A clinical technique and apparatus for simultaneous angiography of the separate retinal and choroidal circulations

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A technique is described which permits making simultaneous angiograms of the separate retinal and choroidal circulations following a single intravenous dye injection. The two sets of angiograms are made using a specially built optical separator with twin motorized 35 mm. cameras which replaces the usual camera body on the standard Zeiss fundus camera. A single injection of solution containing a mixture of indocyanine green dye and sodium fluorescein dye is given to the subject, and the fundus camera with the attached optical separator is otherwise used in the usual manner to produce the angiograms. A technique for producing fluorescent indocyanine green dye in the human is also demonstrated.

Much of what is known about the dynamics of both the retinal and choroidal circulations of the eye is derived from fluorescein angiographic studies. Although fluorescein angiography is a potent diagnostic aid, it does not overcome all of the many problems encountered in attempting to visualize the ocular circulations. The characteristics of sodium fluorescein dye are such, for example, that it can be successfully applied to the study of choroidal circulation only under limited circumstances. Except for the very earliest arterial filling, visualization of choroidal circulation in the normal eye by fluorescein angiography is limited by the spectral characteristics of pigment epithelium and macular xanthophyll which inefficiently transmit both excitation and emission energies of fluorescein and by the rapid extravasation of fluorescein from the choriocapillaris. Consequently, direct and uninterrupted visualization of the choroidal vasculature by fluorescein angiography is possible only in eyes where normal pigmentation and choriocapillaris are absent.

Development of a technique whereby choroidal angiography can be routinely done with equal facility and on the same scale as retinal angiography started with the demonstration of choroidal angiography by Kogure and co-workers. They injected indocyanine green dye into the ca-
rotid arteries of owl monkeys and photographed its passage through the choroidal vasculature using a "false" color technique. Although the angiograms were strikingly clear and detailed, the necessity of making arterial dye injections and the difficulty of determining the proper exposure for each subject eye make it a clinically unacceptable technique.

The feasibility of photographing on black and white infrared-sensitive film the passage of a venous-injected bolus of indocyanine green dye through the ocular circulation was suggested by Hochheimer. The angiograms made by this technique were not of the same quality as those of Kogure and co-workers, however, they demonstrated a photographic technique having a reasonably narrow range of spectral sensitivity and which permits venous injections of indocyanine green dye—an important step toward achieving a clinically acceptable technology.

A further step toward clinically acceptable choroidal angiography was made by placing in front of the light source a narrow band pass filter (15 nm. wide) whose maximum transmission spectrally matches the maximum absorption of indocyanine green dye (about 800 nm.). Using this filtering technique, clinical infrared absorption angiography of the choroid using venous injections of dye was demonstrated to be feasible by Flower. Still, some improvements in technology were necessary to simplify production and interpretation of infrared absorption angiograms of the choroidal circulation before seeking clinical acceptability of the technique.

This paper describes a technique, currently undergoing clinical evaluation at the Wilmer Ophthalmological Institute, which permits simultaneous angiography of the separate choroidal and retinal circulations. Basically, the technique involves intravenous injection of an indocyanine green and sodium fluorescein dye mixture and then simultaneously photographing the passage of the dyes through the ocular vasculatures with two cameras. It is not entirely clear exactly what characteristics of choroidal blood dynamics will ultimately prove to be most important in differentiating normal from abnormal circulation patterns. Hopefully, the ability provided by this technique to compare choroidal filling patterns to simultaneous retinal filling patterns will make identification of those particular characteristics easier. It is, therefore, the purpose of this report only to define the technique and to present a sampling of the data obtained by using it. An in-depth study of choroidal circulation per se will be considered in a separate study.

Principle

Visualization of the separate choroidal and retinal circulations is possible because of the distinct anatomic differences between the vasculatures and because of the different spectral characteristics of indocyanine green and sodium fluorescein dyes. These differences are such that the choroid presents conditions which are ideal for photographing indocyanine green dye and are detrimental for photographing sodium fluorescein.

