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Indocyanine Green Angiograms of Choroidal Nevi: Comparison Between Confocal and Nonconfocal Scanning Laser Ophthalmoscope and Fundus Video Camera

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Purpose: A fundus video camera and a nonconfocal scanning laser ophthalmoscope (SLO) detect direct light and indirect light, whereas a confocal SLO detects mostly direct light. Differences in confocal and nonconfocal SLO images and fundus video camera images are most likely due to their different optical systems. These differences were examined in indocyanine green (ICG) angiograms of a choroidal nevus.

Methods: A confocal SLO, a nonconfocal SLO, and a high resolution digital fundus video camera were used to obtain ICG angiograms of pigmented choroidal nevi in 4 patients for 30 minutes following dye injection.

Results: All the angiograms showed a hypofluorescent region in the nevus until 10–14 minutes after dye injection, except in 1 patient in whom no hypofluorescent region was seen in an early confocal-SLO angiogram. From 20 minutes to 30 minutes postinjection, the hypofluorescent regions were still visible in all fundus video camera angiograms and nonconfocal SLO angiograms but not in confocal SLO angiograms.

Conclusions: Early angiograms taken with the three angiography systems showed a similar appearance of the choroidal nevus. However, late ICG angiograms with a confocal SLO showed different images from those taken with a nonconfocal SLO or a fundus video camera. It is suggested that the angiography system and the aperture size of an SLO should be selected according to the aspect of the pigmented choroidal nevus that is of interest in late-phase ICG angiography. **Jpn J Ophthalmol 2001;45:368–374**

Key Words: Choroidal nevus, confocal scanning laser ophthalmoscope, indocyanine green angiography.

Introduction

Indocyanine green (ICG) angiography is performed using either a scanning laser ophthalmoscope (SLO) or a fundus video camera. Two kinds of SLOs are available: a confocal SLO[1] and a confocal and nonconfocal changeable SLO.[2] A confocal SLO has a small aperture in front of a photodetector, and a focus point illuminated by a laser is optically conjugate to the aperture. Light scattered back directly from the focus point converges on the confocal small aperture and passes through it.[3–8] Light that is scattered back directly from a plane of the laser focus is called direct light.[3] Other light that is scattered at a point outside the focused plane or comes from a point lying off the optical axis is blocked by the aperture.[3–8] The aperture excludes light that has been scattered within the plane of focus.[5,6,8] This blocked light is called indirect light.[3] These optical characteristics make optical sectioning possible in fundus tissue such as an optic disc[9] or a macula.[10] A combination of ICG angiography and optical sectioning is used for observing tumor vessels inside a choroidal melanoma[11] and examining the depth of subretinal neovascular membrane.[12]

Unlike a confocal SLO, a nonconfocal SLO and a

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fundus video camera detect both direct and indirect light from the fundus.[4,6,8] A fundus video camera detects more indirect light than a nonconfocal SLO does when flash is used at the late phase. Laser scanning in both types of SLOs produces less indirect light because of the small laser spot sizes (10–20 μm) on the retinas.[4,8] Thus, a video camera detects indirect light the most, and a confocal SLO detects it the least. Because indirect light reduces contrast in an angiogram,[4] a confocal SLO is thought to produce the clearest image among the three ICG angiography systems. Additionally, the differences in optical characteristics between a confocal SLO and the other two systems are reported to produce different images on ICG angiograms, even in the same fundus. Such differences have been examined only in fundi of serous detachment of retinal pigment epithelium, and indirect light via scattering of fluorescent light in turbid serous fluid was reported to produce a bright region in a fundus video angiogram but not in a confocal SLO angiogram.[8] These differences in ICG angiograms may not be rare. We have been taking multiple ICG angiograms with the different angiography systems on the same patients with fundus diseases,[13] and we have found distinct appearances of a pigmented choroidal nevus in late ICG angiograms.

