined by the algebraic addition of all the wave amplitudes arriving at the point. If the resultant amplitude is zero, because all the individual waves cancel out, a dark speckle is seen at the point; if all the waves arrive at the point in phase, an intensity maximum is observed.

Laser speckle is a random phenomenon and can only be described statistically. GOODMAN [4], has developed a detailed theory, but for this paper only one result is of

major importance. This is an expression for the contrast of a speckle pattern. Assuming ideal conditions for producing a speckle pattern – highly coherent, single-frequency laser light and a perfectly diffusing surface with a Gaussian distribution of surface height fluctuations – it can be shown that the standard deviation of the intensity variations in the speckle pattern is equal to the mean intensity. In practice, speckle patterns often have a standard deviation that is less than the mean intensity, and this is observed as a reduction in the contrast of the speckle pattern. In fact, it is usual to define the speckle contrast as the ratio of the standard deviation to the mean intensity:

$$\text{speckle contrast} = \frac{\sigma}{\langle I \rangle} \leq 1 \tag{1}$$

Although a detailed account of laser speckle statistics is outside the scope of this paper, it is worth mentioning at this point that the scale of the speckle pattern – the size of the individual speckles – has in general nothing to do with the structure of the surface producing it. It is determined entirely by the aperture of the optical system used to observe the speckle pattern. If the speckle pattern is being observed directly by the human eye, it is the pupil of the eye that determines the speckle size. More importantly, if a camera is used, it is the setting of the aperture stop that determines the speckle size. This can have a serious effect if the aperture is used to control the exposure of the photograph.

2.2. Time-varying speckle

When an object moves, the speckle pattern it produces changes. For small movements of a solid object, the speckles move with the object, *i.e.*, they remain correlated. This has been exploited in a technique known as "double-exposure speckle photography" [5]. If a double-exposure photograph is taken of the speckle pattern before and after the movement has occurred, each speckle will be doubled. If the resulting photograph is placed in an unexpanded laser beam, each pair of speckles acts like a pair of pinholes and produces Young's fringes in the far field. The spacing of these fringes can be used to determine the local movement of the object. By scanning the laser beam across the speckle pattern, a map of local movements can be built up.

For larger motions, the speckles "decorrelate" and the speckle pattern changes completely. Decorrelation also occurs when the light is scattered from a large number of individual moving scatterers, such as particles in a fluid. An individual speckle appears to "twinkle" like a star. This phenomenon has come to be known as "time-varying speckle". It is frequently observed when living organisms are observed under laser light illumination and has been proposed as a method of monitoring activity inside botanical subjects [6–9]. One manifestation of the fluctuations is a reduction in the speckle contrast when a photograph is taken with an exposure time that is of the order of the fluctuation period [6]. This effect is used in the technique of laser

speckle imaging, to be discussed below. One of the most important potential applications of speckle fluctuations, first recognized by Stern in 1975, arises when they are caused by the flow of blood [10].

It is reasonable to assume that the frequency spectrum of the fluctuations should be dependent on the velocity of the motion. It should therefore be possible to obtain information about the motion of the scatterers from a study of the temporal statistics of the speckle fluctuations. This is the basis of the study of time-varying speckle, many of whose applications have been in the biomedical field.

Most workers in this field have used the temporal statistics of the fluctuations to analyse the motion of the scatterers. Some of this work, as applied to the measurement of blood flow, has been reviewed by the present author [11]. However, it is also possible to use the spatial statistics, and especially the contrast, of time-integrated speckle patterns. This is the main topic of the present paper. First, though, we should look at the relationship between time-varying speckle and Doppler methods.