Some of those characteristics which make fluorescein useful in retinal angiography are at the same time responsible for its ineffectiveness in choroidal angiography; they are: (1) the absorption and emission spectra of sodium fluorescein are in the visible region of the spectrum (near 490
Fig. 2. A, Schematic drawing of modified Zeiss fundus camera and optical separator. The original fundus camera is indicated by the stippling. B, A photograph of the modified Zeiss fundus camera and optical separator.
nm. and 520 nm., respectively), but the pigment epithelium and macular xanthophyll which overlie the choroid are inefficient transmitters of visible light energy up to about 700 nm. (see Fig. 1); (2) fluorescence of a fluorescein solution takes place most efficiently in a thin surface layer. Due to the increased distance of travel through the solvent, intensity of both excitation and emitted light energy in deeper layers of the solution are attenuated; and, to some extent, light energy emitted from fluorescein deep in the solution is reabsorbed before reaching the surface. In a similar way the presence of fluorescein in the retinal circulation reduces the efficiency of fluorescein fluorescence in the choroidal circulation. Indocyanine green dye, on the other hand, has its absorption spectrum in the near infrared region (near 800 nm.) where the pigment epithelium and macular xanthophyll are relatively transparent (see Fig. 1). When infrared light is used, indocyanine green dye is detectable in both the retinal and choroidal circulations. However, the greater volume of the choroidal circulation tends to overwhelm the lesser retinal volume in infrared absorption angiograms, and only the major retinal vessels are seen superimposed on the choroidal vasculature.¹¹

In general, absorption angiography differs from fluorescent angiography in that the latter involves a re-emission process following absorption of the incident light energy. A small body, such as a capillary can be photographic even though it is below the resolution limits of the optical system if it is self-luminous, as in fluorescent angiography. In absorption angiography, the resolution limit is determined by the characteristics of the entire optical system, consisting of the eye, camera, and film.

Fig. 1 also demonstrates the relative extent to which energy in the range of the excitation and emission spectra of sodium fluorescein and in the range of the absorption spectrum of indocyanine green is absorbed in passing through the entire human ocular media. In traversing the ocular media to the retina, approximately four times the amount of light energy is absorbed in the spectral range of sodium fluorescein (500 nm.) than in the spectral range of indocyanine green (800 nm.). In addition, upon reaching the pigment epithelium and choroid, approximately two times the amount of light energy is absorbed in the sodium fluorescein spectral range than in that of indocyanine green. Consequently, for choroidal angiography, infrared energy is more efficient than...
light energy in the visible region of the spectrum.

Fig. 1 further demonstrates that the wavelength of indocyanine green peak absorption (800 nm.) corresponds to the wavelength at which Falholt found oxyhemoglobin and reduced hemoglobin absorbed light energy equally (the isobestic point).12 If light energy at the wavelength of the isobestic point is used to photograph indocyanine green dye in the ocular vasculatures, its presence in both arterial and venous blood should be equally detectable. Consequently, in order to photograph the indocyanine green dye, a bandpass filter whose peak transmission matches the isobestic point is placed in front of infrared-sensitive film so that only light energy at 800 nm. reflected from the fundus strikes the film. After developing, areas of the film having received the least exposure will correspond to areas of the fundus where light energy was absorbed by indocyanine green dye rather than reflected back toward the camera. Since the dye is entirely confined to the blood vessels (as described below), the lightened film areas must correspond to those vessels.

