

In Vivo Imaging of Human Retinal Flow Dynamics by Color Doppler Optical Coherence Tomography

Siavash Yazdanfar, PhD; Andrew M. Rollins, PhD; Joseph A. Izatt, PhD

Background: Color Doppler optical coherence tomography (CDOCT) combines laser Doppler velocimetry and optical coherence tomography for simultaneous micron-scale resolution cross-sectional imaging of tissue microstructure and blood flow. Recently, CDOCT was adapted to a slitlamp biomicroscope for imaging structure and blood flow in the human retina.

Objective: To demonstrate feasibility of CDOCT for imaging retinal hemodynamics.

Design: Enabling CDOCT to measure retinal blood flow pulsatility in humans.

Setting: Laboratory.

Main Outcome Measures: Time-resolved flow profiles and images of retinal blood flow dynamics for measurement of pulsatility within retinal vessels.

Results: Rapid sequences of images were acquired over selected vessels near the optic nerve head. From these

images, retinal blood flow profiles were extracted and synchronized to an external reference obtained with a photoplethysmograph. Each profile was acquired in less than 10 milliseconds.

Conclusions: Our results indicate that CDOCT provides laser Doppler information in addition to conventional optical coherence tomography, allowing the observation of blood flow dynamics simultaneous to imaging retinal structure. CDOCT is a promising technology for research and clinical studies of retinal blood flow dynamics.

Clinical Relevance: Blood flow dynamics, such as pulsatility and autoregulation, have been shown to change throughout the progression of diabetic retinopathy and glaucoma. Enabling CDOCT to observe retinal dynamics improves its potential as a clinical diagnostic tool.

Arch Ophthalmol. 2003;121:235-239

From the Departments of Biomedical Engineering (Drs Yazdanfar and Rollins) and Medicine (Dr Rollins), Case Western Reserve University, Cleveland, Ohio; and Department of Biomedical Engineering, Duke University, Durham, NC (Dr Izatt). Dr Yazdanfar is currently with the Department of Mechanical Engineering, Massachusetts Institute of Technology, Cambridge.

RECENT ADVANCES in noninvasive and minimally invasive technology have paved the way for improved clinical evaluation of ocular hemodynamics in living patients. Physiologic changes of the retinal vasculature have been associated with several disorders, including diabetic retinopathy, glaucoma, and age-related macular degeneration.¹ It has been noted that these disorders may disturb pressure and metabolic autoregulation of oxygenated blood delivery to the retina, or conversely, disturbed autoregulation may accelerate visual impairment.²⁻⁶

Several optical techniques currently exist for qualitative and quantitative ocular flow measurement. A common technique is angiography, where a map of blood vessels in the retina and partially in the choroid is generated by detection of a

fluorescent dye, typically sodium fluorescein or indocyanine green. Quantitative angiography is achieved by constructing dye-dilution curves, that is, by tracking the fluorescence intensity emitted from a region of interest as a function of time. The intravenously injected dye can cause discomfort, leading to nausea in some patients and a yellow discoloration of the skin for several hours. Laser Doppler velocimetry (LDV),⁴ a noninvasive optical method of measuring velocity of flowing fluids, was first applied to measure blood flows in human retinal vessels in the early 1970s.⁷ Conventional LDV is a single-point detection measurement without axial (depth) localization of flow. Nevertheless, LDV has been used extensively as a valuable research tool to noninvasively examine blood flow and flow dynamics in the human retina,⁸ iris,⁹ and choroid.¹⁰ Combining LDV with a scanning mechanism and con-