2.3. Relationship with laser Doppler

Movement, especially of individual scatterers, causes laser speckle patterns to fluctuate in time. However, laser Doppler techniques also analyse the frequency spectrum of light intensity fluctuations observed when laser light is scattered from moving particles. Are these the same fluctuations? The physics at first sight looks different in the two cases. In the Doppler method, the frequency of light scattered from moving particles is assumed to be frequency-shifted and this "beats" with non-shifted light from stationary parts of the object (or from a reference beam) to give a Doppler signal whose frequency is equal to the difference between the two frequencies. On the other hand, no frequency shift is invoked to explain time-varying speckle – the speckle pattern is produced by interference of light of the same frequency that has traversed different optical path lengths to reach the detector, and the fluctuations are caused by these path lengths changing as a result of the motion of the scatterers. It can be shown, however, that the two techniques yield the same mathematical formula connecting the frequency of the fluctuations and the velocity of the scatterers [11, 12] – they are simply two different ways of looking at the same phenomenon.

Many workers have used the Doppler approach to measure blood flow, starting with RIVA *et al*. [13] in 1972, and the technique is now almost a routine tool in medicine. Some of the work on laser Doppler techniques for measuring blood flow is also reviewed in the work already cited [11].

Whether regarded as Doppler or as time-varying speckle, it should be pointed out that measurements of the temporal statistics of the intensity fluctuations can in principle be carried out only at a single point (a single speckle). If a map of the velocity is required, some method of scanning is necessary. This has been done for both speckle [14–17] and for Doppler [18–21]. In the case of Doppler, commercial instruments are already on the market and some critical assessments of them have been published [22, 23]. The main problem with these scanning instruments is the time taken for a scan to be carried out and the data processed – typically several minutes. It was

for this reason that the technique of laser speckle imaging, which produces a map of velocity in a single shot, was developed.

3. History of laser speckle contrast imaging

3.1. Single-exposure speckle photography

In 1980, the optics group at the University of Essen, Germany, under the leadership of A.F. Fercher, set about the task of finding non-invasive methods of diagnosing problems of the eye. One of the projects targeted the measurement of retinal blood flow, a diagnostic tool in various ophthalmic problems. The classic technique at the time was to inject a fluorescent dye into the blood stream of the patient and wait until it showed up in the retinal blood vessels. Problems such as blocked blood vessels could then be identified. It was felt that a non-invasive optical technique would have advantages both for the patient (no injection of potentially damaging chemicals) and for the ophthalmologist (no need to time his examination for the limited window offered by the dye technique).

The first proposal was to use double-exposure speckle photography [5]. However, it occurred to me that we might be able to adopt a simpler technique by exploiting the effect observed several years earlier, that the contrast of speckle patterns is reduced by speckle fluctuations [6]. If speckle contrast could be used to code velocity, then a single-exposure method might work. Initial results were encouraging, and single-exposure speckle photography was born [24].

The basic argument is that in a finite-time laser photograph, the speckle pattern in an area where flow is occurring will be blurred to an extent that will depend on the velocity of flow and on the exposure time of the photograph. The speckle pattern in an area of no flow, on the other hand, will remain of high contrast. Thus velocity distributions should be mapped as variations in speckle contrast. A preliminary mathematical analysis, making several rather bold assumptions about the statistics involved, produced some promising results [24]. Assuming a Lorentzian velocity distribution, for example, led to the following equation for the speckle contrast ($\sigma/\langle I \rangle$) as a function of the ratio of the correlation time to the exposure time (τ_c/T):

$$\frac{\sigma}{\langle I \rangle} = \left\{ \frac{\tau_c}{2T} \left[1 - \exp\left(-\frac{2T}{\tau_c} \right) \right] \right\}^{\frac{1}{2}} \tag{2}$$

The correlation time τ_c is inversely proportional to the local velocity of the scatterers. The above function is plotted as the curve labelled "Lorentzian" in Fig. 2. It can be seen that the speckle contrast rises from near zero to near its maximum value of 1.0 over about two orders of magnitude of τ_c (and hence of velocity). (For a single exposure, of course, T is a constant.) For flow velocities corresponding to values of τ_c less than about $0.04T$ the speckle contrast is very low, *i.e.*, the speckles

