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Fluorescein and Indocyanine Green Videoangiography of Choroidal Melanomas

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Purpose: This study was performed to determine what role indocyanine green video angiography might play in the evaluation of choroidal melanomas, and to compare this role with that of fluorescein angiography.

Methods: Six patients with posterior segment uveal melanoma underwent digital fluorescein and indocyanine green videoangiography. All patients were women and their mean age was 50.7 years.

Results: In all eyes with melanoma, fluorescein angiography revealed irregular hyperfluorescence in the early phase and staining of the tumor in the late phase. A double circulation pattern was obvious in 1 eye with a mushroom-shaped melanoma. The patterns of indocyanine green videoangiography varied, depending on the degree of tumor pigmentation, thickness, and vascularity. Early frames of indocyanine green video angiography demonstrated hypofluorescence in all eyes, and the intrinsic choroidal vasculature was obvious in 3 eyes. In the late phase of indocyanine green videoangiograms, different patterns (hyperfluorescence, three-ring pattern) were observed.

Conclusion: Indocyanine green videoangiography may be a useful adjunct to fluorescein angiography in the evaluation of choroidal melanomas. **Jpn J Ophthalmol 1999;43:25–30**

Key Words: Choroidal melanoma, fluorescein angiography, indocyanine green videoangiography.

Introduction

A choroidal melanoma in its earlier stage of development is more likely to be observed clinically when it arises in or near the macular area. However, when the eye condition is complicated by hemorrhage, retinal detachment, glaucoma, or cataract, caution should be exercised in making the exact diagnosis.

Like other choroidal tumors, choroidal melanoma is usually diagnosed by indirect ophthalmoscopy.[1] Since McLean and Maumenee[2] described the intense staining of choroidal hemangiomas after an intravenous injection of fluorescein, angiography has become essential in the investigation and diagnosis of fundus mass lesions. In addition, fundus imaging techniques, e.g., fundus photography and fluorescein angiography, have the advantages of providing objective documentation of the growth of the tumor. However, it is not always possible to make a definitive diagnosis of a choroidal tumor on ophthalmoscopic and fluorescein angiographic characteristics alone, and other clinical modalities are often necessary.[3]

Indocyanine green (ICG) diffuses much more slowly from choroidal vessels because it is a more highly bound protein than sodium fluorescein. These properties make it suitable for imaging the choroidal vasculature. Several reports have stressed the usefulness of this dye in the evaluation of different chorioretinal disorders especially choroidal neovascularization.[4–6] Recently, different fluorescence patterns have been shown in choroidal tumors with ICG angiography.[7,8]

In this study, the ICG angiographic characteristics of choroidal melanomas are described and compared with the pattern obtained from fluorescein angiography.

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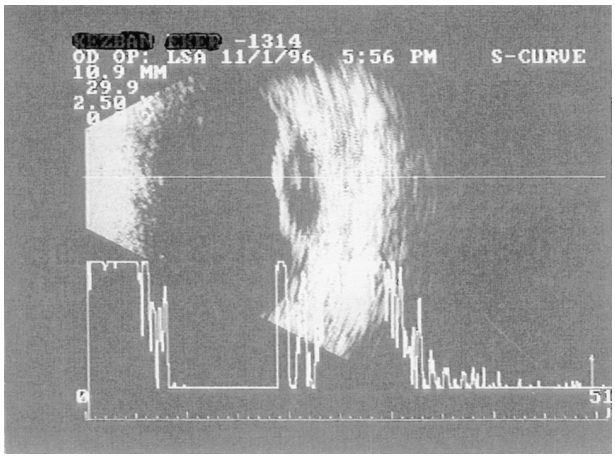

Figure 1. B-scan echogram showing dome-shaped melanoma (case 5).

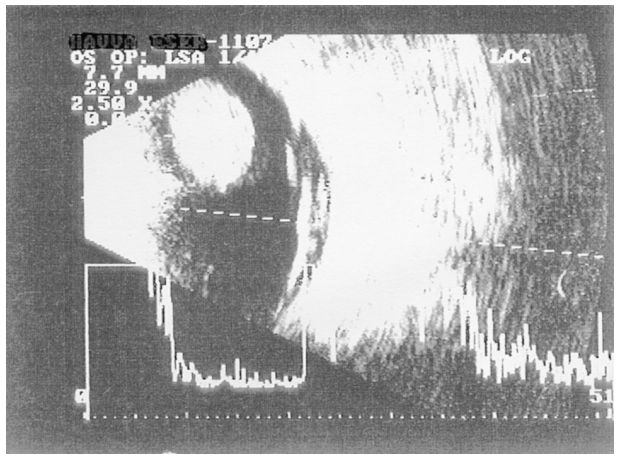

Figure 2. Mushroom-shaped melanoma demonstrating internal sound attenuation at base (case 2).