Fluorescein rapidly diffuses through the vessel walls when it passes through the choriocapillaris and is slowly reabsorbed by subsequent blood flow. This rapid staining of interstitial choroidal tissue accounts for the diffuse "background flush" usually seen in fluorescein angiography. Yet, virtually no extravasation of dye from the choriocapillaris is observed when indocyanine green dye is used. Perhaps the single most important factor in determining the ability to visualize the choroidal vasculature with indocyanine green dye but not with fluorescein is the difference in tendency to bind with blood protein exhibited by each of the two dyes. In blood, from 40 to 85 per cent of injected fluorescein is bound to albumin, whereas 98 per cent of injected indocyanine green is bound to albumin.13-15

Methods

Dye mixture. It should be noted that indocyanine green may not ultimately be the ideal dye for choroidal angiography. However, indocyanine green dye, like sodium fluorescein dye, is a Food and Drug Administration-approved drug, and it has an extensive history of clinical application for purposes other than angiography with no evidence of untoward effects as a survey of the literature shows; choosing it to the exclusion of other non-approved dyes for use in clinical choroidal angiography is, therefore, based primarily on practical considerations.

Although ideally the amount of dye injected should be based on each patient's weight, in keeping with the usual practice of giving the same...
Fig. 4 B-I. For legend see page 252.
standard dose of fluorescein to all adults, a standard dose of the dye mixture was administered to each patient. That dose of dye mixture consisted of 150 mg. of indocyanine green dye dissolved in 3 ml. of 10 per cent sodium fluorescein (i.e., 300 mg. of fluorescein). The dye mixture was administered by rapid injection into the patient's cubital vein. The amount of indocyanine green dye used is within the recommended dose range of 2 mg. per kilogram for the average adult and well below the maximum doses which have been reportedly administered.

Both dyes are virtually chemically inert, and mixing the two together does not alter the physical or spectroscopic properties normally exhibited by either of the dyes individually. Nevertheless, prior to using the dye mixture in human subjects, it was repeatedly administered to 20 rhesus monkeys in doses up to 25 times greater than that given to human subjects, based on body weight and no untoward reactions whatever were observed in any of the monkeys.

Zeiss fundus camera modifications. A Zeiss fundus camera has been modified by several internal changes and by the addition of a new camera recording system. A diagram illustrating the modifications and additions is shown in Fig. 2, A and a photograph of the completed instrument is shown in Fig. 2, B.

A filter holder was placed between the flash lamp and its condenser lens system (Fig. 2, A-O). Filters may also be introduced between the flash lamp condenser lens system and the focusing lamp beam splitter where they are better protected from the heat generated by the flash tube.

An electrically operated shutter was placed just below the focusing lamp (Fig. 2, A-N), and an infrared absorbing filter (Corning 1-69) was placed between the lamp and shutter to protect the shutter blades from heat damage. When a picture is taken, the shutter is automatically closed; it is otherwise kept open for focusing by the observer. A number 47 Wratten filter was placed in the new filter holder instead of in the usual filter wheel provided; thus, white light can be used for viewing without interfering with the blue illuminating light needed for film exposure. Tracking patient movements and focusing is made much easier and more convenient for the photographer.

A new electrical switching system was incorporated by adding two microswitches whose activation is synchronized with the moving mirror in the focusing eyepiece head of the fundus camera. One microswitch activates a relay which closes the electronic shutter below the focusing lamp. A second microswitch is activated when the mirror reaches its full open position and activates the
Fig. 5 B-I. For legend see page 254.
two motorized 35 mm. cameras, initiating the picture-taking sequence.

The observer’s eyepiece and the diagonal mirror which directs the focusing beam from the hinged mirror in the eyepiece head of the fundus camera were rotated 90 degrees to avoid mechanical interference with the optical separator addition. The eyepiece rotation introduces left-right and top-bottom reversals, but the observer quickly accommodates for these orientation changes after using the instrument several times.

A simple patient dental bite was also added to the fundus camera head holder to improve the stability of the patient’s head during angiography. This has been of considerable help in obtaining improved serial angiograms.

The optical separator. The major change in the fundus camera operation results from the addition of a newly designed optical separator system. The system includes filters, relay lenses, twin motorized camera bodies, and a dichroic beam splitter all of which function to separate the infrared reflected energy and visible fluorescent light entering the fundus camera from the eye, suitably filter both beams, and simultaneously record separate pictures from each single flash.

