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A NEW LASER DOPPLER SYSTEM FOR EXAMINING OPTIC NERVE HEAD CIRCULATION

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ABSTRACT

A new laser Doppler system for the noninvasive examination of the human optic nerve head microcirculation is described. The electro-optical component of the system consists of a retinal camera modified with laser input optics and a fiber optic light detection system for collection of the Doppler-shifted scattered light. Data acquisition is carried out in real time under computer control. Automated analysis of the data provides a quantitative measure of the speed of blood cells flowing through the capillaries of the optic nerve head. Unlike previous systems, this system provides results within a few minutes following data acquisition. It is thus appropriate for use in a clinical setting. Analysis of multiple measurements on a patient shows a coefficient of variation of 8.9%. © *1998 Society of Photo-Optical Instrumentation Engineers.* [S1083-3668(98)00304-9]

Keywords laser Doppler technique; optic nerve head; microcirculation.

1 INTRODUCTION

The application of the laser Doppler technique to studies of the human optic nerve head microcirculation was initially described by Riva et al.[1] The work was motivated by the need to develop a noninvasive method to assess the status of the microcirculation and to monitor microcirculatory changes in response to pharmacologic treatment in patients with optic nerve-related diseases, the most prevalent of which is glaucoma.

The technique is based on the Doppler effect: laser light scattered by a moving particle is shifted in frequency by an amount

$$\Delta f = \frac{1}{2\pi}(\mathbf{K_s} - \mathbf{K_i})\cdot\mathbf{V}. \tag{1}$$

$\mathbf{K_i}$ and $\mathbf{K_s}$ are the wavevectors of the incident and scattered light, respectively, each with magnitude $2\pi n/\lambda$, where n is the refractive index of the medium and λ is the wavelength of the laser light *in vacuo*. $\mathbf{V}$ is the velocity vector of the particle.

When examining the optic nerve head microcirculation, an incident laser beam illuminates a small region of the optic nerve head in the back of the eye that is free of surface blood vessels. As the light penetrates the tissue, it is randomly scattered by both nonvascular tissue elements and blood cells circulating through the capillaries that are embedded in the tissue. Each blood cell receives light from a multiplicity of directions. The Doppler-shifted light scattered by each moving cell is also randomly scattered by the surrounding nonvascular tissue prior to detection. The detected scattered light contains a range, or spectrum $S(\Delta f)$, of Doppler-shift frequencies. $S(\Delta f)$ is broadened in direct proportion to the speed of the blood cells flowing through the capillaries. Because the volume fraction of blood in the tissue of the optic nerve head is small, approximately 2%,[2] most of the light collected from the point of illumination is scattered by nonvascular tissue. Thus, $S(\Delta f)$ is detected by heterodyne mixing of the Doppler-shifted light scattered by moving blood cells with the light scattered by tissue.

A theory predicting the shape of $S(\Delta f)$ under heterodyne detection conditions was developed by Stern and Lappe.[3] In their model, the low frequency portion of the spectrum varies as the negative logarithm of Δf:

$$S(\Delta f) = -K \log(\Delta f/\alpha), \tag{2}$$

where K is a measure of the amplitude of the spectrum and the frequency α is a quantitative measure of the broadening of the spectrum. The Doppler broadening parameter α is directly proportional to the speed of the blood cells flowing through the capillaries.