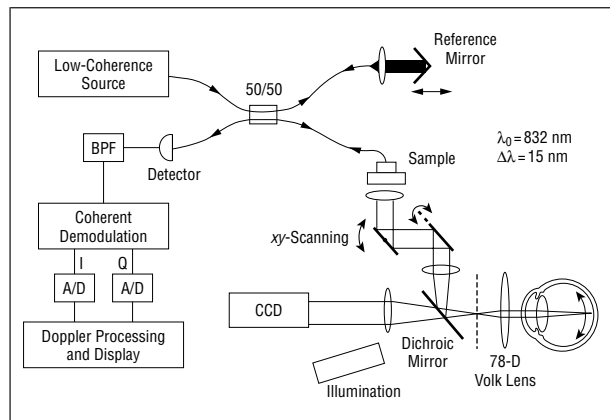


Figure 1. Schematic of the retinal color Doppler optical coherence tomography (CDOCT) scanner. A 78-diopter (D) condensing lens projects the image of the retina onto the image plane indicated by the dashed lines, and the image plane is relayed onto the fiber tip using a pair of lenses. An xy -scanning mirror pair enables transverse imaging in arbitrary linear and circular scan patterns. A charged-coupled device (CCD) camera sensitive to low-intensity visible and near-infrared light was used to visualize the exact scan location on the fundus simultaneous with CDOCT imaging. BPF indicates bandpass filter; A/D, analog-to-digital converter; I, in-phase signal components after phase-sensitive demodulation; and Q, quadrature signal components after phase-sensitive demodulation.

focal detection, termed *scanning laser Doppler flowmetry* (SLDF), enables localization of flow, and 2-dimensional en face retinal blood flow maps at various depths have been imaged with 300- μm axial resolution.¹¹

Recently, we introduced color Doppler optical coherence tomography (CDOCT)^{12,13} for quantitative cross-sectional imaging of flow in blood vessels of the human retina.^{14,15} CDOCT is a functional extension of optical coherence tomography (OCT), a noncontact technique for high-resolution and high-sensitivity cross-sectional imaging of microstructure in biological tissues.¹⁶ Since its early demonstration in living humans,^{17,18} OCT has emerged as a valuable tool for cross-sectional imaging of posterior segment^{19,20} and anterior segment^{21,22} structure at an unprecedented resolution scale. Whereas conventional OCT records only the amplitude of light reflected as a function of depth within tissue, CDOCT uses interferometric phase information to monitor Doppler shifts in the reflected spectrum in a fashion similar to LDV. Phase-sensitive detection of interference of light reflected from the sample and a moving reference mirror enables localization of Doppler shifts arising from motion in the sample, and therefore simultaneous imaging of tissue structure and blood flow. The Doppler shift is localized in depth by use of joint time-frequency analysis algorithms, which generate depth-resolved Doppler frequency spectra of the reflected light. The center frequency of each local spectrum corresponds to the local Doppler shift induced by flowing hemocytes.

Using this approach, CDOCT has been used to measure blood flow profiles in a few milliseconds in the human retina¹⁵ and skin.²³ Rapid acquisition of retinal flow data allows the extraction of dynamic flow properties, such as the retinal vascular response to changes in perfusion pressure or oxygen content. Studies with LDV⁶ have demonstrated that ocular diseases induce a measurable change in retinal flow dynamics (eg, systole to diastole or in response to altered pressure, metabolism, or exposure to light

intensity). Retinal pulsatility increases from healthy patients to patients with diabetic retinopathy and increases further throughout the progression of the disease. Additionally, a slight decrease in arterial flow pulsatility followed pan-retinal laser photocoagulation therapy.²⁴

Both LDV and SLDF have been used in studies of retinal hemodynamics. Herein, we demonstrate the feasibility of CDOCT in measuring retinal blood flow dynamics in humans for the first time. Depth-resolved Doppler flow measurement with OCT may complement or enhance currently developed methods for assessment of ocular hemodynamics.