Materials and Methods

The data collected for this study came from two time periods in which a confocal SLO (Heidelberg Retina Angiograph (HRA); Heidelberg Engineering, Heidelberg, Germany) was used in conjunction with two other noncofocal ICG angiography systems at the same angiography session: one period from May 1996 through October 1996 and the other period from March 1998 through April 1998. During these periods, ICG angiography with the confocal SLO was performed in 48 patients. Among the 48 patients, 4 eyes of 4 patients had choroidal nevus at a posterior pole. They were 42-, 56-, 70-, and 74-year-old men. The 56- and 74-year-old patients (patient 1 and patient 2, respectively) had only a choroidal nevus in their fundi. The 70-year-old patient (patient 3) suffered from age-related macular degeneration in a different region of the same fundus, and the 42-year-old patient (patient 4) suffered from idiopathic choroidal neovascularization in the contralateral eye. Before angiography, the purpose of this study was fully explained, and informed consent was obtained from the patients. This study was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

As shown in the flow chart of Figure 1, early-

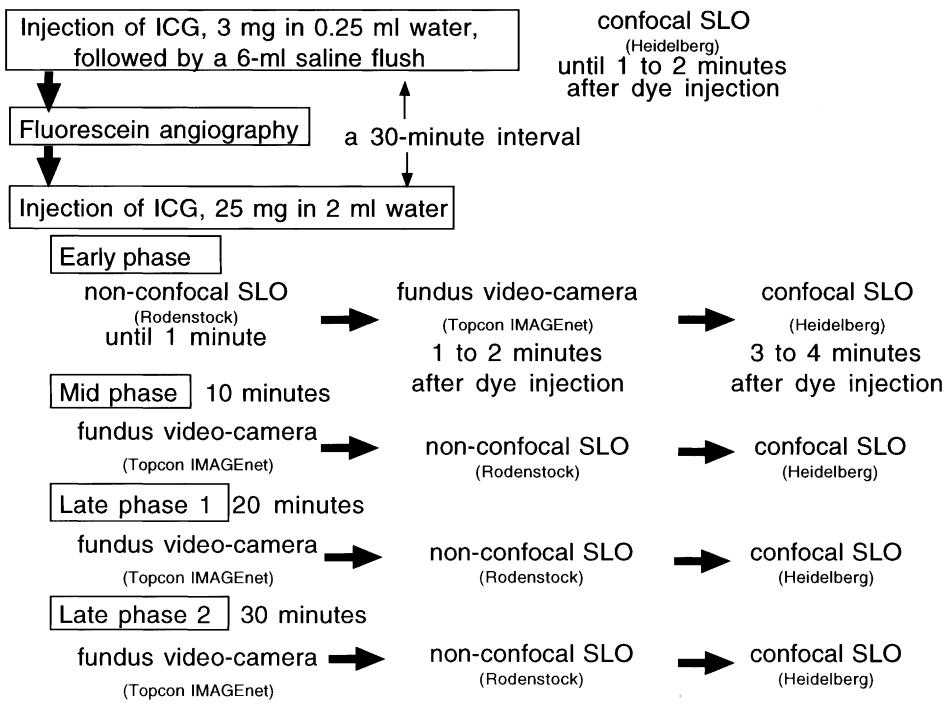

Figure 1. Flow chart of indocyanine green angiography and fluorescein angiography.

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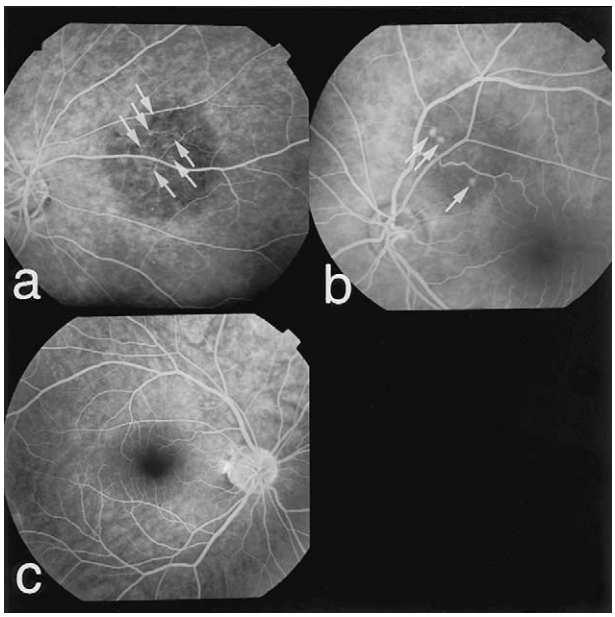

Figure 2. Patients 1, 2, and 4; fluorescein angiograms. (**a**) Patient 1: 1 minute, 3 seconds. (**b**) Patient 2: 1 minute, 21 seconds. (**c**) Patient 4: 3 minutes, 56 seconds. Angiograms show region of decreased background fluorescence at nevus area in patient 1 and patient 2, but not in patient 4. Scattered hyper- and hypofluorescent spots and small hyperfluorescent patches are noted in patients 1 and 2 [arrows in (**a**) and (**b**)].