Materials and Methods

Six patients with choroidal melanoma were included in this study. All the patients were women. Their ages ranged from 39–65 years, with a mean age of 50.7 years. Routine examination of each patient included indirect ophthalmoscopy as well as direct ophthalmoscopy with Goldmann's three-mirror lens. Ultrasonography was done and color fundus photographs were taken of each patient's affected eye. The diagnosis was based on patient history and results of the "classic" examinations mentioned above.

Topcon ImageNET Digital Imaging System linked to a Topcon TRC 50 IA camera was used for angiography. Fluorescein angiography was performed by injecting 5 mL of 20% sodium fluorescein (S. E. R. B. Lab Pharmaceutiques). After the images had been downloaded to the optical disc, the ICG procedure was begun. For this, 25 mg ICG was dissolved in 1.5 mL aqueous solvent (S. E. R. B. Lab Pharmaceutiques) and injected, followed by a 5-mL sterile saline solution. The early, middle, and late phase angiograms were taken. Images were reviewed, then downloaded to the optical disc for storage and analysis. No complication occurred during the angiographies.

Results

Fundus examination of the 6 patients revealed a nonpigmented/hypopigmented tumor in 4 eyes, a pigmented tumor in one eye, and a centrally pigmented tumor in the sixth eye. The lesion was associated with retinal detachment in 4 eyes. The tumor was dome-shaped in 3 eyes and mushroom-shaped in 1 eye. The tumor localization was in the superior nasal quadrant in 2 eyes, temporal macular area in 3, and inferior equatorial region in 1 eye. B-scan echography showed typical findings of an uveal melanoma including acoustic quiet zone, choroidal excavation, and orbital shadowing (Figure 1). A quantitative A-scan demonstrated medium to low reflectivity. In 1 eye with a mushroom-shaped melanoma, B-scan echogram showed an echolucent area at the base of the tumor produced by sound attenuation (Figure 2). All eyes contained medium–large tumors, according to the echographic measurements (Table 1).

In 6 eyes with choroidal melanoma, irregular hyperfluorescence appeared during the arterial phase of the fluorescein angiography. This fluorescence increased markedly with time, and staining of the tumor was observed in the late phase (Figure 3). In 2 eyes, dot-like hyperfluorescent spots accompanied the diffuse hyperfluorescence (Figure 4). In the one eye with a mushroom-shaped melanoma, a double circulation pattern was obvious in the arterial phase (Figure 5).

Three eyes, 2 of which had a pigmented melanoma, showed hypofluorescence in the early phase of the ICG angiogram. In the other 3 eyes that had melanomas with lesser degrees of pigmentation, intrinsic choroidal vasculature was visible within 15 to 25 seconds. Late-phase angiograms demonstrated mild hyperfluorescence due to the leakage from these vessels (Figures 6 and 7). In 1 eye, with a large, pigmented choroidal melanoma, early frames of the ICG videoangiograms demonstrated dense central hypofluorescence within the tumor. In the late phase, a three-ring pattern of staining was seen: a central

Table 1. Patient and Tumor Characteristics

Case No.	Sex	Age	VA	Fundoscopy	Localization	Size (mm)	Treatment
1	F	60	3/10	Hypopigmented, large, RD	Superior nasal	13 × 10	External resection (epithelioid type)
2	F	38	2/10	Nonpigmented, mushroom-shaped, RD	Superior nasal	11 × 7.7	Enucleation (mixed type)
3	F	59	cf 30cm	Nonpigmented, dome-shaped, RD	Temporal macula	11.5 × 5.4	Enucleation (epithelioid type)
4	F	65	1/10	Pigmented, RD	Temporal macula	16.6 × 4.1	Proton irradiation
5	F	44	3/10	Nonpigmented dome-shaped	Temporal macula	10.9 × 5	I^{125} plaque, laser
6	F	38	3/10	Centrally pigmented, dome-shaped, RD	Inferior equatorial	12 × 5.5	I^{125} plaque, laser

RD: Retinal detachment; VA: Visual acuity.