METHODS

A schematic of the fiberoptic Michelson interferometer used in CDOCT is illustrated in **Figure 1**. For retinal imaging, a superluminescent diode with a 15-nm bandwidth centered at $\lambda_0 = 832$ nm (resulting in an axial spatial resolution of 20.4 μm in free space²⁵) illuminated the interferometer. The sample arm of the interferometer contained a standard slitlamp biomicroscope modified for viewing of the fundus simultaneous with OCT imaging. Transverse scanning of the OCT beam was performed using a galvanometric xy -scanning mirror pair, enabling arbitrary scanning patterns on the retina under computer control. The optical power incident on the eye was less than 250 μW , in accordance with the maximum permissible exposure (MPE) limits for near-infrared radiation.²⁶ The most conservative American National Standards Institute MPE standard for 830-nm light is 700 μW , assuming full pupil intra-beam viewing (7-mm pupil aperture) for exposure times up to 8 hours.²⁶ Our experiments were performed for exposures of up to 60 seconds with a less than 250- μW incident on the cornea, considerably lower than the MPE standards for that duration. Imaging was performed over large vessels near the optic nerve head, predominantly in a main superior or inferior temporal vein. Pupillary dilation was not used for these measurements. Experiments were performed on 5 healthy adult volunteers (one eye each) who provided informed written consent under a protocol approved by the University Hospitals of Cleveland Institutional Review Board, Cleveland, Ohio.

Axial ranging was performed by linearly scanning (32.5 mm/s) a retroreflecting mirror in the reference arm while recording the complex envelope of the detected interferometric signal between light reflected from the 2 arms. The interferometric detector signal was coherently demodulated at the Doppler frequency induced by the linear motion of the reference arm (78 kHz). The resulting base-band signal was low-pass filtered at a 20-kHz cutoff frequency, allowing sufficient bandwidth to accommodate the range of Doppler shifts that resulted from the retinal blood flow. To augment the image quality after broad-band Doppler processing, the images were digitally filtered off-line using a 5-kHz bandwidth fourth-order Bessel filter, resulting in an overall detection sensitivity of 90.5 dB.

Depth-resolved Doppler frequency spectra of the demodulated detector response were calculated in software using time-frequency analysis methods described previously.^{13,27} The centroid (f_c) of each depth-localized spectrum was extracted to estimate blood flow velocity (v) according to the following equation:

$$(1) \quad v = f_{s,0} / 2n_t \cos\theta$$

where θ is the angle between the incident light and the direction of blood flow, and n_t is the average tissue index of refraction. Velocity data were thresholded, color coded, and superimposed on the conventional OCT image for a CDOCT display similar to color Doppler ultrasound.

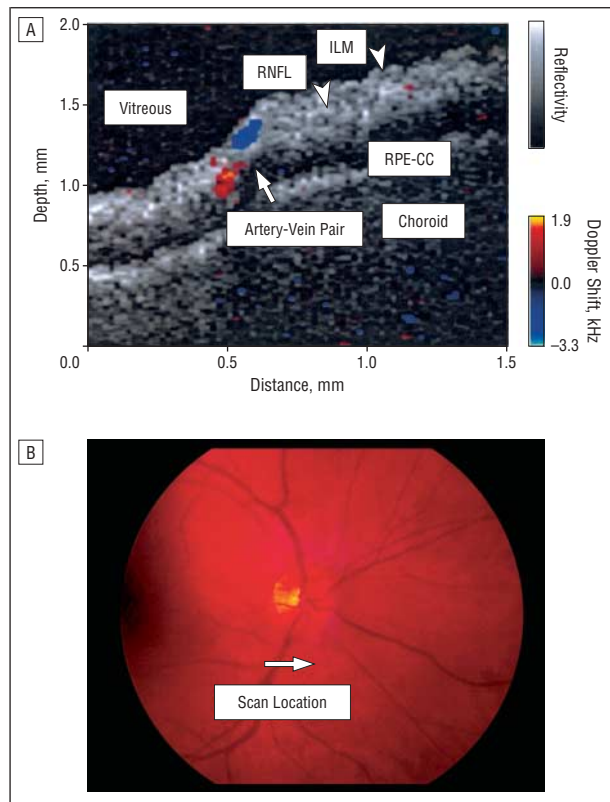


Figure 2. A, In vivo color Doppler optical coherence tomographic (CDOCT) image (2048 axial \times 100 lateral pixels) of bidirectional flow in the human retina acquired in 10 seconds. The axial dimensions indicate optical depth. CDOCT is able to distinguish various layers of tissue and to quantify blood flow magnitude and direction in sub-100- μ m-diameter retinal blood vessels. B, A fundus photograph marked to illustrate the position of the linear scan inferior to the optic nerve head. ILM indicates inner limiting membrane; RNFL, retinal nerve fiber layer; and RPE-CC, retinal pigment epithelium-choriocapillaris complex.