As indicated in Fig. 2, A, light from the patient’s eye is split by a dichroic beam splitter (Liberty Mirror No. 956-1). Visible fluorescent light is reflected by the beam splitter to the upper camera body (Nikon F-36); this camera contains Tri-X film (Eastman Kodak Company, Rochester, N. Y.), sensitive only to visible light. Infrared energy is transmitted through the beam splitter and is recorded on infrared-sensitive film (Eastman Kodak Company High-speed Infrared) in the other Nikon camera body. The Nikon cameras are motor-driven and are capable of taking pictures up to 4 frames per second. The frequency at which angiograms may be taken with this system is limited by the length of the flash unit recycling time. Our angiograms are currently taken at a frequency of one per 1.5 seconds, which is an insufficient time resolution to adequately record the dynamic changes in the choroidal circulation. We intend to improve the time resolution by using the newer Fundus Flash Two with a booster which will permit firing the flash tube every half-second.

The Zeiss fundus camera forms a real image of the patient’s retina at a point posterior to the hinged mirror in the eyepiece head. At this image plane, a 35 mm. diameter, 130 mm. focal length field lens was placed to relay an intermediate image of the patient’s iris into the aperture stop of the relay lenses. This prevents vignetting of these images in the film planes of the two Nikon cameras.

The intermediate images, visible and infrared, of the patient’s retina are relayed to the film planes by 55 mm. focal length Micronikor f/3.5 lenses (Nikon Camera Co., Tokyo, Japan). The cameras were positioned to give an image reduction of approximately 80 per cent in order to provide a focusing range to permit correction of machine tolerances and for unknown infrared chromatic corrections. The full aperture of these lenses is not needed; they are usually closed to an aperture of f/5.6 to reduce stray light at the film plane.

The infrared beam has in its path two thick pieces of glass (¼ inch each), namely, the beam splitter and the interference filter. To correct for the increased optical path’s length, the infrared beam path was lengthened by ½ of the total glass thickness, approximately ¼ inch. In addition to this correction, corrections were made for chromatic aberration of the camera lens systems and the chromatic aberration of the eye. These combined corrections caused the infrared film images to be slightly larger than those of Tri-X film fluorescent images.

Optical filters. For a discussion of the optical components that are used in this fundus camera system, it is useful to divide the system along two optical paths, one for the fluorescein angiograms and the other for the indocyanine green angiograms.

Fig. 3A shows all of the appropriate spectral curves for the fluorescein optical path. The light output of the flash lamp is flat with respect to wavelength when the individual spectral lines of xenon are averaged over any reasonable spectral bandwidth. Light from the flashtube passes through a Kodak Wratten No. 47 filter. Fig. 3A indicates that the No. 47 filter transmits in the blue between 400 to 500 nm. and that the dye mixture also absorbs energy in that region; absorption in this region is due only to fluorescein.

Fluorescein emits energy between 500 to 600 nm., and this light energy is transmitted by the No. 15C Wratten filter and recorded on Tri-X film after being reflected from the surface of the dichroic beam splitter. The No. 15C filter prevents the blue excitation light from reaching the film. This filtering technique is more or less standard for most fluorescein angiography and is quite well documented.

Fig. 4B shows the curves appropriate to the optical path for indocyanine green angiography. Light from the flash lamp is transmitted by the No. 47 filter which, in addition to the blue peak, has a transmission peak in the near infrared spectrum above 700 nm. The dye mixture has a strong absorption near 800 nm. due to the indocyanine green. The 15C filter in front of the optical separator transmits infrared light energy as well as fluorescent light energy. Light energy at approximately 770 nm. is transmitted by the 15 nm. wide bandpass interference filter (Baird-Atomic, Bed-

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ford, Mass.) and is recorded on Kodak High-Speed Infrared film after being transmitted through the dichroic beam splitter (Liberty Mirror 956-1).