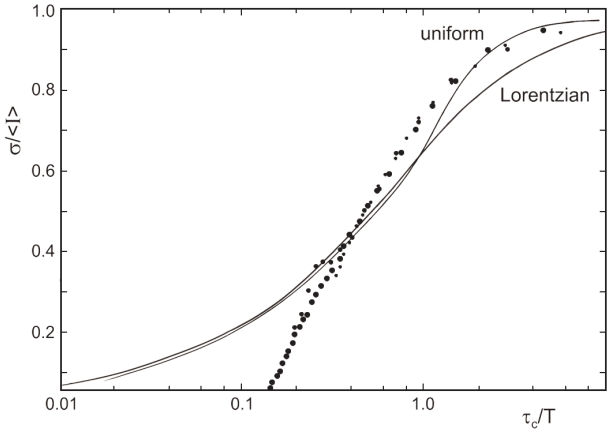

Fig. 2. Plots of speckle contrast against the ratio of correlation time to exposure time for two velocity distributions; the dots are experimental points using a rotating disc as the object.

are completely blurred out by the motion. For velocities corresponding to values of τ_c greater than about $4T$ the speckle pattern remains almost fully developed, with maximum contrast. Between these limits, the photographs will map the velocity distribution as a variation in speckle contrast.

If a different velocity distribution is assumed, for example a Gaussian or a uniform distribution, the curve is slightly different, but still shows this characteristic *S*-shape. The dynamic range – the range of velocities that can be covered – remains similar. The curve for a uniform velocity distribution is also plotted in Fig. 2. Some (previously unpublished) experimental results, using a rotating disc as the object, are also plotted in Fig. 2. These show that a more realistic dynamic range for the technique might be one order of magnitude – the speckle contrast follows the upper part of the curve, but tends to continue to fall to zero rather than follow the low-contrast tail of the curve.

It should be pointed out that the curves and plots of Fig. 2 have been normalized in order to compare them – they do not naturally fall in the same range of τ_c/T. This is not surprising, considering the sweeping assumptions made in the derivation of Eq. (2). From the start, we have stressed that Eq. (2) is only a model to show the mechanism [24], in practice, the technique must be calibrated against known flow velocities.

In practice, contrast variations are difficult for the human eye to detect and some method of enhancing the contrast maps is necessary. We found that a simple optical filtering process, using a high-pass spatial filter, worked quite well [25]. The original photograph of the flow field, as a transparency or negative, is placed in the arrangement of Fig. 3. The argument is that where the speckle contrast is high, much of the light will be diffracted (the dotted rays in Fig. 3) and will be collimated by the middle lens. Where the speckle contrast is low, most of the light will pass directly through the photograph (the continuous rays) and will be focused by the middle lens. A stop

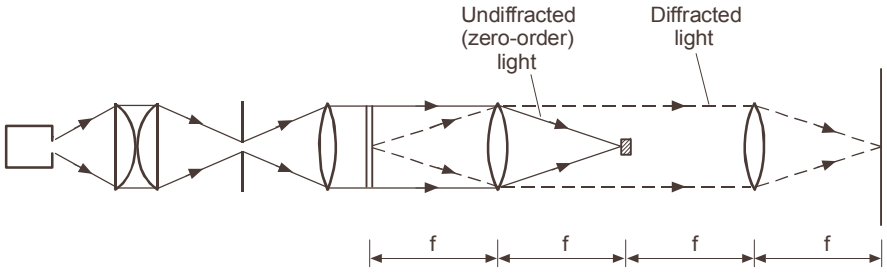

Fig. 3. Spatial filtering arrangement for converting speckle contrast variations to intensity variations.

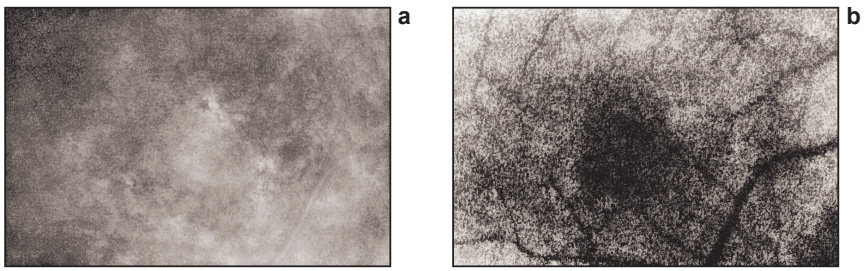

Fig. 4. Single-exposure speckle photography – raw image of part of a retina (**a**), and its processed version (**b**).

in the focal plane of this lens blocks the undiffracted light and therefore acts as a high-pass filter – only the diffracted light reaches the final image plane. The higher the speckle contrast, the more light from that part of the original image reaches the final image: contrast variations are converted to intensity variations.