The applicability of the Stern and Lappe theory to the optic nerve head microcirculation was substantiated in an experimental study[4] in which laser Doppler findings were compared to results obtained using the microsphere impaction technique. As described in that study, the theory is valid when

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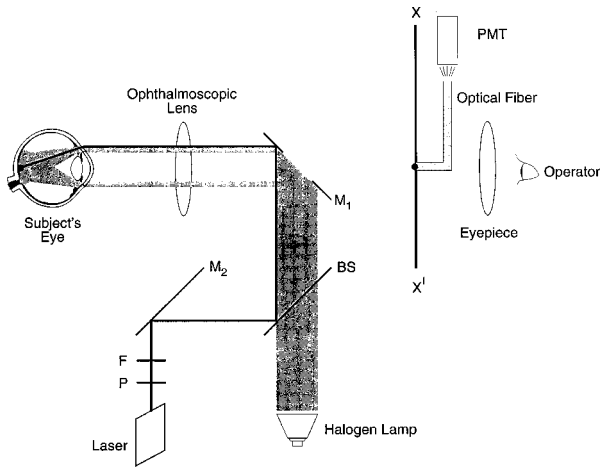

Fig. 1 Schematic diagram of the illumination and light detection system. Light from a halogen lamp passes through a laser line beam splitter (BS), and is reflected into the subject's eye by mirror *M*, which has an opening in its center. Light returning from the eye passes through the opening, and forms an image of the posterior pole at the plane (x,x'). The operator views the image through an eyepiece. The linearly polarized beam from an HeNe (633 nm) laser is attenuated by a rotatable polarizer *P* and a neutral density filter *F*. The beam is reflected by mirror M_2 and then by the beam splitter (BS) into the illumination pathway. Detection of the scattered laser light is via a 450-μm-diam optical fiber positioned in the image plane (x,x') of the posterior pole of the eye. The light collected by the fiber is transmitted to the cathode of a photomultiplier tube (PMT).

applied to terminal vessels up to 15 μm in diameter. The blood cell speed in such vessels is less than 1 mm/s. The Stern and Lappe theory has been successfully applied to characterize the speed of blood cells flowing in the capillaries of the optic nerve head in limited studies of normal aging,[5] of response to acute increases of intraocular pressure,[1] of neurogenic optic atrophy[6] and chronic ocular hypertension,[7] and of response to intraocular pressure-lowering pharmacological agents.[8,9] These studies were all conducted in a laboratory setting, however, and the data analysis procedures employed were laborious and time consuming. In this article, we describe a new laser Doppler system for examining the optic nerve head circulation that can be used effectively in a clinical setting.

2 ELECTRO-OPTICAL SYSTEM

A standard retinal camera (Topcon TRC-50X, Tokyo, Japan) was modified with laser input optics and a fiber optic light detection system for collection of the Doppler-shifted scattered light. Figure 1 is a simplified schematic diagram of the modified camera system. The posterior pole of the subject's eye is illuminated with light from a 100 W halogen lamp. The light is reflected into the eye off of mirror M_1 which has an opening in its center. Light returning from the eye passes through the opening, and forms an image of the posterior pole at the plane (x,x'). Three magnifications are available (1.9×, 2.6×, and 3.7×), corresponding to three subtended angles (50°, 35°, and 20°). The operator views the image through a 10× eyepiece.

Laser light is directed to the eye along the optical path of the camera illumination system. The linearly polarized beam from a 0.5 mW HeNe (633 nm) laser (Uniphase, Manteca, CA) is attenuated by a rotatable polarizer P and a neutral density filter F. The beam is reflected by mirror M_2 and then by a laser line beam splitter (BS) (Melles Griot, Irvine, CA) into the illumination path. The beam is substantially collimated as it emerges from the ophthalmoscopic lens, and is focused onto the optic nerve head by the cornea and lens of the subject's eye. The power of the beam entering the eye is 18 μW, a level that is safe for up to 10 min of exposure.[10]

Detection of the scattered laser light is achieved using a scanning microscope eyepiece (Gamma Scientific, San Diego, CA). The input aperture of the unit is the face of a 450-μm-diam optical fiber that is positioned in the image plane (x,x'). The light collected by the fiber is transmitted to the cathode of a photomultiplier tube (PMT) (Hamamatsu, Bridgewater, NJ). The entire detector assembly is rotatable, allowing r-θ positioning of the collection face at any point of the image. In practice, the operator centers the collection face of the fiber on the illuminated region of the optic nerve head by rotating the assembly and then using a micrometer adjustment for the radial position of the fiber. Depending on the camera magnification used, scattered light is collected from a circular region of the optic nerve head approximately 240, 170, or 120 μm in diameter.