To measure dynamics in the pulsation of retinal blood flow, the reference arm scan rate was increased by a factor of 4 to 130 mm/s. High-frequency quadrature detection electronics were used to demodulate the signal at its center frequency of 312 kHz and obtain the in-phase and quadrature signal components from which the amplitude and phase were calculated. The probe beam was repeatedly scanned over a blood vessel of interest near the optic nerve head, where the lateral scan dimensions were restricted to slightly greater than the blood vessel diameter. Forty sequential images composed of 5 depth scans each were acquired in 5.0 seconds. A blood volume waveform was obtained externally using an infrared photoplethysmograph placed on the participant's ear, assuming that blood flow within the earlobe was approximately in phase with ocular blood flow. Centerline flow profiles were extracted from the images and correlated to the different phases of the cardiac cycle to measure pulsatility. Nonlinear least squares regression parabolic fits to these profiles provided the depth, diameter, and peak Doppler shift of the vessel.

RESULTS

Cross-sectional imaging of structure and blood flow was performed in the retina of the undilated human eye using a slitlamp biomicroscope adapted for OCT imaging. **Figure 2A** presents an in vivo CDOCT image demonstrating the observation of sub-100- μ m-diameter vessels within the retina. The conventional reflectivity OCT

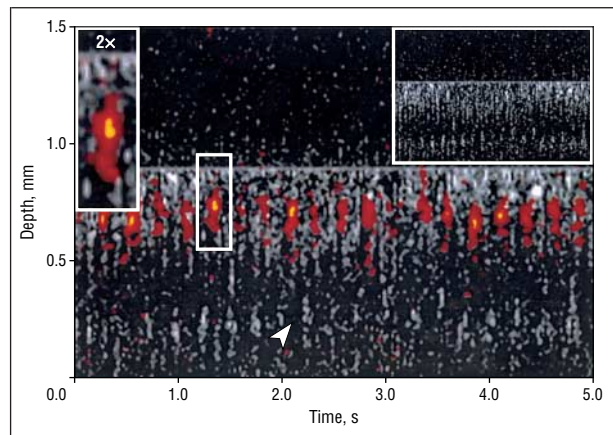


Figure 3. A sequence of images of a selected retinal blood vessel for measurement of flow dynamics (eg, extraction of pulsatility). The left inset is a single image of the vessel magnified by a factor of 2. The right inset is the amplitude-only image underlying the Doppler processing. Note the low reflectivity of the retinal pigment epithelium-choriocapillaris complex, as indicated by the arrowhead, below the blood vessel.

image (gray scale) clearly delineates retinal layers associated with OCT examination of the fundus. A fundus photograph (Figure 2B), indicating the location of the scan, confirms that a large artery-vein pair in the inferior temporal quadrant was imaged in Figure 2A. In this image, structural information is encoded in gray scale, where white indicates regions of high reflectivity (eg, retinal pigment epithelium-choriocapillaris complex), and black indicates low or no reflectivity (eg, vitreous humor). For velocity information, the direction and magnitude of blood flow are designated by color (red or blue) and intensity, respectively. Both microstructural and flow information were acquired simultaneously, and the flow data signal processing and display were performed off-line. Identification of blood vessels during image acquisition was aided by the fundus photographs acquired in real-time by a charged-coupled device camera with sufficient responsiveness to view the scanning infrared beam on the fundus. Before flow processing, the blood vessels sometimes appeared as low-reflectivity regions in the OCT image because of the increased scattering and absorption of light in blood relative to the surrounding tissue.

