Laser Doppler measurement of relative blood velocity in the human optic nerve head

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The Doppler shift frequency spectrum (DSFS) of laser light scattered from red blood cells (RBCs) moving in the microcirculation of the optic nerve head has been recorded in normal volunteers by means of a fundus camera laser Doppler velocimeter. The width of the DSFS, which varies in proportion to the speed of the RBCs, has been characterized by a parameter \( \alpha \). With the use of a model for the scattering of light by tissue and RBCs and for the RBC velocity distribution, values of \( \alpha \) recorded at normal intraocular pressure (IOP) suggest that the RBCs that contribute to the Doppler signal are flowing in capillaries. The parameter \( \alpha \) was found to vary markedly with the IOP and with the phase of the ocular pressure pulse at elevated IOP. The return of the speed of RBCs toward normal, which is observed after a step increase of IOP above normal and after a step decrease below normal, has been attributed to an autoregulatory response of the optic nerve circulation. (INVEST OPHTHALMOL VIS SCI 22:241-248, 1982.)

**Key words:** laser Doppler velocimetry, red blood cell velocity, optic nerve, intraocular pressure, autoregulation

To study normal and pathologic hemodynamic conditions of the human optic nerve head, a technique for measuring tissue blood flow in that region of the eye is required. Various methods have been devised.\(^1\)\(^2\) Based on the dye dilution technique in which the passage of sodium fluorescein through the vasculature of the nerve head is recorded. Although they may reveal gross hemodynamic disturbances, their application is severely limited because the sites of dye inflow and outflow in the optic nerve cannot be determined.

An alternative approach to study hemodynamics in the optic nerve head tissue is the noninvasive technique of laser Doppler velocimetry (LDV). The technique was first applied to the measurement of tissue blood flow in the skin by Stern et al.\(^3\) As we describe and illustrate in this article, the LDV technique allows quantitative determination of changes in the speed of red blood cells (RBCs) in discrete regions of the nerve head microcirculation.

LDV is based on the Doppler effect: laser light scattered by a moving particle is shifted...
Fig. 1. Fundus camera laser Doppler velocimeter. The beam from a helium-neon laser is delivered to the eye through the optics used for fundus illumination. The beam is adjusted at the fundus by means of a rhomboid prism (RhP) and a rotary prism (RP). BS-1 and BS-2, Beam splitters; DF, density filter for attenuating the laser beam power; GIF, interference filter that allows red-free illumination of the fundus. The light scattered from the optic nerve tissue RBCs passes through the aperture filter wheel (FW), is focused on the aperture of an optical fiber in the image plane of the fundus, and is transmitted to a photoreceptor.

in frequency by an amount \( \Delta f = \frac{2\pi}{\lambda} (\vec{K}_s - \vec{K}_i) \cdot \vec{V} \). \( \vec{K}_i \) and \( \vec{K}_s \) are the wave vectors of the incident and scattered light, respectively. \( \vec{V} \) is the velocity of the particle, and \( \lambda \) is the wavelength of the incident light; \( \Delta f \) is detected by optical mixing spectroscopy. When laser light impinges on many RBCs moving with different velocities, the scattered light contains a spectrum of \( \Delta f \), called a Doppler shift frequency spectrum (DSFS), which corresponds to the distribution of velocities. RBCs moving in microvessels embedded in a tissue that strongly scatters light receive the laser light from innumerable directions of incident light. The multiplicity of \( \vec{K}_i \)-vectors produces a broadening of the DSFS that would be obtained without tissue scattering. Further broadening results from the multiplicity of \( \vec{K}_s \)-vectors that reach the detector from each RBC because of scattering by the tissue or other RBCs. Exact determination of the velocity distribution of RBCs from the broadened DSFS is difficult because it requires knowledge of the scattering properties of the tissue and RBCs and of the prob-
abilities that light is scattered by 1, 2 . . . n different RBCs before reaching the detector. However, if these properties and probabilities remain constant in spite of flow changes, the DSFS scales in width in proportion to the velocity distribution of the RBCs.

Two theories have been generated to obtain a first order approximation of the DSFS based on single scattering (n = 1) from the RBCs. The theory of Stern and Lappe^5 assumes that (1) the direction of the scattering vector \( \mathbf{K} = \mathbf{K}_s - \mathbf{K}_r \) relative to the velocity vector \( \mathbf{V} \) associated with each RBC is randomly distributed, (2) the distribution of RBC velocities, \( P(V) \), is equal to a constant up to a value \( V_{\text{max}} \) and zero for \( V > V_{\text{max}} \), (3) scattering of light by RBCs is isotropic, and (4) detection of the DSFS is achieved by heterodyne mixing of light scattered from tissue (reference beam) with light scattered by RBCs. Under these conditions the low frequency portion of the DSFS is a logarithmic function of frequency, \( \log \left( \frac{\alpha}{\Delta f} \right) \), where the parameter \( \alpha = \frac{2}{\lambda} V_{\text{max}} \).