3 REAL TIME DATA ACQUISITION

On-line data acquisition is carried out in real time under computer control. The computer system (P5-133, Gateway 2000, North Sioux City, SD) is equipped with an analog-to-digital converter (Data Translation, Marlboro, MA) set to acquire ten thousand samples per second of the photomultiplier output signal. The controlling software is written in DT virtual engineering environment (VEE) (Data Translation, Marlboro, MA).

Figure 2 is a flow chart of the data acquisition procedure. The operator initiates the process by activating a foot switch which transmits a start pulse to the computer. The computer emits an audible signal to confirm receipt of the start pulse. It then proceeds to digitize the incoming photomultiplier tube signal at a rate of 10 kHz gated for one-second intervals. Each one-second signal interval is displayed on the monitor screen and automatically evaluated to determine whether it is sufficiently above the noise level to represent scattered laser light, and sufficiently free of large amplitude fluctuations arising from eye movements. Only the intervals that pass the signal evaluation tests are

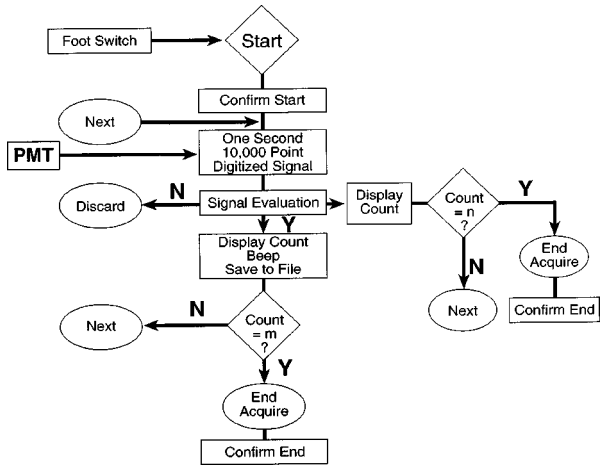

Fig. 2 Flow chart of the data acquisition procedure.

saved as data files. The computer emits an audible signal each time an interval is saved, and a running count of the number of saved intervals is displayed. A running count of the total number of intervals evaluated is also displayed. When the number of saved intervals reaches a preset value m the data acquisition program ends and the computer emits an audible signal to alert the operator that it has ended. The program also ends if the total number of intervals evaluated reaches a different preset value n before the number of saved intervals reaches m. The same audible signal alerts the operator. In initial tests of the program, the values $m = 12$ and $n = 60$ were used. The maximum exposure time at one optic nerve head site was thus 60 s.

4 DATA ANALYSIS

Analysis of the data is completed in approximately two minutes, and thus may be carried out with the study subject present. Figure 3 is a flow chart of the

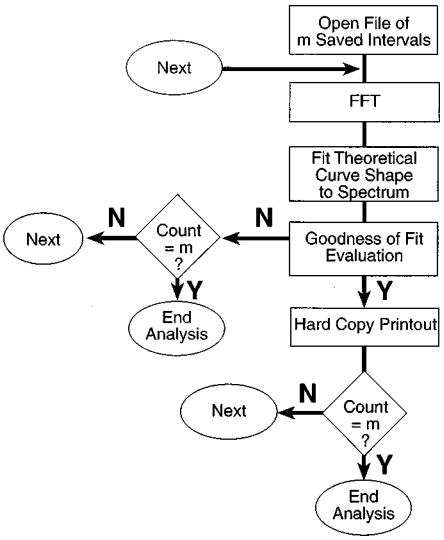

Fig. 3 Flow chart of the data analysis procedure.