Reducing CDOCT image acquisition time facilitated measurement of retinal hemodynamics. A pulse plethysmograph signal was acquired synchronously from the ear as an external reference for comparison. After increasing the reference arm speed and reducing the lateral image size, several images of major retinal vessels were acquired rapidly during each heartbeat, as shown in **Figure 3**. The centerline flow profiles were extracted from the images and correlated to the phases of the cardiac cycle measured from plethysmographic waveforms, as shown in **Figure 4A** for a single participant. Parabolic fits to these profiles provided the depth, diameter, and peak Doppler shift of the vessel. Pulsatility of a given vessel was then extracted from a series of profile fits as follows:

$$(2) \quad P = (v_{\text{syst}}) / (v_{\text{dias}})$$

where v_{syst} and v_{dias} are the peak systolic and end diastolic blood flow velocities, respectively, calculated from

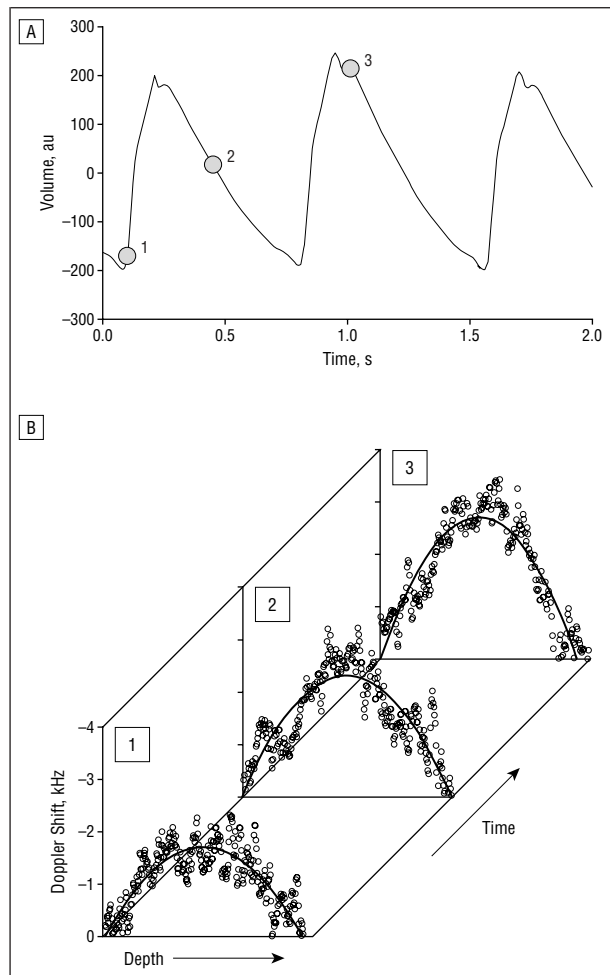


Figure 4. A, A portion of the periodic cardiac pulse waveform obtained with an infrared ear photoplethysmograph during acquisition of sequential color Doppler optical coherence tomographic (CDOCT) images of a selected central vein branch inferior to the optic nerve head. au Indicates arbitrary units. B, A sequence of extracted flow profiles demonstrates approximate laminar flow corresponding to the phases of the cardiac cycle numbered in part A. Solid lines represent parabolic fits to the raw flow data. Waveform 1 corresponds to diastole and waveform 3 to systole. The CDOCT data corresponding to each profile was acquired in fewer than 5 milliseconds, and the flow profiles are not averaged.

equation 1. As expected, Figure 4B indicates that the highest and lowest peak flows were during the systolic and diastolic phases of the heartbeat, respectively. The profiles remained approximately laminar throughout the heartbeat, indicating that parabolic fits are acceptable, despite the pulsatile variation of the measured flow rate over time. In the vein imaged in this figure (diameter = $159.4 \pm 17.7 \mu\text{m}$, assuming an average tissue index of refraction of 1.38), the measured pulsatility was 1.6. The peak centerline Doppler frequency in CDOCT is comparable to the measurement obtained with conventional LDV devices.²⁴ Although the scattering angle θ was not exactly determined in the current setup, equation 2 is normalized and thus independent of scattering angle (θ) ambiguities. Also, since the data corresponding to each profile are acquired in 5 to 10 milliseconds, instantaneous relative to flow fluctuations, the profile represents an accurate snapshot of the blood flow information.