phase ICGl angiograms were taken first with the confocal SLO, which had a 400-μm diameter barrier filter, until 1–2 minutes after dye injection. Then the ICG angiography was stopped, and fluorescein angiography was performed in succession. About 30 minutes after the initial ICG angiography, ICG angiography was repeated with the quick, successive use of the three systems: the confocal SLO, a nonconfocal SLO (Rodenstock, München, Germany), which is a first generation SLO with a 22-mm diameter barrier filter, and a high resolution fundus video camera (IMAGEnet system, Topcon, Tokyo). The order in which the three angiography systems were used and the schedule for angiograms are summarized in Figure 1. In this study, the early phase of ICG angiography was defined as up to 5 minutes after dye injection. The late phase was defined as 20 minutes or more after dye injection. The period between these two was defined as mid phase.

Results

Fluorescein Angiography

Fluorescein angiograms showed a region of decreased background fluorescence at a nevus area in 2 patients (patient 1, Figure 2a; patient 2, Figure 2b) but no abnormality in the other 2 (patient 3; patient 4, Figure 2c). Scattered hyper- and hypofluorescent spots were noted in patient 1 (arrows in Figure 2a), and small hyperfluorescent patches corresponding to drusen were observed in patient 2 (arrows in Figure 2b).

Indocyanine Green Angiography

Because the largest difference between systems occurred in late angiograms of the fundus video camera and those of the confocal SLO, late angiograms of these two systems are presented, except for patient 1.

Early ICG angiograms taken during the first 5 minutes after dye injection showed hypofluorescence throughout the nevus region in 3 of the 4 patients (eg, patient 1: Figures 3a, 4a, and 5a); patient 4

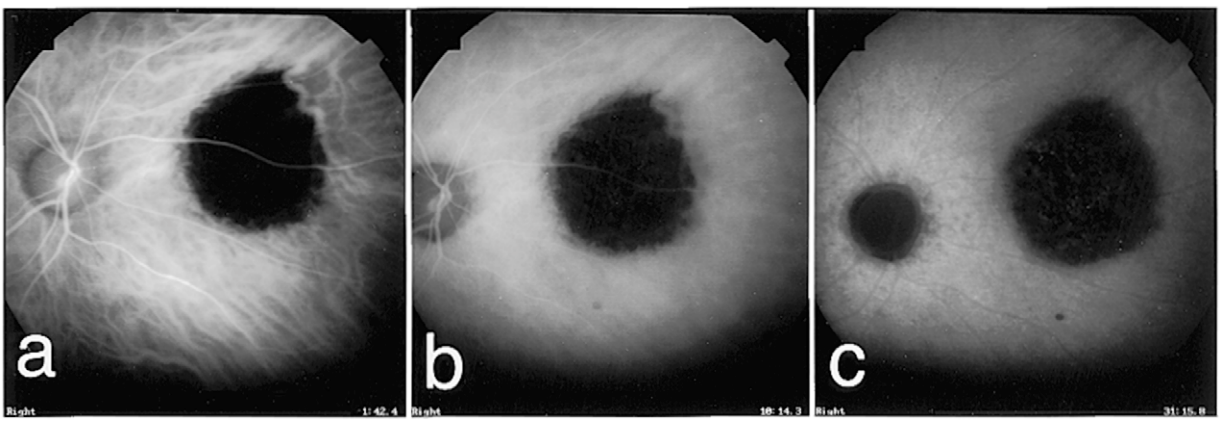

Figure 3. Patient 1; fundus video camera indocyanine green (ICG) angiograms. (a) 1 minute, 42 seconds. (b) 10 minutes, 20 seconds. (c) 31 minutes. Hypofluorescent region of choroidal nevus is seen until late phase. [Figure 3(**c**) from Shiraki et al[13], reprinted with permission.]