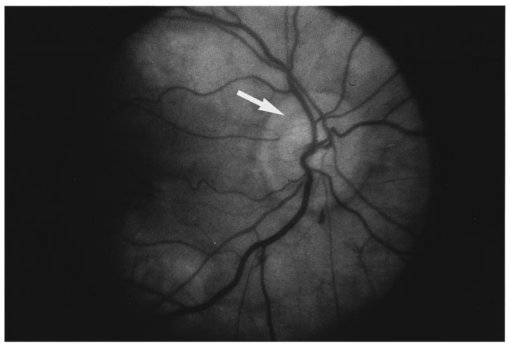

Fig. 4 Photograph showing the optic nerve head of the right eye of a patient under treatment for glaucoma. The laser Doppler measurement site is indicated.

data analysis procedure. First, the operator identifies and opens the appropriate data file consisting of the m saved signal intervals. The analysis program then automatically performs a fast Fourier transform (FFT) on the first saved interval and displays a five thousand point Doppler-shift spectrum $S(\Delta f)$ in the range 0–5 kHz. The shape of $S(\Delta f)$ is analyzed according to the Stern and Lappe theory.[3] The zero-amplitude value is taken as the baseline noise level, calculated as the average value of $S(\Delta f)$ in the range 4–5 kHz. A least squares regression analysis is then used to determine the optimal fit of the function $-K \log(\Delta f/\alpha)$ to the spectrum in the range 100–500 Hz. The lower end of the range was chosen to ensure that contributions to $S(\Delta f)$ from eye movements, known to occur at frequencies below approximately 50 Hz,[1] would be minimized. The upper end of the range was chosen to minimize the effects of multiple scattering of the laser light by the blood cells circulating through the optic nerve head capillaries on the shape of the spectrum. Significant contributions to $S(\Delta f)$ from multiple scattering occur at frequencies above approximately 800 Hz.[5] Both the spectrum and the superimposed extrapolated fit curve are then displayed. The value of R^2, the coefficient of determination, is calculated as a "goodness of fit" parameter. If R^2 exceeds a preset threshold value, the spectrum and the superimposed fit curve are automatically printed out. The next saved signal interval is then processed in the same manner. If the value of R^2 does not exceed the threshold, the spectrum and fit curve are discarded, and the next saved signal interval is processed. The program continues until all of the signal intervals have been transformed and evaluated.

5 SAMPLE RESULT

Figure 4 is a photograph showing the optic nerve head of the right eye of a 91-year-old female patient under treatment for glaucoma. The location of the measurement site on the nerve head surface is indicated. During the measurement, twelve one-second