Optical examination techniques such as CDOCT and LDV are particularly favorable for measurement of retinal blood flow in humans for several reasons. First, the vitreous is relatively transparent in the wavelength range of 600 to 1000 nm (visible and near infrared) due to the lack of chromophores and the low absorption coefficient of water in this spectral window.^{28,29} Within this region, sufficient photons survive the round-trip journey through the vitreous to provide a detectable signal collected at the optical fiber. Second, the short wavelength of light permits highly localized measurement of perfusion in the retina with micrometer-scale resolution. Currently, only optical techniques can maintain high spatial resolution at the retina. High-frequency (50- to 100-MHz) ultrasound biomicroscopy has been demonstrated for high-resolution blood flow imaging of the anterior segment,³⁰ approaching 15- to 20- μm spatial resolution. However, the rapid attenuation of ultrasound at higher frequencies³¹ prevents imaging of the retina with adequate resolution. In contrast to ultrasound, optical modalities for measuring flow do not require immersion of the eye in a water bath, resulting in greater patient comfort and potentially reduced preparation time. Unlike fluorescein angiography, CDOCT (as well as LDV and SLDF) is entirely noninvasive and does not require dilation of the pupil. Finally, fiberoptic delivery makes optical techniques amenable to integration with ophthalmoscopes and slitlamp biomicroscopes.

CDOCT offers some additional advantages. Using a broad-band light source in the interferometer enables depth localization of retinal flow with unprecedented axial resolution. Unlike CDOCT, LDV detects a signal that is composed of Doppler shifts from both the superficial and deep tissue layers, so the relative contributions are difficult to isolate in the retina.³² Although SLDF is also able to localize flow longitudinally, its ability to do so depends on confocal rejection of out-of-focus light in the retina. Therefore, the numerical aperture of the ocular lens determines the axial spatial resolution, which is on the order of 300 μm . In addition to decreasing the spatial resolution to approximately 10 to 20 μm , low-coherence interferometry improves the rejection of light outside the focal volume, resulting in a higher signal-to-noise ratio than confocal detection alone. Furthermore, CDOCT operates at longer wavelengths than conventional LDV, so light exposure times can be safely increased.

In summary, we have demonstrated the feasibility of using CDOCT for measuring retinal flow dynamics in the human vasculature. Cross-sectional imaging of blood flow in the retina is an important complement to conventional reflectance OCT imaging. Depth-resolved quantification of retinal hemodynamics may prove helpful in understanding the pathogenesis of several ocular diseases. These promising results should stimulate more comprehensive studies of retinal blood flow with CDOCT, similar to prior work with more mature laser Doppler technologies. Thus far, we have used CDOCT only for imaging of large vessels near the optic nerve head. Improvement of both the spatial and velocity resolutions is

required for imaging retinal microvasculature, which is composed of smaller-diameter vessels with slower-flow velocities. Since the spatial resolution in OCT is inversely related to the optical bandwidth of the source used in the interferometer, the resolution can be improved simply by using a broader bandwidth source, as demonstrated recently for ultrahigh-resolution (2- to 3- μm) structural imaging in the human retina.³³ The velocity resolution depends on the amount of time spent in detecting the Doppler shifts at a given location in the tissue. Therefore, to improve velocity resolution for detecting smaller blood flow velocities, the CDOCT image acquisition time has to be increased, which precludes imaging in a moving sample such as the human retina. However, we and others^{23,34,35} have recently demonstrated that by calculating Doppler flows across sequential scans, the velocity resolution can be improved by orders of magnitude without compromising the image acquisition time. Incorporating these 2 technologies into the existing setup will allow CDOCT to image smaller retinal blood vessels. CDOCT is the first technique to determine simultaneously, with micron-scale resolution, the depth, diameter, flow rate, and flow dynamics of blood vessels within the living retina.