Bonner et al.\(^6\) modified this model by expressing the RBC light scattering in terms of the Rayleigh-Gans approximation derived for optically homogenous spheres (radius, \( a \), equals \( 3 \mu m \)) in which most of the light is scattered into a small angle region along the forward direction. In addition, they assume that the velocity distribution of the RBCs is gaussian. In this case the low frequency part of the DSFS recorded under heterodyne conditions decays exponentially as \( e^{-\beta \Delta f} \), where \( \beta = 6.9 \frac{a}{<V^2>} \), \( <V^2> \) is the root mean square (standard deviation) of the RBC velocity distribution.

The case where light is multiply scattered by RBCs has been analyzed by Stern and Lappe.\(^5\) These authors conclude that the first order term (n = 1) will dominate the total spectrum at low frequencies, whereas multiple scattering will affect only the high-frequency portion of the DSFS.

**DSFS from the human optic nerve head.** DSFSs were recorded from discrete sites of the optic nerve head with a fundus camera laser Doppler velocimeter (Fig. 1).\(^7\) The beam from a helium-neon laser was focused onto areas (approximately 200 \( \mu m \) in diameter) where no discrete blood vessels were visible when the disc was observed in red-free light. Laser irradiance at the fundus was approximately 0.05 W/cm\(^2\), a value below the maximum permissible retinal irradiance for continuous exposure.\(^8\) The light scattered from the RBCs that emerged from the pupil was collected by an optical fiber with its aperture in the image plane of the fundus camera. The diameter of this aperture, which defined the sampling areas of the scattered light, was approximately 180 \( \mu m \). The dimension of the entrance pupil of the camera, determined by the size of the opening in filter wheel, was 1 mm. Light collected by the optical fiber was transmitted to a photomultiplier after passing through a Kodak Filter No. 29 that blocked the red-free light used to illuminate the fundus. The output signal from the detector, which could be heard through a loudspeaker, was recorded by an FM-tape recorder for subsequent analysis by a spectrum analyzer (Model 4520, two-channel digital signal analyzer; Unigon Industries, Inc.). Each DSFS was plotted on a strip-chart recorder. Fig. 2 displays a typical DSFS recorded from the temporal rim of the nerve head of a normal volunteer, at normal intraocular pressure (IOP). Most of the spectral power is concentrated below 300 Hz. The shape of DSFS recorded from five normal volunteers could be fitted by \( \log (\frac{\alpha}{\Delta f}) \) functions as well as by exponential functions at significant levels (p < 0.01) up to frequencies typically of 300 to 600 Hz. The coefficient of determination for the logarithmic fit was generally better than that for the exponential fit, and therefore the changes in RBC speed were characterized in this study by changes in the parameter \( \alpha \), the frequency at which the logarithmic fit intersected the baseline (shot-noise level) of the DSFS.

To determine the logarithmic fit, the recorded curves were smoothed by hand and
Fig. 2. Typical DSFS from the temporal rim of the nerve head of a normal volunteer and its logarithmic fit. The baseline is determined by the shot-noise level of the detector. The value of \( a \) is the frequency at which the logarithmic fit (solid line) intersects the baseline (dashed line). The \( a \) value varies proportionally to the speed of the red blood cells. Inset, DSFS replotted on a semi-logarithmic scale to evaluate the frequency at which the data points depart from a straight line (here approximately 200 Hz).

Values of \( a \) obtained from normal volunteers lead to estimates of \( V_{\text{max}} \) of the order of 0.12 to 0.2 mm/sec. Corresponding values of \( \langle V^2 \rangle \) determined by the model of Bonner et al. were larger by an order of magnitude.

Although the RBC speeds calculated from both models differ significantly, their magnitude still suggests that the scattered light is detected predominantly from RBCs flowing in the microvessels of the optic nerve tissue. This observation is supported by methacrylic ester casts of the optic nerve parenchyma of monkeys, which demonstrate large areas with homogenous distribution of capillaries between major nerve-head branchings of retinal vessels.

The DSFS in Fig. 2 was recorded in 30 sec. For five successive 30 sec recordings from the same site of the optic nerve head in each of three subjects, the coefficient of variation for \( a \) was less than 10% and less than 15% for five successive 11 sec recordings. Changing the angle of incidence of the incident laser beam did not significantly affect \( a \) as expected, since light scattered from the optic nerve tissue is dominated...
by multiple interactions with static tissue elements.