**Photographic films.** Kodak Tri-X and Kodak High-Speed Infrared films were selected for use in the dual cameras of the optical separator; the sensitivities of these two film emulsions are indicated in Fig. 3. The relative sensitivity and resolution for various development times for the two films were determined by photographing with the modified fundus camera a small standard resolving power chart (AF 1951) mounted behind a 32 mm. microscope objective to simulate the optics of the eye. Exposure of the film was varied from photograph to photograph, and the exposed films were developed at 70°F. in Kodak D-11 (diluted 1:1) or in Kodak X-ray developer which is similar to D-19. The results of this experiment are summarized in Tables I and II.

The fluorescein pictures on Tri-X film give consistently good results when developed in D-11 for 6 minutes, and the High-Speed Infrared film needs only minor variations in development from patient to patient for optimum results. These variations are brought about by changing the amount of indocyanine green dye injected or by the varying degrees of pigmentation in different patients. An educated guess as to the correct development time was found to be satisfactory. The data in Table I support this observation; for in D-11, Tri-X film sensitivity does not change greatly from 6 to 12 minutes, while the infrared film sensitivity changes by a factor of 2. Thus, with D-11 developer, the desired small changes in infrared film sensitivity needed to offset the variation in pigmentation from patient to patient may be achieved by varying development time, while the Tri-X film sensitivity remains almost constant.

Film resolution is a function of film exposure, but this is only a slowly varying function. The data in Table II indicate that the film resolution also varies somewhat with developers and development time—but again not drastically so. The results of the experiment indicate that the best resolution which can be achieved in photographing the ocular fundus with the modified fundus camera is approximately 7 to 8 microns. A carefully focused fluorescein retinal photograph was taken and the smallest visible vessel diameters measured; this also indicated a retinal resolution of about 7 microns. The best visual resolution through the fundus camera eyepiece is about 4 microns which indicates that the resolving power of the film is a major limiting factor for ultimate resolution.

In order to get the maximum possible choroidal detail on the infrared film, the fact that the choroid is behind the retinal plane must be taken into account. Therefore, the film plane of the infrared film camera on the optical separator was moved approximately 1.2 mm. toward the Zeiss fundus camera. For a magnification of 2.5 from fundus to film, this change of 1.2 mm. in the film focal plane corresponds in the eye to a change in focal plane of about 200 microns posterior to the retina.

Resolution was also determined as a function of focus with the focus knob of the Zeiss Fundus camera. When this knob is turned 3/4 of a revolution, the best visual focus through the eyepiece changed from 4 to 7 microns. Therefore, without very careful focusing by the observer, the best resolution possible (i.e., the film-limiting resolution) in photographing the ocular fundus will not be reached.

**Results**

To date simultaneous angiograms using this technique have been made of 47 patients. One example of these angiograms has been previously published, and two others are presented here. As with the previous example, the selected pairs of angiograms shown in Figs. 4 and 5 were selected to correspond to the major phases of filling associated with standard fluorescein angiography.

The angiograms in Fig. 4 were made of a 69-year-old female Caucasian with a macular degeneration. Ophthalmoscopy showed clear ocular media with disc and vessels within normal limits. There was an elevation of the retinal pigment epithelium and sensory retina in the area of the macula, and some thickening of the retina was evident. There was no evidence of wrinkling of the internal limiting membrane or cystoid change in the retina. A red-free photograph of the fundus is shown in Fig. 4A.