The technique was applied to the original aim of monitoring blood flow in the retina. An early example, taken from our 1982 paper [26], is shown in Fig. 4. The quality is not excellent, but it demonstrates the effect of the spatial filtering in allowing the retinal blood vessels to be seen.

Although the feasibility of single-exposure speckle photography had been demonstrated, the fact that it was a two-step process (the photograph had first to be processed, then the resulting transparency placed in the spatial filtering setup and a second photograph taken) reduced its attractiveness to clinicians and researchers. This, combined with the break-up of the Essen group in the mid-eighties, led to the method being shelved.

3.2. Laser speckle contrast imaging – a digital version of single-exposure speckle photography

By 1990, digital techniques were sufficiently advanced to justify another look at single-exposure speckle photography. If the photographic stage could be eliminated and the contrast measured directly and converted to a false-colour image, the main

disadvantage of the technique could be avoided. At Kingston University we started a project to investigate the possibility, and the technique showed some promise. As the procedure no longer involved photography, a new name was needed, and we called the technique LASCA (LAser Speckle Contrast Analysis) [27]. (Some researchers have continued to use this name [28–30], but a more general term is "laser speckle contrast imaging", or even "laser speckle imaging".)

The experimental setup for laser speckle contrast imaging is very simple. Diverging laser light illuminates the object under investigation, which is imaged by a CCD camera (or equivalent). The image is captured by a frame grabber (or equivalent) and the data passed to a personal computer for processing by custom software. The operator usually has several options at his disposal. In the original LASCA technique [31], this included the exposure time, the number of pixels over which the local contrast was computed, the scaling of the contrast map and the choice of colours for coding the contrast. The choice of the number of pixels over which to compute the speckle contrast is important: too few pixels and the statistics will be compromised, too many and spatial resolution is sacrificed. In practice, it is found that a square of 7×7 or 5×5 pixels is usually a satisfactory compromise. (A square with sides of an odd number of pixels was chosen so that the computed contrast could be assigned to the central pixel.) The speckle contrast is quantified by the usual parameter of the ratio of the standard deviation to the mean ($\sigma/\langle I\rangle$) of the intensities recorded for each pixel in the square (see Eq. (1)). The pixel square is then moved along by one pixel and the calculation repeated: this overlapping of the pixel squares results in a much smoother image than would be obtained by using contiguous squares, and at little cost in terms of additional processing time. It must be remembered, though, that this overlapping of the squares does not lead to an increase in resolution, which is determined by the size of square used: there is a trade-off between spatial resolution and reliable statistics.

If the object under investigation contains moving scatterers, such as blood cells, each speckle will be fluctuating in intensity. A time-integrated image therefore shows a reduction in speckle contrast because of the averaging of the intensity of each speckle over the integration time. In practice, the exposure time can be very short, typically 0.02 seconds, and the processing time is less than one second for the whole frame [32], making it effectively a real-time technique.

One complicating factor for the technique is that of speckle size. As mentioned in Section 2.1., this is determined entirely by the aperture of the imaging system used (in this case the camera). The pixels of the detector are effectively sampling the speckle pattern. If the speckles are smaller than the pixels, some averaging will occur and the technique rapidly becomes less effective. If the speckles are much larger than the pixels, only a few speckles will be sampled by the square of pixels used, and the statistics will become unreliable. The best compromise is to arrange for the speckle size to be equal to the pixel size [33]. This is achieved by choosing an appropriate setting for the aperture of the camera lens. However, this removes the possibility of using the aperture to control the amount of light reaching the detector, the usual

function of a variable lens aperture. Further, the shutter speed cannot be used to do this, as it is determined by the need to match the velocities being measured. Hence there is a need to find another method of controlling the amount of light reaching the detector, such as a neutral-density (or possibly polarizing) filter.