**Application of the technique.** Recording DSFS within seconds allows changes in RBC speed induced by various physiologic stresses to be quasicontinuously monitored. Fig. 3 demonstrates the effect on DSFS of sudden increases in IOP to systolic ophthalmic artery pressure. The IOP was elevated stepwise by means of a Langham suction cup (Digilab) applied to the temporal sclera and was kept constant at each level during the recording time. It was measured with a Model 30R Digilab Pneumatonometer. Recording time of each DSFS was approximately 20 sec, except for the one recorded at systolic ophthalmic artery pressure, which was 6 sec. As the IOP was raised, the spectral power shifted markedly toward lower frequencies (decrease in $\alpha$). The spectral power of the DSFS recorded at systolic ophthalmic artery pressure is most probably due to the effect of eye motion. A low-frequency component was also observed by Stern et al.\(^3\) and Stern\(^10\) in the skin of the fingertip at pressures above systolic levels. It was attributed to artifacts resulting from tissue motion.

In the three normal subjects tested, modulation in pitch, which was synchronous with the heart cycle, could be clearly perceived when the IOP was raised to a few mm Hg below diastolic ophthalmic artery pressure. This modulation was attributed to the speed of the RBCs varying with the pressure pulse. To record the speed variations (Fig. 4), the pulse pressure signal from the finger tip was used to trigger the spectrum analyzer for 0.1 sec at various phases of the pressure pulse.\(^{11}\) For each phase the spectral power was averaged over 22 cardiac cycles. As expected for RBCs flowing in capillaries, the change in speed ($\alpha$ as in Fig. 4) with the pulse pressure is considerably dampened compared with the change in speed of RBCs moving in retinal arteries at normal and elevated IOP.\(^{11,12}\)

If after a step increase from normal the IOP is kept approximately constant for a few minutes and then rapidly decreased to below normal, $\alpha$ varies in time as shown in Fig. 5.

Data were obtained from successive DSFSs, each one recorded in 11 sec. The same experiment was repeated three times on separate occasions in the same subject. Blood pressure and resting IOP were not significantly different in each experiment.

The IOP was raised with a Langham pressure-cup system set at a suction pressure of 120 mm Hg. Because the IOP could not be measured during the LDV recording, the time course of the IOP displayed in Fig. 5, $B$, was determined at a different occasion under the same experimental conditions.

With IOP elevation the speed of the RBCs markedly decreased. It then increased toward normal and reached a constant level within approximately 2 to 3 min. Release of the suction cup caused a rapid drop in IOP and resulted in a marked increase in the speed of the RBCs above the baseline.
Within minutes, however, the speed returned to the baseline level.

During the period between 15 sec and 3 min after the step elevation of IOP, the speed of the RBCs increases by approximately 60%, whereas the IOP decreases from 38 to 35 mm Hg. The percent increase in perfusion pressure (mean ophthalmic artery pressure \( \bar{P} \) minus IOP) corresponding to this 3 mm Hg decrease in IOP is equal to 38 mm Hg. \( \bar{P} \) is generally calculated as
\[
\frac{100 \Delta P}{P - \text{IOP}} = 3 \left( \frac{100}{57.8 - 38} \right) = 15%.
\]

A 15% increase in perfusion pressure should produce only an equal increase in RBC speed. The most plausible explanation for the additional 45% speed increase appears to be an autoregulatory response of the optic nerve circulation that attempts to normalize blood flow. This interpretation is supported by the similarity between the time course of the speed increase of RBCs in the optic nerve and that of blood-flow autoregulation in the retinal macular capillaries.\(^{13}\)

Similarly, the 25% decrease in the speed of

Fig. 4. A, Variation of \( \alpha \) during the heart cycle recorded at an IOP a few mm Hg below diastolic ophthalmic artery pressure. The ±1 S.D., shown here for two data points, was determined on the basis of 10 DSFSs recorded at normal IOP. The spectrum analyzer was triggered for 0.1 sec during each heart cycle, and each DSFS was averaged over 22 of these cycles. B, Time course of the pulse pressure signal from the fingertip of the subject. This signal was used to trigger the spectrum analyzer for 0.1 sec at 10 different phases of the heart cycle.
Fig. 5. A, Relative variation of $\alpha$, as a function of time, when the IOP is varied as shown in B. The error bars represent ±1 S.D., calculated from data obtained from identical experiments conducted in the same normal volunteer on three separate occasions. The ±1 S.D. for the starting value of $\alpha$ (baseline) is based on three successive recordings obtained before elevating the IOP.

The RBCs occurring after release of the cup (between 7 and 9 min, Fig. 5) strongly suggests the presence of an autoregulatory response because the magnitude of this decrease cannot be caused by the 4% decrease in perfusion pressure occurring during this 2 min interval. To our knowledge the return of RBC speed to baseline after removal of the suction cup is the first demonstration in man of an autoregulatory response to a decrease in IOP below resting value.

The LDV technique appears to provide a new means for studying noninvasively the flow of blood in the normal and pathologic optic nerve. Monitoring short-term changes in blood velocity, as demonstrated in this paper, illustrates the potential application of this noninvasive technique. Direct microcomputer processing of the data is now under development and will soon allow on-line RBC speed measurement in the optic nerve head.

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REFERENCES