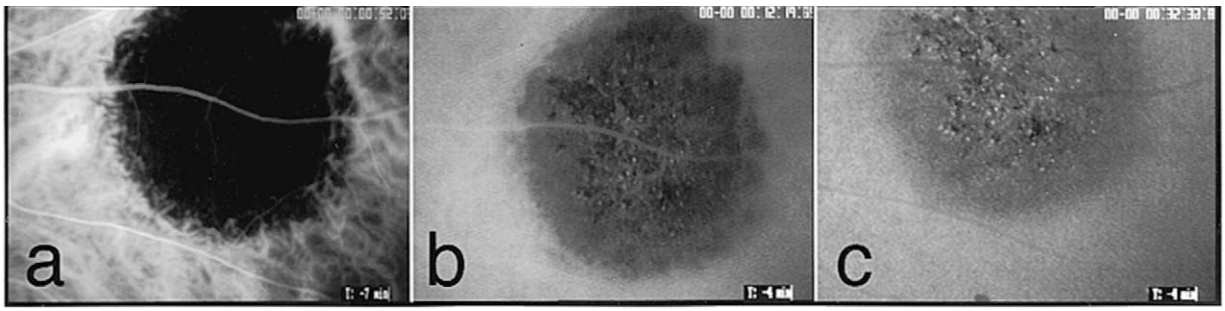

Figure 4. Patient 1; nonconfocal scanning laser ophthalmoscope indocyanine green angiograms. (**a**) 52 seconds. (**b**) 12 minutes, 19 seconds. (**c**) 32 minutes. Hypofluorescent region of choroidal nevus lasts until late phase. Scattered hyper- and hypofluorescent spots are noted at mid-phase (**b**) and more clearly at late phase (**c**). [Figure 4(**c**) from Shiraki et al[13], reprinted with permission.]

showed no hypofluorescence with all systems. Mid-phase ICG angiograms taken 10 to 15 minutes after dye injection continued to show hypofluorescent regions, and the regions were surrounded by a ground-glass appearance of fluorescence in all 4 patients with all the systems (eg, patient 1: Figures 3b, 4b, and 5b). Late ICG angiograms taken 20 minutes or more after dye injection continued to show similar hypofluorescent regions in fundus video camera angiograms and nonconfocal SLO angiograms in all patients (patient 1, Figures 3c and 4c; patient 2, Figure 6a; patient 4, Figure 7a) but not in confocal SLO angiograms (patient 1, Figure 5c; patient 2, Figure 6b; patient 4, Figure 7b).

The late confocal SLO angiograms of patient 1 showed only a scattered appearance of hyper- and hypofluorescent spots (Figure 5c), which were seen also in the late nonconfocal SLO angiogram (Figure 4c) and were seen faintly in the late video fundus camera angiogram (Figure 3c).The late confocal SLO angiograms taken in patient 2 similarly showed only scattered hyperfluorescent patches (Figure 6b), which were seen also in the late video fundus camera angiogram (Figure 6a). Three hyperfluorescent patches corresponded to drusen (arrows in Figures 6a, 6b). In late confocal SLO angiograms of patient 3 and patient 4, choroidal nevi had disappeared without leaving any findings relevant to the nevi (Figure 7b).

Discussion

Our results indicate that early ICG angiograms taken during the first 5 minutes after dye injection usually show hypofluorescent regions of choroidal nevi, irrespective of the angiography system used. However, late ICG angiograms taken 20 minutes or more after dye injection continue to show hypofluorescent regions with a video fundus camera and non-