Submitted for publication May 14, 2002; final revision received October 9, 2002; accepted October 23, 2002.

This study was supported by a Biomedical Research Partnerships grant (EY13015) and a Training Grant (5T32-GM-07535, Dr Yazdanfar) from the National Institutes of Health, Bethesda, Md.

We thank Zeiss Humphrey Systems (Dublin, Calif) for providing the slitlamp-based scanning apparatus used in these measurements. We also thank Brian Wolf for technical support.

Corresponding author and reprints: Joseph A. Izatt, PhD, Department of Biomedical Engineering, Duke University, 136 Hudson Hall, Box 90281, Durham, NC 27708-0281 (e-mail: jizatt@duke.edu).

REFERENCES

- Alm A. Ocular circulation. In: Hart WM, Jr, ed. *Adler's Physiology of the Eye: Clinical Application*. 9th ed. St Louis, Mo: Mosby-Year Book Inc; 1992:198-227.
- Hickam JB, Frayser R. Studies of the retinal circulation in man: observations on vessel diameter, arteriovenous oxygen difference, and mean circulation time. *Circulation*. 1966;23:302-316.
- Ernest JT. Retinal circulation in diabetes mellitus. *Arch Ophthalmol*. 1986;104:986-988.
- Riva CE, Petrig BL, Grunwald JE. Retinal blood flow. In: Shepherd AP, Öberg PÅ, eds. *Laser-Doppler Blood Velocimetry*. Boston, Mass: Kluwer Academic Publishers; 1990:349-383.
- Harris A, Ciulla TA, Chung HS, Martin B. Regulation of retinal and optic nerve blood flow. *Arch Ophthalmol*. 1998;116:1491-1495.
- Grunwald JE. Laser Doppler velocimetry studies of retinal hemodynamics in diabetes mellitus. In: Weinreb RN, Joyner WL, Wheeler LA, eds. *Biology of the Ocular Microcirculation*. Amsterdam, the Netherlands: Elsevier Science Publishers BV; 1991:149-159.
- Tanaka T, Riva C, Ben-Sira I. Blood velocity measurements in human retinal vessels. *Science*. 1974;186:830-831.
- Riva CE, Grunwald JE, Sinclair SH, Petrig BL. Blood velocity and volumetric flow rate in human retinal vessels. *Invest Ophthalmol Vis Sci*. 1985;26:1124-1132.
- Chamot SR, Movaffaghy AM, Petrig BL, Riva CE. Blood flow in the human iris measured by laser Doppler flowmetry. *Microvasc Res*. 1998;57:153-161.
- Riva CE, Petrig BL. Choroidal blood flow by laser Doppler flowmetry. *Opt Eng*. 1995;34:746-752.
- Michelson G, Schmauss B. Two dimensional mapping of the perfusion of the retina and optic nerve head. *Br J Ophthalmol*. 1995;79:1126-1132.
- Chen ZP, Milner TE, Dave D, Nelson JS. Optical Doppler tomographic imaging of fluid flow velocity in highly scattering media. *Opt Lett*. 1997;22:64-66.
- Izatt JA, Kulkarni MD, Yazdanfar S, Barton JK, Welch AJ. In vivo bidirectional color Doppler flow imaging of picoliter blood volumes using optical coherence tomography. *Opt Lett*. 1997;22:1439-1441.
- Yazdanfar S, Rollins AM, Izatt JA. In vivo imaging of blood flow in human retinal vessels using color doppler optical coherence tomography. *Proc Soc Photo Opt Instrum Eng*. 1999;3598:177-184.
- Yazdanfar S, Rollins AM, Izatt JA. Imaging and velocimetry of the human retinal circulation using color Doppler optical coherence tomography. *Opt Lett*. 2000;25:1448-1450.
