Electro-optic Fundus Imaging

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Abstract. Fundus imaging and photography are cornerstones of modern ophthalmic practice. The recent developments in electro-optic and computer imaging technology resulted in many improvements in the acquisition and analysis of fundus images, which already are being used in commercial fundus imaging systems. This paper reviews the basic aspects of the electro-optic methods for fundus imaging, with emphasis on the differences between these new techniques and conventional, film-based, fundus photography. Potential benefits of these systems in image acquisition, archival, communication, processing, and quantitative analysis, as well as their current advantages and shortcomings are discussed. (Surv Ophthalmol 34:113–122, 1989)

Key words. Fundus imaging • fundus photography • image analysis • ophthalmoscopy • optic nerve • retina

Ophthalmic practice is second only to radiology in application of imaging. The transparent nature of the eye enables imaging in the visible spectrum, in addition to X-ray, nuclear magnetic resonance, and ultrasound. Photography of the anterior segment, the vitreous cavity, and the retina are commonplace in clinical practice. Color photography of the retina is used for general evaluation of the fundus, and stereo-pair images for subjective appreciation and measurement of depth. Black and white photographs are taken in red-free light to enhance the visibility of the nerve fiber layer in fundus photography and the vascular pattern in fluorescein angiography. The wide availability and applicability of retinal images together with recent developments in computerized image analysis have led to important research in this field. In conventional fundus photography, a high-resolution still image is obtained on film using the fundus camera. The processed film is stored in a paper file for documentation and future comparison and analysis. The image is analyzed by a trained observer, usually with the aid of optical magnification. Analysis is usually qualitative or at best semi-quantitative, estimating parameters such as cup-to-disc ratio or the intensity and area of optic nerve pallor.

The new ophthalmic imaging systems offer alternatives to acquisition, storage, and evaluation of fundus images. Images are acquired electro-optically instantaneously, usually in a video format. The images can be evaluated immediately and, if inappropriate, a new image obtained. Once satisfactory, the image is permanently stored as a computer file that can be readily accessed at the same location and at remote locations in another building or city. The most important benefits of these systems are the immediate availability of the images and the ability to process the images to obtain measurements of parameters that may be important diagnostically.

Currently, four commercial units using the basic fundus camera imaging optics are available: The
ImageNet system (Topcon, International Corporation of America, Paramus, NJ) (previously the IS-2000 Ophthalmic Imaging System, PAR Technology Corporation, New Hartford, NY); the Optic Nerve Head Analyzer (G. Rodenstock Instrumente GMBH, Munich, West Germany); the IPS Ophthalmic (Kontron Bildanalyse, Munich, West Germany); and the latest system, the Retinal Analyzer (Humphrey Instruments, San Leandro, CA).

A different group of instruments using a new imaging modality, the Scanning Laser Ophthalmoscope (SLO) has been presented as prototypes by two companies: The Scanning Laser Ophthalmoscope (Rodenstock) and the Laser Tomographic Scanner (LTS) (Heidelberg Instruments, Heidelberg, West Germany). These instruments are discussed separately here.

I. Image Acquisition

The simplest method of acquiring a fundus image for the computer is by using a film transparency taken with the fundus camera. Since this method is important for processing pictures taken in the past using standard fundus photography, it is provided by most commercial systems. The transparency is back-illuminated, and a video camera used to photograph the image. To obtain the image in its digital form, the video analog signal is digitized by an analog-to-digital converter. The digitized video signal is stored in the computer. To redisplay an image, a different circuit, a digital-to-analog converter, shapes a video signal from numbers stored in the computer memory. If color imaging is desired, the video image should be acquired three times, each time with a different color filter in front of the camera, a process similar to color separation in standard photography.

Direct image acquisition is a means of obtaining the video image directly from a patient's fundus without the intermittent film step by connecting a video camera rather than a filmback to the fundus camera. In both cases, a color image can be obtained. Color video images are obtained by splitting the image into the red, green, and blue signals, using a beam splitter and acquiring them with three monochrome cameras simultaneously. The resolution of video color cameras is still inadequate for this application. The red, green, and blue channel signals generated by the cameras are digitized and then stored in the computer.

American video systems continuously generate 30 images or frames per second. To obtain a properly illuminated image, the fundus camera flash should be synchronized with the beginning of the video frame. The electronic flash period of about 1/1000th of a second is much shorter than one video frame (1/30th of a second); however, the flash allows a full image to be recorded because of the relatively slow decay of the video tube's phosphor. The flash results in an "afterimage" on the video tube's faceplate that can be obtained even after the

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*A similar instrument was recently introduced by Carl Zeiss, Oberkochen, W. Germany."
light is extinguished. However, because the image decay starts as soon as the flash light disappears, the amount of decay needs to be corrected so that the bottom of the digitized image remains as bright and contrasting as the top.