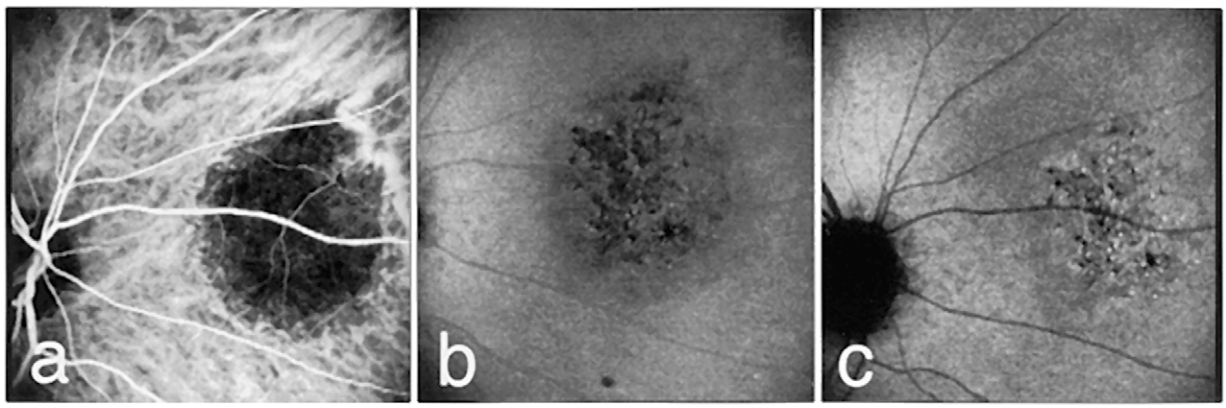

Figure 5. Patient 1; confocal nonconfocal scanning laser ophthalmoscope indocyanine green angiograms. (**a**) 1 minute, 41 seconds. (**b**) 14 minutes, 9 seconds. (**c**) 33 minutes. Hypofluorescent region of nevus is seen at early phase (**a**). Hypofluorescent region is barely noted in mid-phase angiogram (**b**). However, late angiogram (**c**) shows only scattered hyper- and hypofluorescent spots. [Figure 5(**c**) from Shiraki et al[13], reprinted with permission.]

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confocal SLO, but the hypofluorescent regions of the nevi disappear in late confocal SLO angiograms.

ICG fluorescent light that reaches a detector of an angiography system can be direct light or indirect light (Figure 8, left column). Excitation light hits the dye directly at a focus plane and fluorescent light is emitted. The fluorescent light that is transmitted directly back to a detector is direct fluorescent light. In contrast, indirect fluorescent light comes via various other pathways. First, fluorescent light emitted from a dye from a focal plane is scattered at the sclera, and the scattered fluorescent light is transmitted back to the detector. As a second pathway, excitation light can be scattered similarly at the sclera. The scattered excitation light hits the dye to produce indirect fluorescent light.

In the early phase, ICG dye is within a choroidal vascular lumen, and a choroidal nevus blocks any fluorescent light emitted from underlying choroidal vessels. A fundus video camera and a nonconfocal SLO detect the decreased intensities of both direct and indirect fluorescent light over the nevus, and the two systems show the nevus as a hypofluorescent region (Figure 8, upper left). A confocal SLO detects decreased intensity of direct fluorescent light over the nevus and shows the nevus similarly as a hypofluorescent region (Figure 8, upper right) unless the nevus is thin enough so that the infrared fluorescent light can penetrate it. Therefore, all three angiograms show the nevus as a hypofluorescent region in the early phase. Toward the mid phase, ICG dye gradually diffuses from choriocapillaries to an extravascular space[14,15] and produces the ground-glass

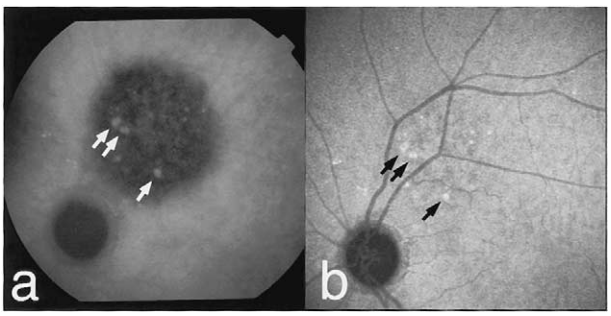

Figure 6. Patient 2; late indocyanine green angiograms. (**a**) Fundus video camera angiogram, 32 minutes. (**b**) Confocal scanning laser ophthalmoscope angiogram, 35 minutes. Fundus video camera angiogram (**a**) shows hypofluorescent appearance of choroidal nevus along with diffuse faint fluorescence covering nevus area. Confocal scanning laser ophthalmoscope angiogram (**b**) no longer shows hypofluorescent nevus. Small hyperfluorescent patches are noted at drusen in both angiograms (arrows).

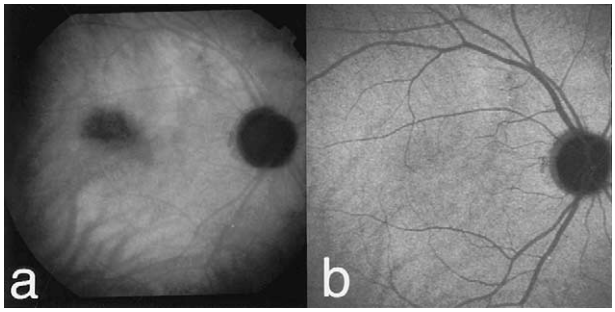

Figure 7. Patient 4; late indocyanine green angiograms. (**a**) Fundus video camera angiogram, 31 minutes. (**b**) Confocal scanning laser ophthalmoscope (SLO) angiogram, 35 minutes. Hypofluorescent region of choroidal nevus, which is clearly noted in fundus video camera angiogram (**a**), is no longer apparent in confocal SLO angiogram (**b**).