- Huang D, Swanson EA, Lin CP, et al. Optical coherence tomography. *Science*. 1991;254:1178-1181.
- Fercher AF, Hitzinger CK, Drexler W, Kemp G, Sattmann H. In vivo optical coherence tomography. *Am J Ophthalmol*. 1993;116:113-114.
- Swanson EA, Izatt JA, Hee MR, et al. In vivo retinal imaging by optical coherence tomography. *Opt Lett*. 1993;18:1864-1866.
- Hee MR, Izatt JA, Swanson EA, et al. Optical coherence tomography of the human retina. *Arch Ophthalmol*. 1995;113:325-332.
- Puliafito CA, Hee MR, Lin CP, et al. Imaging of macular diseases with optical coherence tomography. *Ophthalmology*. 1995;102:217-229.
- Izatt JA, Hee MR, Swanson EA, et al. Micrometer-scale resolution imaging of the anterior eye in vivo with optical coherence tomography. *Arch Ophthalmol*. 1994;112:1584-1589.
- Radhakrishnan S, Rollins AM, Roth JE, et al. Real-time optical coherence tomography of the anterior segment at 1310 nm. *Arch Ophthalmol*. 2001;190:1179-1185.
- Zhao Y, Chen ZP, Saxer C, Xiang S, de Boer JF, Nelson JS. Phase-resolved optical coherence tomography and optical Doppler tomography for imaging blood flow in human skin with fast scanning speed and high velocity sensitivity. *Opt Lett*. 2000;25:114-116.
- Grunwald JE, Riva CE, Sinclair SH, Brucker AJ, Petrig BL. Laser Doppler velocimetry study of retinal circulation in diabetes mellitus. *Arch Ophthalmol*. 1986;104:991-996.
- Danielson B, Whittenberg C. Guided-wave reflectometry with micrometer resolution. *Appl Opt*. 1987;30:2975-2979.
- American National Standards Institute. *Safe Use of Lasers*. Orlando, Fla: Laser Institute of America; 2000. ANSI Z 136.1-2000.
- Yazdanfar S, Kulkarni MD, Izatt JA. High resolution imaging of in vivo cardiac dynamics using color Doppler optical coherence tomography. *Opt Express*. 1997;1:424-431.
- van den Berg TJTP, Spekreijse H. Near infrared light absorption in the human eye media. *Vis Res*. 1997;37:249-253.
- Itzkan I, Izatt JA. Medical use of lasers. In: Trigg GL, ed. *Encyclopedia of Applied Physics*. Vol 10. Washington, DC: VCH Publishers Inc; 1994:33-59.
- Pavlin CJ, Christopher DA, Burns PN, Foster FS. High-frequency Doppler ultrasound examination of blood flow in the anterior segment of the eye. *Am J Ophthalmol*. 1998;126:597-600.
- Foster FS, Pavlin CJ, Lockwood GR, et al. Principles and applications of ultrasound biomicroscopy. *IEEE Trans Ultrason Ferroelectr Freq Control*. 1993;40:608-617.
- Petrig BL, Riva CE, Hayreh SS. Laser Doppler flowmetry and optic nerve head blood flow. *Am J Ophthalmol*. 1999;127:413-425.
- Drexler W, Morgner U, Ghanta RK, Kartner FX, Schuman JS, Fujimoto JG. Ultrahigh-resolution ophthalmic optical coherence tomography. *Nat Med*. 2001;7:502-507.
- Westphal V, Yazdanfar S, Rollins AM, Izatt JA. Real-time high velocity-resolution color Doppler optical coherence tomography. *Opt Lett*. 2002;27:34-36.
- Yazdanfar S, Rollins AM, Izatt JA. Ultrahigh velocity resolution imaging of the microcirculation in vivo using color doppler optical coherence tomography. *Proc Soc Photo Opt Instrum Eng*. 2001;4251:156-164.