Stereo images are used to measure depth and evaluate the topography of retinal features, such as the optic nerve head. Both simultaneous and sequential stereo image pairs may be obtained depending on the fundus camera used. With most fundus cameras, sequential stereo pairs may be obtained using the Allen stereo separator. Simultaneous stereo-image pairs may be obtained with the use of a stereo fundus camera. In this case, both images appear on the same video frame. The main benefit of acquiring simultaneous stereo pairs is a fixed, known stereo base that provides fixed relationships between depths measured at different times. Thus, the actual depth may be compared over time with such a system. Only relative depth is obtainable from the sequential (variable base) stereo pairs. Thus, we can determine which of two points is deeper, but not by how many millimeters. This can prevent accurate follow-up of depth and volume changes over time.

Simultaneous stereo-pair images together with special illumination may aid in the depth measurements for those images. A set of parallel stripes is projected on a retina and the stereoscopic image pair recorded with this stripe pattern (Fig. 1). The small deformations in the stripe patterns simplify the calculations required to obtain the depth measurement from the stereo pair and reduce the errors. Other illumination techniques for image acquisition include illumination by monochromatic light and indirect illumination; in the former, the wavelength can be selected throughout the visible spectra. Images taken with the green and red illumination area are used for measuring pallor of the optic disc. In indirect illumination, the illumination and recording of the image are done through a narrow, horizontal, rectangular slit scanned vertically across the fundus. If the illumination and recording areas differ slightly, the acquired image represents a view of the retina illuminated indirectly by light scattered through neighboring areas, similar to the local view seen next to the slit of light with the slit-lamp. The indirect view offers a different image of the retina that may be clinically significant. In addition, time-resolved imaging, in which small parts of the object are sequentially illuminated and the reflected light recorded at different times and displayed together to form the image, improves the contrast of the image, because it reduces intraocular light scatter from one retinal point to another.

Unsteady fixation as well as normal eye movements of the patient often misalign camera optics and the eye, causing variable illumination, vignetting, and different compositions of the fundus image. These changes present little difficulty to the trained observer comparing two images, but changes in illumination and position may alter significantly the results of quantitative image analysis. To minimize the effect of these artifacts, some instruments offer automatic alignment. An eye movement-monitoring device aligns the camera position with either the center of the pupil or the cornea, enabling a more consistent illumination and positioning of the fundus on repeated photographs tak-
Fig. 3. Pallor map with color coding to represent local disc pallor values. The pallor code indicated in the bar color code below ranges from red on the left to white on the right. The histogram on the right represents the frequency distribution of various pallor values within the disc. (Photo courtesy of Ulrich Klingbeil, Ph.D., G. Rodenstock Instrumente GMBH, Munich, West Germany.)

Fig. 4. Topographic map for representation of depth measurements obtained with the Rodenstock Optic Nerve Head Analyzer. The original image is compared with the topographic color-coded overlay map (left), where the color is used to code the depth information. Each color step represents a change in depth of 200 µm. The black-and-white image on the right represents the same topographic map coded in brightness rather than color. (Photo courtesy of Ulrich Klingbeil, Ph.D., G. Rodenstock Instrumente GMBH, Munich, West Germany.)

en at different times. The alignment also improves the image quality by properly centering the camera with the optics of the eye.

The approximately 500 lines of resolution common to most video systems are substantially lower than the potential resolution of photographic film. The manufacturer's data suggest that film commonly used for fundus photography have a resolving power of the order of 1000 line pairs per frame for low-contrast and 2500 for high-contrast images. However, evaluation of the film's resolution in two different fundus cameras indicates that the cameras' optics seriously limit the resolution that can be obtained in fundus photography. The resolution of the same films in the fundus camera is of the order of 400 line pairs for low-contrast, and 1000 line pairs for high-contrast testing targets.

II. Images in Computers

Images are represented in computers as two-dimensional arrays of numbers. The position of each number in the array corresponds to a point in the image, and the value of each point represents the grey level or brightness of the point. To represent a full-color image, three two-dimensional arrays are required, the images of which are used to drive the red, green, and blue electron guns of the color video screen.

