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Optical Coherence Tomography Angiography Characteristics of Iris Melanocytic Tumors

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Purpose: To evaluate tumor vasculature with optical coherence tomography angiography (OCTA) in malignant iris melanomas and benign iris lesions.

Design: Cross-sectional observational clinical study.

Participants: Patients with iris lesions and healthy volunteers.

Methods: Eyes were imaged using OCTA systems operating at 1050- and 840-nm wavelengths. Three-dimensional OCTA scans were acquired. Iris melanoma patients treated with radiation therapy were imaged again after I-125 plaque brachytherapy at 6 and 18 months.

Main Outcome Measures: OCT and OCTA images, qualitative evaluation of iris and tumor vasculature, and quantitative vessel density.

Results: One eye each of 8 normal volunteers and 9 patients with iris melanomas or benign iris lesions, including freckles, nevi, and an iris pigment epithelial (IPE) cyst, were imaged. The normal iris has radially oriented vessels within the stroma on OCTA. Penetration of flow signal in normal iris depended on iris color, with best penetration seen in light to moderately pigmented irides. Iris melanomas demonstrated tortuous and disorganized intratumoral vasculature. In 2 eyes with nevi there was no increased vascularity; in another, fine vascular loops were noted near an area of ectropion uveae. Iris freckles and the IPE cyst did not have intrinsic vascularity. The vessel density was significantly higher within iris melanomas (34.5%±9.8%, $P < 0.05$) than in benign iris nevi (8.0%±1.4%) or normal irides (8.0%±1.2%). Tumor regression after radiation therapy for melanomas was associated with decreased vessel density. OCTA at 1050 nm provided better visualization of tumor vasculature and penetration through thicker tumors than at 840 nm. But in very thick tumors and highly pigmented lesions even 1050-nm OCTA could not visualize their full thickness. Interpretable OCTA images were obtained in 82% of participants in whom imaging was attempted.

Conclusions: This is the first demonstration of OCTA in iris tumors. OCTA may provide a dye-free, no-injection, cost-effective method for monitoring a variety of tumors, including iris melanocytic lesions, for growth and vascularity. This could be helpful in evaluating tumors for malignant transformation and response to treatment. Penetration of the OCT beam remains a limitation for highly pigmented tumors, as does the inability to image the entire iris in a single field. *Ophthalmology 2016;■:1–8 © 2016 by the American Academy of Ophthalmology*

Optical coherence tomography angiography (OCTA) is a new, noninvasive microvascular imaging method that provides angiography by detecting changes in the optical coherence tomography (OCT) signal as blood cells travel through the vessel lumen. This technique does not require injected contrast, which makes it safer and less expensive than traditional ophthalmic angiography techniques. To evaluate posterior segment eye conditions such as retinopathies or choroidal neovascularization, OCTA was initially applied.[1,2] Evaluation of intratumoral vessels in humans with OCTA is an emerging technique,[3] as is OCT of the anterior eye.[4] Most clinical ophthalmic OCT systems operate at 840-nm wavelength, which penetrates poorly through tumor tissue. We have developed an OCTA system operating at a longer wavelength of 1050 nm to improve penetration into turbid (highly scattering)[5] tissues such as the iris and tumors. The approach was chosen because scattering loss decreases with a longer wavelength,[6] and we use this system to investigate OCTA in iris tumors for the first time.

Iris melanomas represent approximately 4% of uveal melanomas, and although they tend to be less aggressive than posterior uveal melanomas arising in the ciliary body and choroid, these tumors are associated with risk of metastatic disease as well as vision loss.[7,8] Decreased vision can occur owing to direct tumor effects, such as development of cataract or progressive glaucoma, or be associated with treatment of iris tumors with excisional surgery or radiation. Metastatic disease associated with iris melanomas occurs in 3% to 11% of patients and remains very difficult to treat, causing death in the majority of those patients in whom

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Table 1. Summary of Cases with Iris Lesions

Case	Gender	Age	Eye	Eye Color	Iris Lesion
1	M	61	OS	Green	Freckle
2	F	73	OS	Blue	Nevus
3	F	44	OS	Blue	Freckle, nevus
4	M	86	OS	Blue	Freckle, nevus
5	M	80	OD	Brown	Iris pigment epithelial cyst
6	M	45	OD	Blue	Melanoma
7	M	69	OS	Blue	Melanoma
8	M	48	OD	Blue	Melanoma
9	F	92	OD	Blue	Freckle, melanoma

F = female; M = male; OD = right eye; OS = left eye.

metastatic disease develops.[8–10] Owing to the significant morbidity of treatment, many iris tumors, even some felt clinically to be melanomas, are observed until they show signs associated with high risk of metastasis. One of the clinical features likely to be indicative of a more aggressive tumor with metastatic potential is increased vascularity.

The purpose of this pilot study was to characterize iris lesions using OCTA, comparing vascular patterns and vessel density between iris melanomas and other melanocytic lesions or lesions that may simulate melanomas. We also present OCTA imaging of iris melanomas treated with radiation to evaluate changes in vascularity associated with tumor regression after treatment.