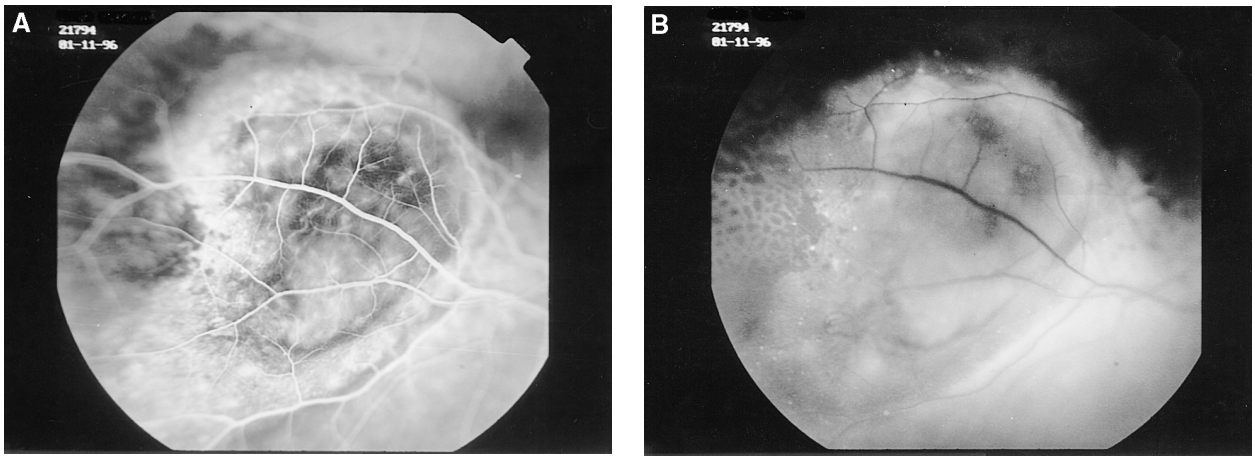

Figure 3. (**A**) Early venous phase fluorescein angiography of a choroidal melanoma showing irregular fluorescence (case 5). (**B**) Late venous phase of fluorescein angiography in the same eye.

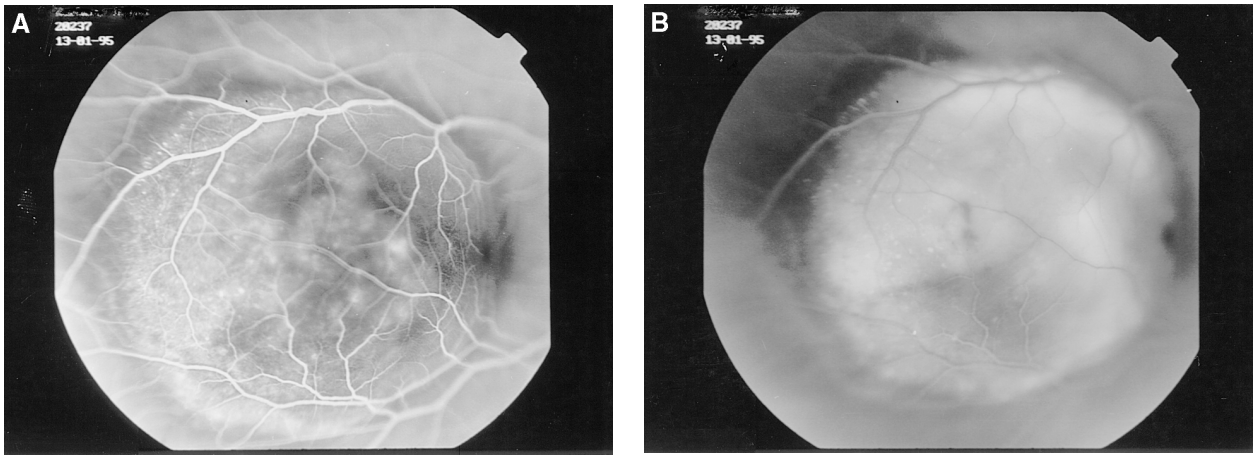

Figure 4. (**A**) Early venous phase of fluorescein angiography of a choroidal melanoma showing irregular fluorescence with dot-like hyperfluorescent spots (case 3). (**B**) Late venous phase of fluorescein angiography in the same eye.