The image resolution or quality is determined by the size of the array and the size of the number representing each point. Most imaging instruments are built to represent images up to $512 \times 512$ picture elements (pixels). Such representation requires large computer memory and storage capabilities; thus, a $256 \times 256$ resolution is used frequently. Fig. 2 illustrates the effect of reducing the resolution further on a fundus photograph. In most applications, image brightness is displayed at 256 different levels, which represent standard computer data word size (one byte, eight bits). For most
applications, a coarser quantitation (only five bits or 64 levels) would be sufficient, but further reduction would deteriorate image quality.

III. Image Storage and Retrieval

Acquired fundus images should meet standard medical needs and be adequate for patient records. Because images taken in the past should be available to compare with current studies, they should be stored safely for future use. Film files, the current mode of storing fundus images, may be inefficient because of the time required to obtain an image and the danger of lost or misplaced slides. Digitized video images may be stored more efficiently using nondestructive optical digital storage offered on optical discs with a Write Once Read Many (WORM) characteristic. Images can be stored temporarily on computer magnetic disc or magnetic tape, and after the image has been deemed satisfactory, stored permanently on the optical laser disc. Each laser disc, an efficient storage medium, can save up to 108,000 color video images (LV-200 Videodisc, TEAK, Montebello, CA). Storing an image takes less than one second, and an image can be recalled and redisplayed in about the same time. Whether images are stored on optical discs or in magnetic computer discs, the archival properties of the system are superior to the paper film file. Image lists can be accessed easily by the computer, and selecting the image to be retrieved and displayed is fast and convenient.

An important benefit of the electronic archival system is the ability to access images from different work stations, e.g., a doctor can recall the image directly on a screen in his or her office without going to the photography room. This office can be either in the same building as the system or elsewhere. Images can be mailed electronically with a referral letter or retrieved from the referring physician.
Film records still may be required for publication and educational purposes. Those may be provided with a separate film record option. However, any digitized image could be rephotographed using a video film recorder and thus placed on film. The images also could be recorded on a video cassette recorder or video still recorder now available. Thus, electro-optic archives of fundus images offer the benefits of computerized data base management, telecommunications capabilities, and a safe, compact, and fairly inexpensive means of storage. Lower-quality images may be printed using either regular or laser printers to serve as notes in the patient’s record.

IV. Image Processing

Digital image processing has been applied widely in recent years to research involving fundus images. Measurements of the optic nerve head in glaucoma were a main target for this research, including studies of cupping, pallor of the optic nerve head, the striations of the retinal nerve fiber layer, and fluorescein angiograms. Image processing techniques were used to measure blood flow in retinal vessels and detect microaneurysms in diabetics, estimate the extent of diabetic macular nonperfusion, and evaluate changes in exudates and drusen patterns. Image processing in conjunction with pattern recognition methods was used in the automatic detection of the vascular pattern from fundus photographs and identification of arteries, veins, and their relative positions. Pattern recognition using color information was used to identify hemorrhages and exudates and to analyze arterial vein crossings in systemic diseases. Similar methods were applied to identify many fundus features in normal and diseased retinas. Image enhancement techniques were used to enhance fundus photographs. Gilchrist recently presented a review of this topic.

Image processing is the most important benefit of the new fundus imaging instruments. Most of the available processing programs concentrate on measuring the optic nerve head in glaucoma. The simplest image-processing capability involves delineating fundus features with a light pen or graphics bit-pad (planimetry). The operator marks the disc margin and the edge of the cup on the image displayed on the screen. The computer then calculates the cup-to-disc ratio easily, based on the relative area or ratio of horizontal and vertical diameters. Other parameters, e.g., neural rim area, can be calculated. All the commercial systems are implementing this technique, which can be used to measure other features of the fundus such as tumors or scars.

Fig. 7. Enhancement of fundus photographs taken through cataract. Top left, photograph taken in 1979 before cataract developed. Top right, cataractous image of the same eye taken in 1985 after cataract development. Bottom images represent enhancement of the cataractous image using two different enhancement techniques described in reference 28.

Automated analysis of pallor of the optic nerve head offers an objective measurement. Color analysis of fundus images requires images in more than one color illumination. Images taken in red and green light can be used to calculate the pallor of the disc and to generate a color-coded pallor map (Fig. 3). The relative area of the pallor can then be calculated from the ratio of green to red levels to give a pallor map of the disc. It should be noted that this pallor definition, based on intensity only, is different than the definition used by Nagin et al., who measured the pallor area, tracking the intensity changes along the pallor boundary and applying the knowledge of the general size and shape of pallor area.