Methods

Subjects

Participants of this cross-sectional observational pilot study were recruited at Casey Eye Institute, Oregon Health and Science University (Portland, OR) from October 2014 to December 2015. This study followed the tenets of the Declaration of Helsinki and was in accord with the Health Insurance Portability and Accountability Act of 1996. The study protocol was approved by the Oregon Health and Science University institutional review board. Clinical trial registration was not required owing to the observational nature of the study. All subjects were at least 18 years old. Written informed consent was obtained from all subjects. Participants with iris lesions

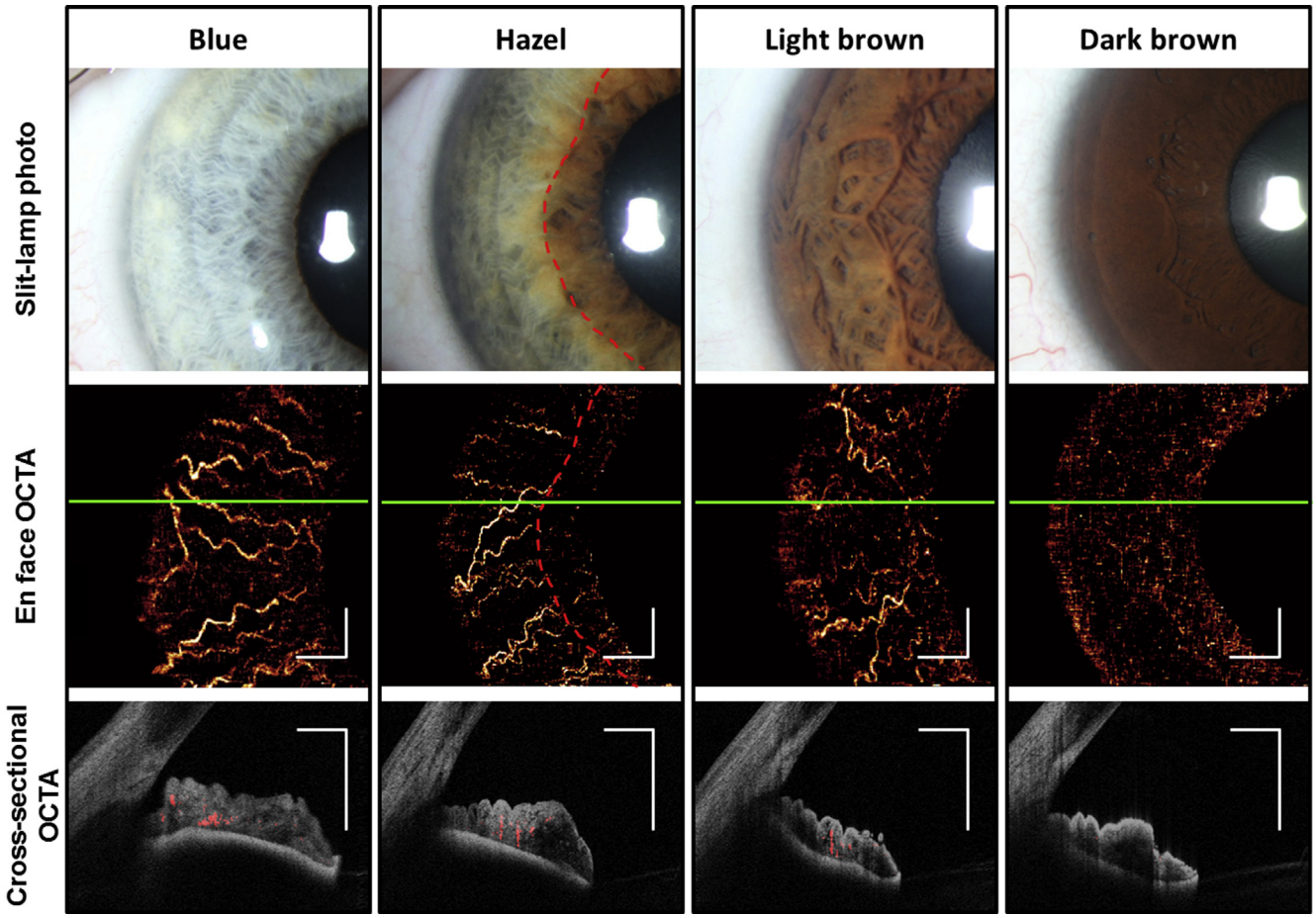

Figure 1. Shown are 1050-nm optical coherence tomography (OCT) and OCT angiography (OCTA) of normal irides with light to dark pigmentations. En face OCTA of iris shows iris vessels in all except the dark brown iris and in the thicker and more pigmented areas of the hazel iris near the pupillary margin (inside *red dashed lines*). White scale bars are 1 mm in length. *Green solid lines* indicate the levels at which the cross-sectional OCTAs were obtained. Cross-sectional OCTAs show vessels (flow signal in *red*) within the iris stroma (reflectance signal in grayscale). The posterior iris epithelium was visible in all irides. However, both reflectance and flow signals in the stroma were faint in the dark brown iris, presumably owing to blocking by the dense pigmentation in the anterior stroma.