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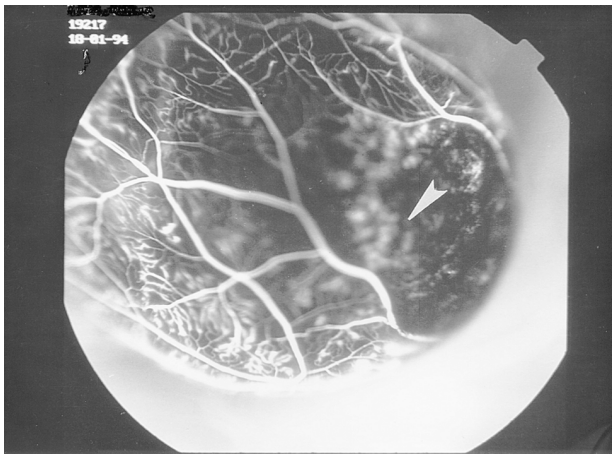

Figure 5. Mid-venous phase of fluorescein angiography of a mushroom-shaped choroidal melanoma demonstrating double circulation (case 2).

region of dense hypofluorescence, a ring of mild hyperfluorescence, and a peripheral ring of hypofluorescence (Figure 8, Table 2).

The treatment modalities of our cases that were performed in other clinics and their pathologic findings are shown in Table 1.

Discussion

Studies of the pathology specimens of eyes enucleated with the presumed diagnosis of uveal melanoma have shown that the misdiagnosis rate was 20% in the 1960s,[9,10] but had improved to 1.9%[11] during the same time period at a center with advanced diagnostic facilities. The Collaborative Ocular Melanoma Study has recently reported the lowest incidence (0.48%) of incorrect diagnosis.[11] It is believed that this low incidence of incorrect diagnosis is more the result of greater awareness of the clinical appearance of lesions, than the availability of more ancillary tests, which play a limited role in a physician's decision.

Indirect ophthalmoscopy plays an important role in the diagnosis of melanomas because of the wide field of view and stereopsis. Char et al[3] reported the incidence of correct diagnosis was 95% with this method.

The diagnostic accuracy of fluorescein angiography in the evaluation of suspected melanomas is limited.[13] There is no pathognomonic angiographic sign for a choroidal melanoma. A blockage of the background fluorescence, spotty hyperfluorescence due to changes in the pigment epithelium, an independent vascular network, and late staining as the dye leaks from the tumor vessels can be observed. In dome-shaped melanomas a "double circulation" pattern is evident in the early phase of the angiograms.[12] With these findings, it is possible to differentiate melanomas from subretinal hemorrhage, exudative maculopathy, and posterior scleritis, but it is still difficult to differentiate melanomas from choroidal hemangioma and choroidal metastases.[12] In this study, the early venous-phase angiograms showed irregular fluorescence, and, in 2 eyes, dot-like hyperfluorescent spots accompanied the irregularity. In 1 eye with mushroom-shaped melanoma, a double-circulation pattern was obvious.

It has been more than 20 years since the initial investigations of choroidal circulation by ICG angiography. Advances in imaging techniques have im-