The fluorescein angiograms (Fig. 4 B through E) indicate a normal filling pattern except in the macular area where considerable leakage occurs around the edge of the lesion. The field shown in these angiograms was chosen to show an area of normal fundus as well as the macular lesion. In the later phase of the angiograms, a large sensory epithelial detachment extending from the superotemporal down to the inferior temporal vessels is seen.
Table I. Relative film sensitivity

<table>
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<th>Developer and Developer time</th>
<th>Tri X relative sensitivity</th>
<th>High-Speed infrared sensitive sensitivity</th>
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<tr>
<td>D 11* 3 min.</td>
<td>1</td>
<td>1</td>
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<tr>
<td>D 11* 6 min.</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>D 11* 12 min.</td>
<td>2+</td>
<td>4</td>
</tr>
<tr>
<td>X-ray 3 min.</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>X-ray 6 min.</td>
<td>1+</td>
<td>4</td>
</tr>
<tr>
<td>X-ray 12 min.</td>
<td>2</td>
<td>4+</td>
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*Diluted 1:1; + sign indicates slightly greater values.

Table II. Film resolution (equivalent resolution on retina in microns)

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<tr>
<th></th>
<th>X-ray 3 min.</th>
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<tr>
<td>D 11* 3 min.</td>
<td>7.0</td>
<td>7.0</td>
<td>7.0</td>
</tr>
<tr>
<td>D 11* 6 min.</td>
<td>7.9</td>
<td>7.9</td>
<td>7.9</td>
</tr>
<tr>
<td>D 11* 12 min.</td>
<td>7.0</td>
<td>7.0</td>
<td>7.0</td>
</tr>
<tr>
<td>X-ray 3 min.</td>
<td>6.3</td>
<td>7.0</td>
<td>7.0</td>
</tr>
<tr>
<td>X-ray 6 min.</td>
<td>7.0</td>
<td>7.0</td>
<td>7.9</td>
</tr>
<tr>
<td>X-ray 12 min.</td>
<td>7.0</td>
<td>8.2</td>
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Simultaneously made infrared absorption angiograms (Fig. 4 F through I) show the filling of choroidal vessels in the same eye. It is possible to see both major retinal arteries and veins superimposed over the choroidal vasculature throughout the series of angiograms. This is due to the fact that the volume of indocyanine green dye contained in the larger retinal vessels is sufficient to better absorb the infrared light impinging on the retina than the underlying choroidal vessels. Some residual staining in the area of the macular lesion can be seen in Fig. 4 H and I.

The second set of angiograms is of a 26-year-old male Caucasian who had a history suggesting night blindness since age 4. Ophthalmoscopy at that time indicated only a possible abnormal pigment distribution. Subsequent examinations indicated gradual pigmentation changes progressing to a retina of mottled appearance which led finally to depigmentation of the retina. The red-free photograph (Fig. 5A) shows the retinal vascular pattern and depigmentation so that choroidal vessels are clearly seen.

A comparison of the fluorescein angiograms (Fig. 5B through E) and the infrared absorption angiograms demonstrates the clarity of visualization of filling of the larger choroidal vessels which may be achieved by use of indocyanine green dye. In this case, since retinal pigment is absent, improved visualization of the choroidal vessels is attributable solely to the fact that while unbound fluorescein extravasates into choroidal tissue, thus obliterating choroidal vascular detail, indocyanine green is confined to the choroidal vessels. This is particularly obvious in the later arterial filling phase, Fig. 5C and G, even though the vascular patterns appear to be somewhat unusual.

Discussion

Comparison of simultaneous fluorescein and indocyanine green angiograms. It is clear from the examples which have been shown that the choroidal vessels seen in infrared absorption angiograms are not as clear and well resolved as the retinal vessels seen in fluorescein angiograms. The reason for this is twofold: (1) The vessels of the retina are effectively confined to a two-dimensional plane and fill at right angles to the optical axis. The choroid, on the other hand, is composed of a network of convoluted vessels which lie in three distinct, major layers and, unlike the retinal vasculature, this three-dimensional volume of vessels tends to fill parallel to the optical axis of the eye. (2) As mentioned earlier in the section entitled "Principle," higher resolution may be achieved in photographing selfluminous bodies such as are seen in fluorescein angiography than may be achieved in absorption angiography where the resolution limit is determined by characteristics of the entire optical system including the eye being photographed. Nevertheless, the technique of infrared absorption angiography does permit uninterrupted visualization of the choroid throughout its filling with indocyanine green dye.
which cannot be accomplished with fluorescein angiography except in cases where unusual anatomic conditions exist.