Calculating the three-dimensional topography of the optic nerve head for objectively evaluating the cup-to-disc ratio and volume measurements is probably the most interesting and difficult of the techniques offered. The computer program correlates local brightness levels in the two images to find corresponding points in the stereo pair. Calculating the disparity between the two images enables the system to calculate the depth of each point. Once the depth for all required points within the disc is known, the three-dimensional structure of the disc can be presented as a contour map (Fig. 4), a wire frame model of the optic nerve head (Fig. 5), or a
series of depth profiles of the nerve head (Fig. 6). The edge of the cup then can be calculated based on a predetermined rule. It is frequently difficult to determine the cup edge position, especially when there is a shallow slope with no clear inflection point. Arbitrarily depth, below the retinal surface, is, therefore, used in most instruments. Once the cup edge and disc edge are determined, the system can calculate cup-to-disc ratios based on cup area, diameters, or even volume.

Image processing also is used to enhance images. By properly distorting the appearance of an image, specific features become more visible. Common image enhancement techniques include contrast modification, edge enhancement (spatial filtering), and noise reduction. Image enhancement techniques may improve the visibility of fundus photographs taken through cataracts or other media opacities (Fig. 7), and the visibility of fine retinal features such as the retinal nerve fiber layer.

V. Commercial Instruments

It is interesting to review the reported measurement capabilities of the systems, even though any reference to properties of the commercial units becomes rapidly outdated because of advancements in the field. The IPS Ophthalmic system offers programs to compare two independently generated pictures, enabling accurate assessment of fundus changes such as tumor growth and displacement of vessels with accuracy of ±18 μm.

Topographic measurement of the disc is under investigation and development for the Humphrey Retinal Analyzer. Reproducibility of repeated measurements on 10 images was reported as 1.4–4.9% for the rim area and 0.25–3.3% for the disc area in normals. The results in glaucoma patients were similar, 1.8–7.5% and 0.5–4.9% for rim and disc areas, respectively. Basic capabilities in this area are available with the Topcon Image-Net system; the resolution on a model eye was reported to correspond to 20 μm of depth and the variability of the measurements ranged from 0.7% to 25.5% in one study and 1% to 18% in another study. The Rodenstock Optic Nerve Head Analyzer was designed specifically to perform these measurements. Its stripe-coded illumination enables more reliable calculation of depth from the stereo-pair images. The depth resolution offered by the Optic Nerve Head Analyzer varies on repeated measurements by less than 60 μm. The reproducibility of repeat measurements on about 10 images are on the order of up to 10% for cup-to-disc ratios and rim area and about 25% for volume measurements. Other studies found median reproducibility for cup-to-disc ratio (7.9% and 3.1%), rim area (7.5% and 7.5%), and cup volume (7.6% and 1.5%). In one study, the mean reproducibility was 2% and 18%, respectively. A recent study evaluated total variability using three images from each eye and found the variability to range from 0.069–0.078 for cup-to-disc ratio. The variability of measurements from glaucoma patients was found to be similar to the variability of measurements from normals, and the largest component of variability was the result of acquisition of separate images at different times.

The reproducibility of pallor measurements with the Optic Nerve Head Analyzer was reported in a study to be worse than 30%, making it inadequate to detect small changes. Another study found variability of optic disc pallor measurements ranging only from 1.7% to 10.8%. Unfortunately, variability was defined in this study as the standard deviation of nine repeat measurements expressed as percentages, making comparison between studies difficult.

VI. Scanning Laser Ophthalmoscopes

The SLO, developed at the Eye Research Institute, Boston, and the LTS, developed jointly at Heidelberg University and the University of California at San Diego, employ a unique ophthalmoscopy principle that differs considerably from other methods of retinal imaging, and provides many advantages. A videoimage is obtained that can be displayed on a television monitor, and recorded on a videocassette recorder. However, the imaging principle is not equivalent to the imaging with a videocamera attached to a fundus camera, as in the other instruments already discussed. The SLO uses a dim, focused laser beam to scan the retina. The videoimage is generated by collecting the reflecting light from one retinal point at a time. The detected signal is displayed as the intensity of the spot on the videomonitor. The resolving power of the SLO is limited by the size of the laser spot on the retina, not by the optics of the fundus camera and the characteristics of the videocamera as in other imaging devices.