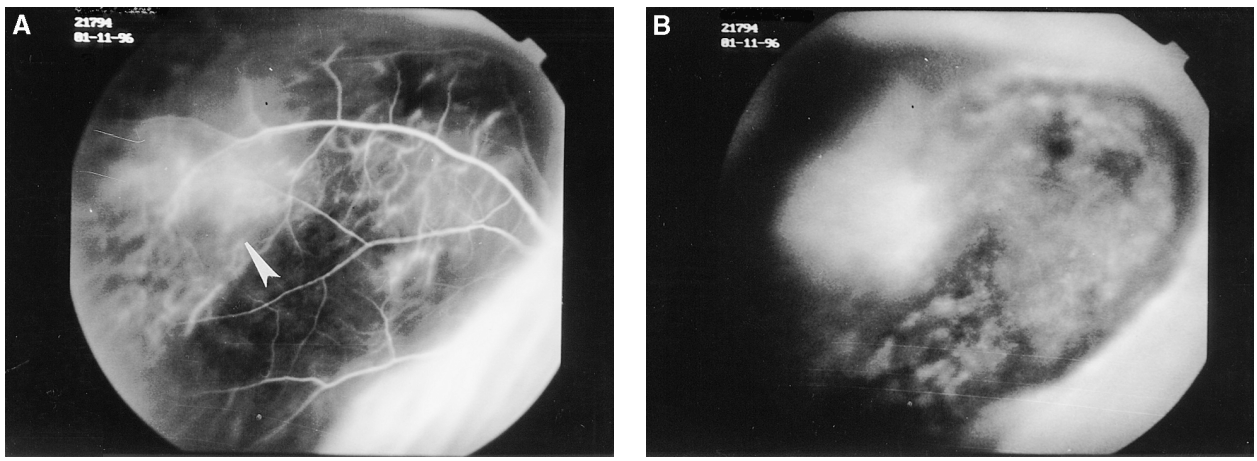

Figure 6. (**A**) Mid-phase indocyanine green angiography (ICGA) at 3 minutes, showing mild leakage from intratumoral vessels (arrowhead) (case 5). (**B**) Late phase ICGA in the same eye at 37 minutes.

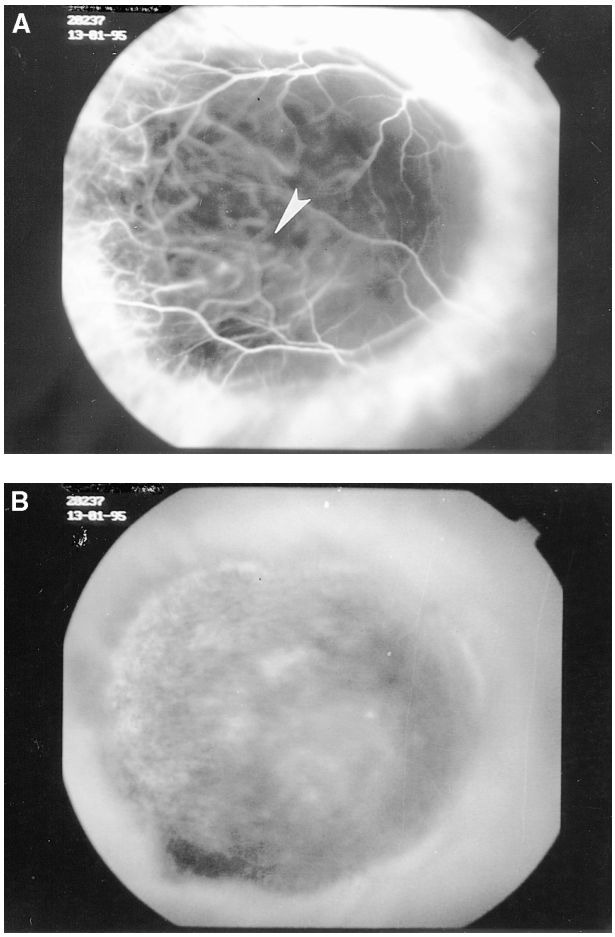

Figure 7. (**A**) Early phase indocyanine green angiography (ICGA) at 29 seconds showing intratumoral choroidal circulation (case 3). (**B**) Late phase ICGA in the same eye at 36 minutes.

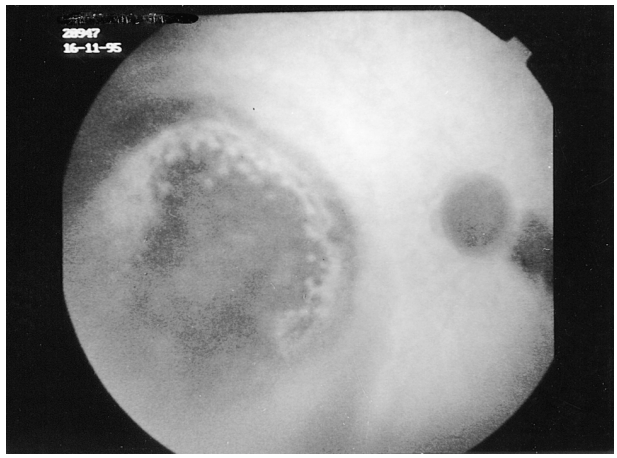

Figure 8. Late phase indocyanine green angiography at 33 minutes showing a "three-ring pattern" (case 4).