Some examples of the original LASCA technique are given in Figs. 5 to 7, taken from previous publications [11, 27]. (To avoid potential problems connected with

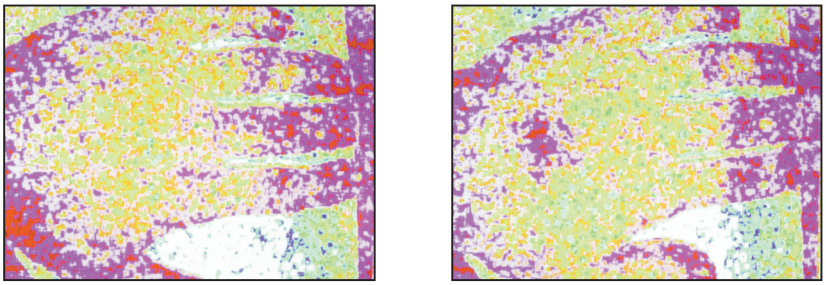

Fig. 5. LASCA images of the back of a hand, showing perfusion before and after gently rubbing a small area.

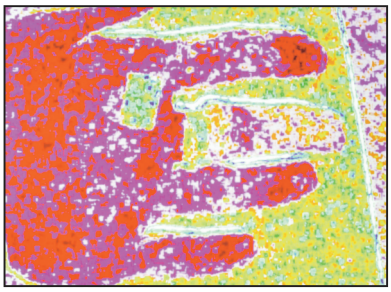

Fig. 6. LASCA image of a hand, showing the reduction in perfusion caused by a rubber band around the base of a finger. (The rectangle is a control patch to ensure there was no gross movement of the hand.)

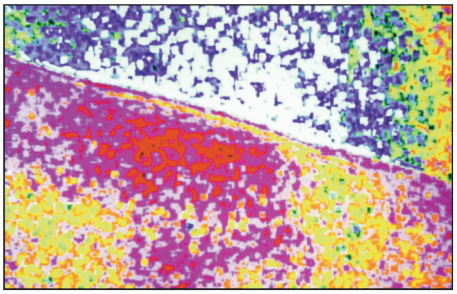

Fig. 7. LASCA image of part of a forearm, showing increased perfusion around a superficial hot-water burn.

safety and Ethics Committees, we switched our target area from retinal blood flow to subcutaneous capillary blood flow.)

3.3. Some recent work on laser speckle contrast imaging

The Kingston group was disbanded in 1999 and work stopped on the project. I am pleased to report, however, that the technique has been taken forward by others. At least thirty groups in at least seventeen countries are known to be either using the technique or developing it further.

Developments include optimization of the exposure time [34], noise reduction [35], and some significant contributions to the theory [36, 37]. Some workers [38] have identified "errors" in the original theoretical formulations (such as Eq. (2)). We have always stressed, however, that our theoretical model was very tentative and based on many assumptions [24] – it was proposed merely as a starting point for a more rigorous treatment. Some recent work (as yet unpublished) shows that our model still forms a reliable basis on which to quantify velocities from the contrast measurements.

Applications have been mainly in the medical field, as expected, with a lot of activity in using the technique to monitor cerebral blood flow during animal experiments [29, 30, 33, 39, 40] and investigations into migraine [41]. Other medical applications have included microcirculation investigations [42, 43], the characterization of atherosclerotic plaques [44], and a return to ophthalmological problems [45, 46]. Non-medical applications have included measuring the velocity of tracked vehicles on snow and ice [47] and watching paint dry [48]. (It is stressed that these examples are just a selection from the large amount of work that is going on – the list is not meant to be exhaustive.)