In all fundus imaging devices, separation of the illumination and light-gathering pathways at the patient's pupil is important to reduce specular reflections and light scatter from media turbidity. Because the illuminating laser beam's diameter at the pupil is so small, it is possible to use a large portion of the pupil to collect light reflected from the retina, partly accounting for the SLO light efficiency. The SLO, therefore, offers fundus imaging at light levels that are orders of magnitude lower than those used in indirect ophthalmoscopy, making fundus examination more comfortable and safe for the patient. The efficient light collection also enables
fluorescein angiography to be performed with only one tenth of the normal fluorescein dose. The angiography provides a continuous video signal and may be recorded with a time resolution of 30 frames per second on a videocassette recorder to be reexamined and analyzed later.\textsuperscript{16,20a} The low dose of fluorescein also permits repeated angiographies to evaluate both eyes on the same day for abnormalities of the early phase, as well as pre-and post-photoagulation angiogram analysis.

The laser beam intensity during the scan can be controlled by a computer. Thus, any graphic material that can be displayed on the computer screen also can be generated in the laser raster directly on the patient’s retina and at the same time observed by the clinician on the television screen. Since the exact location of any displayed detail is viewed directly, many functional testing procedures can be performed at specific, known retinal locations. This capability has been used to perform fundus perimetry,\textsuperscript{7,35} acuity testing at various retinal locations,\textsuperscript{16} and study the use of residual retina for reading by patients with macular diseases.\textsuperscript{34}

The SLO may be used in the same way to evaluate eye movements and fixation patterns in nystagmus, amblyopia, and learning disabilities. It is especially attractive for pediatric evaluation of function (i.e., fixation and eye movements) as well as retinal health because of the low light levels and the ability to display computer games to the patient (Fig. 8-top), and thus maintain the child’s interest during the examination.\textsuperscript{16}

The confocal SLO uses the double scanning principle, i.e., illuminating laser light is scanned across the retina, as well as by the detection system, thus enabling the detector to be limited only to light that is apparently directly reflected from the illuminated retinal point. Light scattered back from optical media turbidities thus misses the detector and does not reduce the image quality.\textsuperscript{29,38} This may offer improvement in image quality obtained through cataract, vitreous haze, and other turbidities, and also increases the contrast of images taken from clear-media eyes. The improved contrast compensates for the relatively low resolution, and the image quality may approach the quality of fundus photographs. With such improvements, the SLO may offer good imaging of the retinal nerve fiber layer even with red laser light and without pupillary dilation (Fig. 8-bottom). Variation in the size and shape of the confocal aperture enables indirect imaging that is similar but more flexible than that offered by the Humphrey Retinal Analyzer in which a full line is illuminated rather than a single point.

The LTS is designed to provide topographic measurements of the cornea and fundus as well as confocal laser imaging. By scanning one meridian on the cornea or retina repeatedly while changing the focal plane continuously, the instrument provides an optical section image of the structure with high resolution and details. The images are digitized directly, and the integral image processing system can provide measurements of corneal curvature, thickness, or depth of corneal incisions. Similar methods are used to obtain volumetric and topographic measurements of the optic disc\textsuperscript{12a,40} and thickness profiles of the nerve fiber layer.\textsuperscript{3}

The high visibility of the nerve fiber layer, result-
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from the high-contrast imaging inherent in the confocal laser scanning configuration can be enhanced further using digital image enhancement techniques.26,29 The polarization properties of the nerve fiber layer can be explored by implementation of polarization differential contrast imaging.29 Using two images obtained simultaneously in two orthogonal polarization directions, the difference image is obtained and displayed in real time. These images may be processed to provide estimates of nerve fiber layer thickness. The variability, accuracy, and sensitivity of these measurements have not yet been verified.

VII. Summary

Although commercial interest in high-tech fundus imaging is a sign that the technology is needed and marketable, the price ($35,000 to $150,000) is prohibitive for most private practices. However, these systems are being used to conduct clinical research in major medical centers. The value of image processing and the anticipated reduction in price of this electro-optic technology may result in widespread use of these instruments in the near future. Some systems offer programs for processing other ocular images, i.e., pupil and cornea. Using these programs in conjunction with a photo slit-lamp extends the applicability of these systems to anterior segment evaluation as well.

As in many other computer systems, a serious drawback is the limited availability and high cost of developing and maintaining the highly specific software. Although many manufacturers promise future delivery of software, caution should be exercised. "Vaporware" (software that is promised but never completed and delivered) is a common problem in the computer industry. When shopping for an image processing system, one should first determine if the available software suits one's specific requirements. Developing image processing software is expensive and should, in most cases, be undertaken by the manufacturer, not the user.

The clinical value of these instruments is still unknown. The potential benefit from the ability to evaluate changes over time needs to be studied. The accuracy of the instrument and what accuracy is needed to provide meaningful clinical information are unknown. Only partial information exists regarding the reproducibility of the measurements in patient populations. Studies investigating these questions, in relation to various conditions, are under way in many centers.

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References


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