Because of the complex vascular pattern of the choroid, what constitutes normal choroidal filling in a healthy eye or what characteristics are indicative of a particular pathologic condition can be determined only after a sufficiently large volume of data on human subjects has been accrued. Therefore, at this time a few examples of simultaneous angiograms are presented solely to demonstrate the technique which is the subject of this report. The clinical applications of the technique and interpretation of the simultaneous angiograms are deferred as the subject of a future study.

**Visualization of the choriocapillaris.** A clear visualization of the choriocapillaris filling is not to be expected of infrared absorption angiography. Since the choriocapillaris is a relatively uniform, thin layer of vessels, and although there is no extravasation of indocyanine green dye from them into choroidal tissue, the absorptive capacity of dye in these vessels is small by comparison to that of the dye contained in the larger, underlying choroidal vessels. Consequently, viewing the filling of the larger choroidal vessels through the choriocapillaris in infrared absorption angiography is analogous to viewing them through an optical filter with fairly high transmission capabilities. However, use of indocyanine green dye might make possible visualization of the choriocapillaris specifically by making use of the fact that indocyanine green dye does, under some conditions, fluoresce in the near infrared region of the spectrum.

Indocyanine green dye has an emission
spectrum with a maximum wavelength near 845 nm. Consequently, fluorescent infrared angiography of the eye can be done in much the same way as standard fluorescein angiography; that is, an appropriate filter (one which does not transmit energy above 800 nm.) is placed in front of the excitation light source, and an appropriate barrier filter (Wratten Gelatin Filter No. 87C) which cuts out the lower wavelengths, including the excitation wavelength, is placed in front of the infrared-sensitive film. In terms of the photographic technique employed, the difference between visible and infrared fluorescent angiography lies only in the fact that each is done within a different spectral range. In terms of the resulting angiograms, however, the difference could be highly significant.

Indocyanine green is not as efficient a fluorescing dye as sodium fluorescein, the former being about 30 per cent maximum efficient while the latter is nearly 100 per cent efficient. Indocyanine green dye, therefore, would not be a likely substitute for angiography of the retinal vessels. However, since the dye does not extravasate from the choriocapillaris and since dye fluorescence is primarily a surface phenomenon, fluorescent indocyanine green dye might be detectable in the choriocapillaris in spite of its concurrent presence in the larger, underlying choroidal vessels.

Fig. 6 shows four frames of a fluorescent indocyanine green angiographic study made at a frequency of one every 0.6 seconds. The angiograms were made of a young woman with a histoplasmosis-like lesion in the macular region. Note that the first filling of the retinal arteries is seen in Fig. 6, D approximately 1.8 seconds after its appearance in the choroidal arteries. In the later frames, all detail becomes lost because of the graininess of the film caused by maximum forced development. This problem, which prohibits visualization of the details of the choroidal capillaries, might be overcome by using an image intensifier in front of the camera so that less grainy film than the high speed infrared can be used. Such a modification to our present camera system is now underway.

Grateful acknowledgment is made to Mr. Charles F. Bradley (A.P.L.) who, in addition to contributing to its design, constructed the optical separator and Mr. Salvatore D’Anna (J.H.M.I.) for his technical assistance. The indocyanine green dye (Cardio-Green) used in this study was generously provided by Hynson, Westcott & Dunning, Baltimore, Md. In addition to that of Drs. A. E. Maumenee and A. P. Patz, we appreciate the advice and encouragement of Drs. I. P. Pollack, S. J. Ryan, C. J. Courgott, H. S. Schatz, and D. H. Nicholson.

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