The recent work on laser speckle contrast imaging has, of course, been accompanied by improvements in the images produced. Three examples are reproduced here. Figure 8 is from David Boas' group at Harvard Medical School,

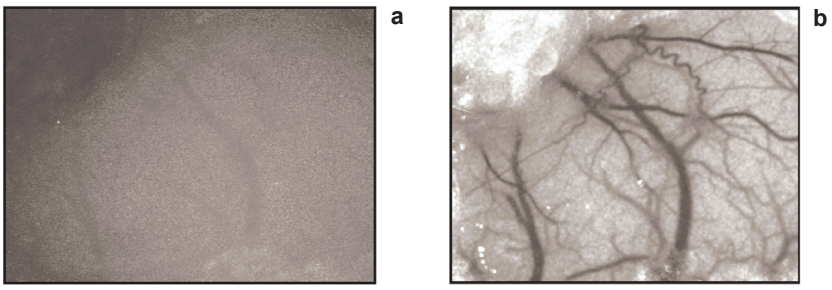

Fig. 8. Raw image of part of a rat cortex (**a**), and its processed version (**b**) (source: D. Boas, Harvard Medical School).

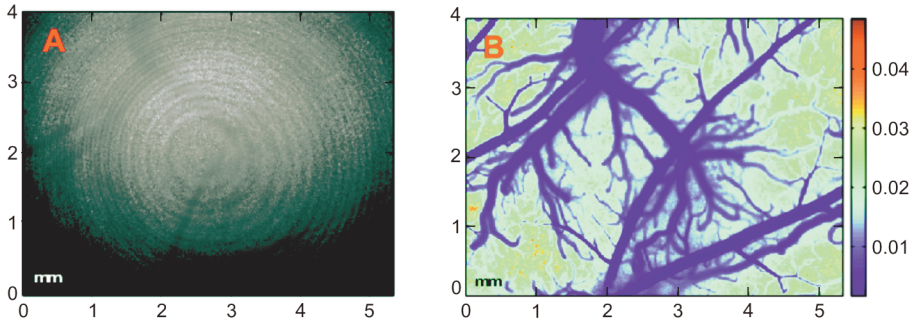

Fig. 9. Speckle image of the barrel cortex of a rat (**a**), and its processed version (**b**) (source: F. Scheffold, A. Völker and P. Zakharov, University of Fribourg, and B. Weber, University of Zurich).

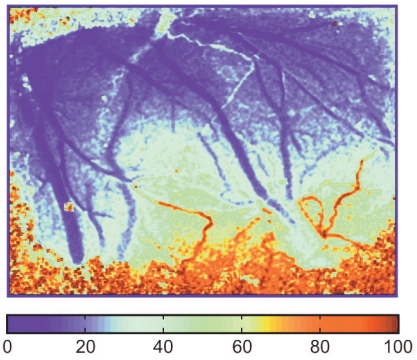

Fig. 10. Blood flow changes during stroke: relative cerebral blood flow ten minutes after occlusion of the middle cerebral artery in a rat, demonstrating the spatial gradient in the blood flow deficit due to the ischemia (source: A.K. Dunn, University of Texas).

Figure 9 is from Frank Scheffold, Andreas Völker and Pavel Zakharov of the University of Fribourg and Bruno Weber of the University of Zurich, and Figure 10 is from Andrew Dunn at the University of Texas. In all three cases the improvement in the quality of the images is clear.

A major development has taken place recently (late 2006) with the announcement of a real-time video capability by Moor Instruments of Axminster, UK. For the first time, this allows the researcher or surgeon to follow changes of blood flow in real time.

4. The future of laser speckle contrast imaging

It is clear that there is a lot of activity around the world involving laser speckle contrast imaging. After a history of twenty-five years, the technique is finally being recognized as a valuable tool, especially for monitoring blood flow. Its strengths

are its simplicity and its cheapness; its main weaknesses are the lack of robustness in the models used to interpret the images and its relatively low spatial resolution. Its main competition comes from scanning laser Doppler techniques, but at present these cannot compete on speed – laser speckle imaging is effectively a real-time technique (even a real-time video technique with recent developments), whereas a Doppler scan can take several minutes. But the future probably lies with the Doppler approach. Several groups are known to be working on the parallel processing of the Doppler signals from each pixel, using such techniques as on-chip processing. Once these techniques are perfected, laser Doppler may also be able to produce full-field images in virtually real time, and Doppler should then win on account of its inherently higher spatial resolution. However, such an approach is likely to be very expensive to implement, and laser speckle contrast imaging may still have a role to play, by competing on cost.

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