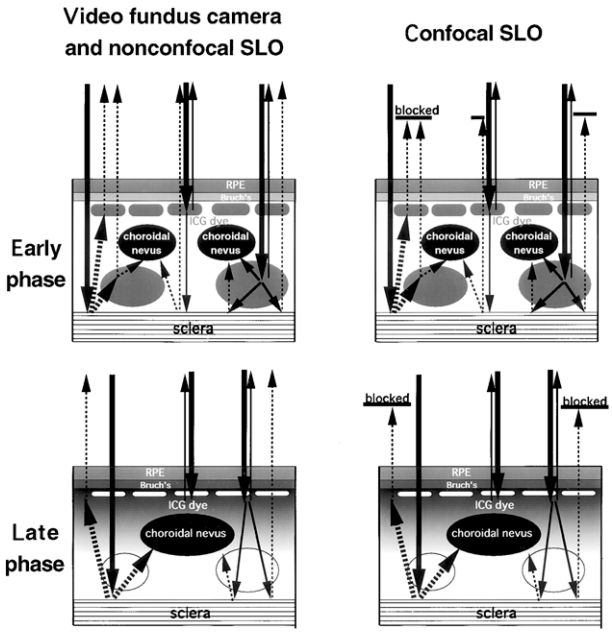

Figure 8. Pathways of excitation light and fluorescent light reaching and emitting from fundus with choroidal nevus in nonconfocal angiography systems and confocal scanning laser ophthalmoscope (SLO). Solid lines: direct light, interrupted lines: indirect light, thick lines: excitation light, thin lines: fluorescent light. Fundus video camera and nonconfocal SLO (left column) detect both direct and indirect light. Confocal SLO detects only direct light, and its aperture blocks indirect light (right column, blocked). At early phase (upper row), indocyanine green (ICG) dye is within choroidal vessels. At late phase (lower row), ICG dye is at Bruch's membrane-choriocapillary complex and at superficial choroid over nevus. RPE: retinal pigment epithelium, Bruch's: Bruch's membrane.

appearance of diffuse fluorescence seen around the hypofluorescent nevus. Thereafter, as the concentration of ICG dye decreases in plasma, the dye is gradually removed from the extravascular space of the choroid. If the dye concentration decreases evenly in the choroid, a confocal SLO would presumably show a hypofluorescent nevus because of a decreased amount of fluorescent light over the nevus. However, disappearance of hypofluorescent nevi in our late confocal SLO angiograms is contrary to this hypothesis. Because a confocal SLO detects only direct fluorescent light emitting from illuminated dye, the light pathway between the dye and a detector is not interrupted by a nevus. Therefore, the illuminated ICG dye is over the nevus, namely at a retinal pigment epithelium-Bruch's membrane complex and a superficial choroid (Figure 8, lower row). The results of recent histologic study with a fluorescence microscope support this hypothesis; ICG fluorescence was observed at the retinal pigment epithelium-Bruch's membrane complex 7 minutes after dye injection, and this fluorescence lasted until 50 minutes postinjection.[16] In our present study, the clearer appearance of scattered hyper- and hypofluorescent spots seen in patient 1 and hyperfluorescent patches of drusen[17,18] in patient 2 support the supposition that a late confocal SLO angiogram shows fluorescent light emitting from ICG dye at a retinal pigment epithelium-Bruch's membrane complex and a superficial choroid over the nevus.

In the late phase, fluorescent light that has been emitted from a retinal pigment epithelium-Bruch's membrane complex and a superficial choroid can be scattered at the sclera and transmitted back to a detector as indirect fluorescent light. In other pathways, excitation light is scattered at the sclera and may produce other indirect fluorescent light from ICG dye in a retinal pigment epithelium-Bruch's membrane complex and a superficial choroid. A fundus video camera and a nonconfocal SLO detect a decrease in intensity of these indirect fluorescent light transmissions over the nevus. Thus, the nevus appears hypofluorescent (Figure 8, lower left). When flash is used with a fundus video camera, more light scattering is produced, resulting in more contrast between the nevus and surrounding region.

Based on our present results, we consider that a late fundus video camera angiogram is suitable for determining the size of a pigmented mass in a choroid and that a late confocal SLO angiogram is useful for examining changes in a retinal pigment epithelium-Bruch's membrane complex and a superficial choroid. We suggest that the angiography system and the aperture size of an SLO should be selected according to the aspect of the pigmented choroidal nevus that is of interest in late-phase ICG angiography.

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