proved the resolution of the choroidal angiograms. Recently, the role of ICG angiography in diagnosis of choroidal melanomas was discussed by several authors.[7,8] Other reports have focused on the usefulness of ICG in various choroidal disorders, especially poorly defined choroidal neovascularizations.[4,6]

The findings of ICG angiography in choroidal tumors were superficially described in the early developmental years of dye technology.[13,14] It was found that vascularization of nonpigmented tumors could be studied and the angiogram could provide a topographic parameter for delineating the size and growth of choroidal tumors. Due to the deficient resolution of the early imaging systems, the details of pigmented choroidal tumors were not clearly observed. In recent years, with the new technology of ICG videoangiography, various angiographic findings have been identified in pigmented and nonpigmented choroidal melanomas.[7,8]

ICG fluorescence findings for choroidal melanomas vary, depending on the tumor pigmentation, thickness, and vascularization.[15] In general, the less pigmented and more vascular tumors demonstrate more fluorescence. The greater the thickness of the tumor, the greater fluorescence due to the large-caliber intrinsic vessels. In Shield's study, the maximum fluorescence was achieved at an average time of 18.2 minutes, and although this period varied, it was not dependent on tumor thickness and color.[8]

In most cases, the intrinsic choroidal vasculature of the tumor can be observed as well as the normal retinal and choroidal circulation. Tumor vessels are tortuous, have random direction, and show abnormal branching. These vessels are more pronounced on ICG angiography, depending on the amount of pigmentation.[7] In this study, these vessels were clearly seen with ICG videoangiography in the 3 eyes with dome-shaped, nonpigmented melanomas. In the late phase, diffuse hyperfluorescence due to vascular leakage was observed. The presence of abnormal vascular leakage with late dye leakage on ICG angiography may be considered an indicator of malignancy. It is better to follow these tumors with ICG angiography.[7]

The ICG videoangiographic image of pigmented choroidal melanomas was variable. These tumors usually showed well-defined hypofluorescence throughout the angiogram. This hypofluorescence is caused by blockage from the tumor pigment, and the lack of obvious intrinsic tumor vascularity, RPE proliferation, hemorrhage, and necrosis.[8] In minimally ele-

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Table 2. Fluorescein and Indocyanine Green Angiographic Findings

Case No.	FA		ICGA	
	Early	Late	Early	Late
1	Irregular hyper	Hyper	Hypo	Irregular hyper
2	Double circulation	Hyper	Hypo with intratumoral vessels	Irregular hyper
3	Irregular hyper	Diffuse hyper	Hypo with intratumoral vessels	Mild hyper
	Dot-like hyper spots			
4	Irregular hyper	Diffuse hyper	Hypo	3-Ring pattern
	Dot-like hyper spots			
5	Irregular hyper	Hypo in the central, hyper in the periphery	Hypo with intratumoral vessels	Irregular hyper
6	Hypo in central, hyper in periphery	Diffuse hyper, dot-like hyper spots	Hypo	Hypo, hyper in superior

FA: fluorescein angiography. Hypo: hypofluorescence. Hyper: hyperfluorescence. ICGA: indocyanine green angiography.

vated pigmented melanomas, late phase ICG angiograms often reveal hypofluorescence, but a fuzzy, mild fluorescence can be observed as well. In most cases, the fluorescence is homogenous, but in some cases a three-ring pattern of staining is seen. We observed this pattern in 1 eye with a large, pigmented melanoma in the late frames at 30 minutes.

In this study, exudative retinal detachment accompanied the tumor in 4 eyes, and 3 of these eyes had a dome-shaped melanoma. In these eyes, delineation of tumor edges was difficult and the base of the lesion could barely be visualized by fundoscopy or fluorescein angiography. ICG videoangiography defined the margins of these tumors better than previous methods.

In conclusion, fluorescein and ICG angiographies demonstrated various fluorescence patterns, depending on the characteristics of the tumor. None of these findings is pathognomic for a choroidal melanoma. The major advantage of ICG angiography is the better delineation of the tumor, providing an objective documentation of tumor growth. This is especially important in the follow-up of suspected melanomas. ICG angiography should always be combined with fluorescein angiography as well as other current diagnostic techniques, especially ultrasonography.

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