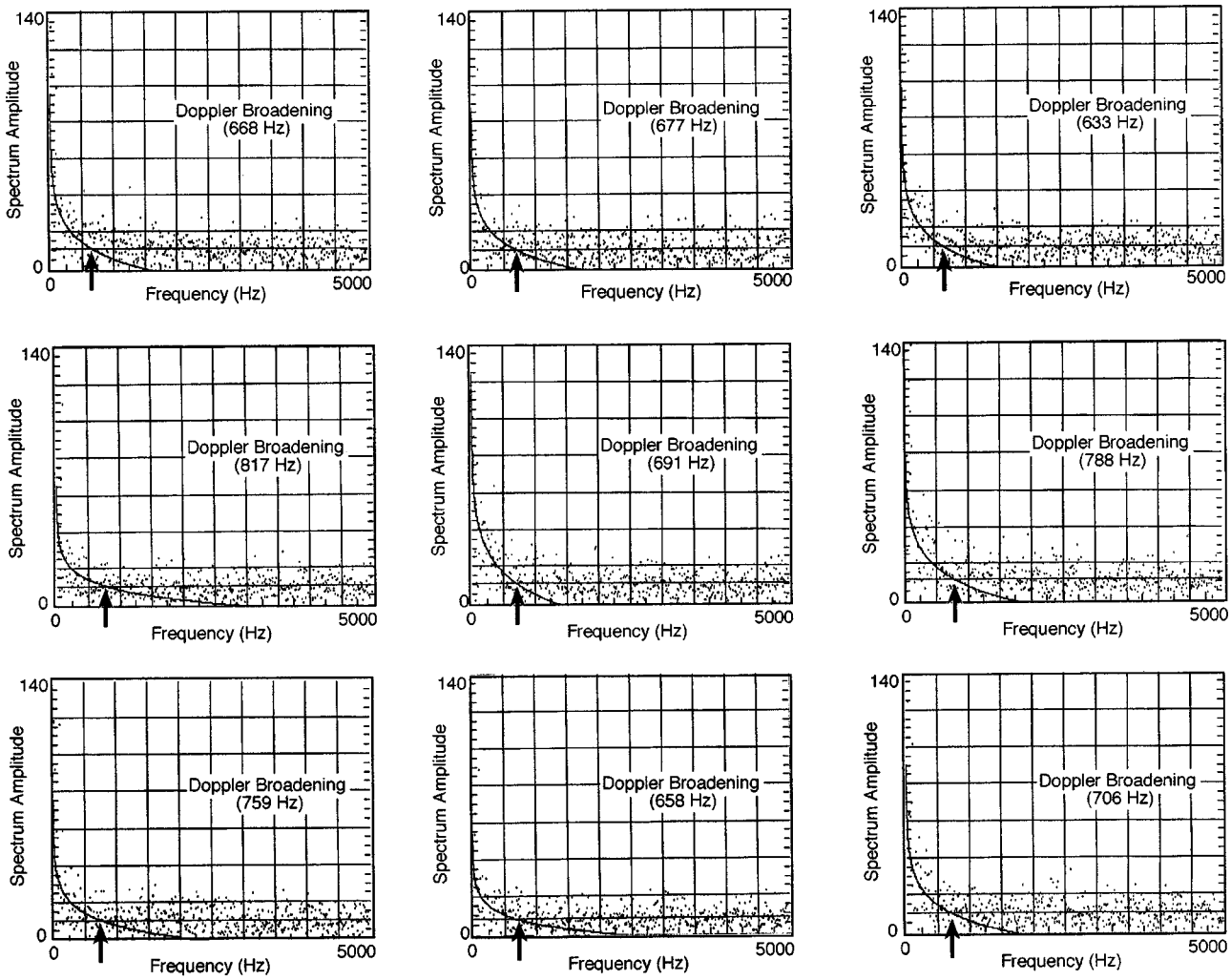

Fig. 5 Nine Doppler-shift frequency spectra of laser light scattered from blood cells flowing through the optic nerve head capillaries at the site indicated in Figure 4. The best fit logarithmic curve to each spectrum is shown, and the Doppler broadening parameter, the frequency at which the fit curve intersects the baseline (shown by the arrows) is displayed.

duration signal intervals were saved. The goodness of fit criterion was satisfied by nine Doppler-shift spectra. Figure 5 shows these nine spectra. For clarity, only every tenth point of each five thousand point Doppler-shift spectrum is plotted. The frequency range is 0–5000 Hz. The best fit logarithmic function [(Eq. 2)] is shown, and the value of the Doppler broadening parameter, α, is displayed. Graphically, α is the frequency at which the fit curve intersects the baseline. The mean and standard deviation (SD) of the Doppler broadening for the nine spectra is 711 ± 63 Hz. The coefficient of variation [(SD/mean)$\times$100] is 8.9%. This value is similar to the average coefficient of variation of 8% previously reported[5] in a study using a laboratory-based instrument that required laborious and time-consuming data analysis procedures to yield results.

6 CONCLUSION

We have described a new laser Doppler system for examining the optic nerve head circulation that can be used in a clinical setting. It is anticipated that the system will be used to assess the status of the circulation in patients with optic nerve-related diseases and to monitor circulatory changes in such patients during treatment.

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