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Quantitative OCT Angiography Evaluation of Peripapillary Retinal Circulation after Plaque Brachytherapy

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Purpose: To study peripapillary retinal capillary circulation in eyes treated with iodine 125 (I^{125}) plaque brachytherapy for uveal melanoma using optical coherence tomography angiography (OCTA).

Design: Cross-sectional study of 10 participants imaged with OCTA before uveal melanoma treatment and 15 participants imaged after development of radiation retinopathy, optic neuropathy, or both.

Participants: After institutional review board approval, participants were enrolled from an academic ocular oncology clinical practice. All participants had uveal melanoma in 1 eye, and treatment with I^{125} plaque brachytherapy was planned or had taken place previously. Patients with low vision at baseline and uncontrolled hypertension were excluded. In the posttreatment group, 7 participants were men and 8 were women; age range was 38 to 81 years. Visual acuities in the irradiated eyes ranged from 20/20 to counting fingers. Visual acuities in the untreated fellow eyes were 20/25 or better.

Methods: Peripapillary retinal capillary circulation was measured by OCTA (Optovue, Inc). Optic disc scans measuring 4.5 × 4.5 mm were obtained.

Main Outcome Measures: The relationship of the peripapillary retinal capillary density (PPCD) as measured by OCTA to the calculated dose to the optic nerve (the dose to 50% of the disc [D50]) and visual acuity in logarithm of the minimal angle of resolution units were evaluated.

Results: No significant differences were observed in the PPCD as measured by OCTA when comparing the eye with melanoma with the fellow eye before brachytherapy; however, the PPCD was significantly lower in treated eyes (52.9% ± 22.4%) than in fellow eyes that did not receive radiation (73.3% ± 13.7%; $P = 0.004$). There was an inverse linear correlation between D50 and the PPCD (Pearson's $r = -0.528$; $P = 0.043$) and between visual acuity and the PPCD (Pearson's $r = -0.564$; $P = 0.028$).

Conclusions: Among patients with clinically apparent radiation retinopathy, radiation optic neuropathy, or both, PPCD was lower in the treated eye and correlated with the radiation dose to the optic nerve and the visual acuity. Optical coherence tomography angiography provides a measure of capillary changes after radiation and may serve as a quantitative end point to address visual prognosis. *Ophthalmology Retina 2017;■:1–7 © 2017 by the American Academy of Ophthalmology*

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Uveal melanomas are the most common primary intraocular malignancy in adults, with an incidence of approximately 5 to 6 cases per 1 million population.[1–3] Eye-sparing treatment with radiation is an option for many patients diagnosed with uveal melanoma, but often leads to significant loss of vision. The degree of vision loss varies widely, with some patients experiencing only mild decline in measured visual acuity and others becoming entirely blind in the treated eye.[4–7] In the landmark Collaborative Ocular Melanoma Study (COMS), 43% of patients treated with plaque brachytherapy were found to have measured visual acuity in the severely compromised range at 3 years after radiation.[8]

Vision loss after radiation therapy typically occurs because of radiation optic neuropathy and retinopathy caused by vascular compromise leading to ischemia and edema.[9–13] Advanced vascular compromise can be observed with traditional fluorescein angiography, which shows retinal vascular leakage and capillary dropout in eyes with radiation-induced damage.[14,15] Optical coherence tomography angiography (OCTA) is a new, noninvasive method for imaging retinal vasculature and providing quantitative information regarding ischemia in the retina.[16–20] The association of radiation maculopathy with decreased parafoveal capillary density as measured by OCTA has been reported previously.[21] Optical coherence tomography angiography findings may allow for earlier detection of radiation maculopathy.[22] We hypothesized that OCTA can measure radiotherapy-induced changes in retinal vasculature associated with

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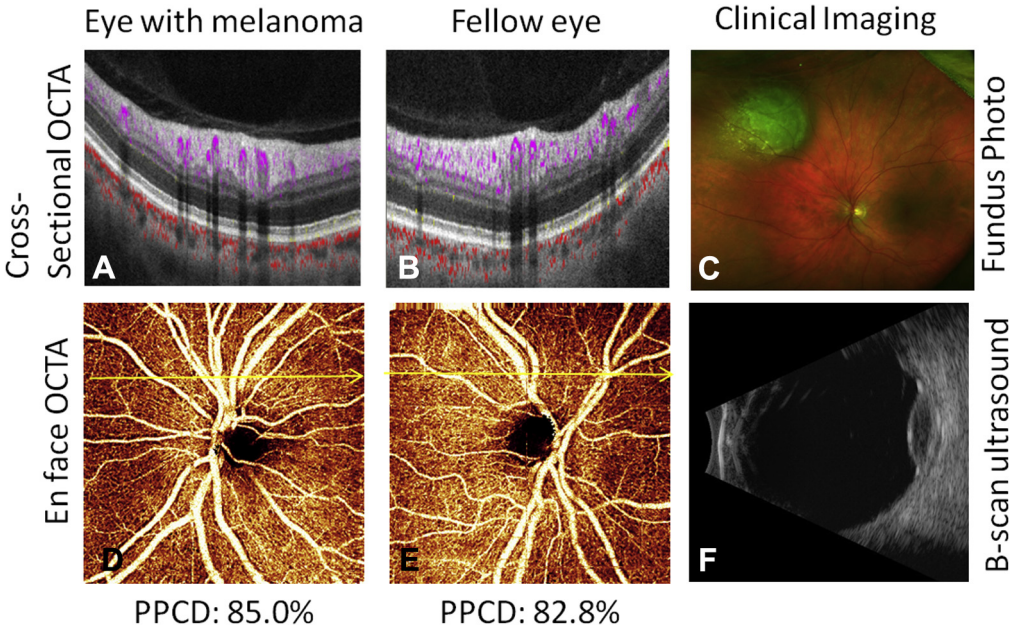

Figure 1. Representative example of peripapillary capillary density (PPCD) before treatment in an eye with uveal melanoma located in the superonasal periphery as compared with the normal fellow eye. **A**, **B**, Cross-sectional OCT angiography (OCTA) image for each eye (retinal flow shown in *purple*, and choroidal flow shown in *red*). **D**, **E**, En face OCTA of the peripapillary region. The location of the cross-sectional OCTA image is indicated with a *yellow arrow*. The PPCD for each eye is shown. The clinical imaging included (**C**) Optos fundus photography and (**F**) longitudinal B-scan ultrasonography.

radiation optic neuropathy. Herein, we describe for the first time the use of OCTA to evaluate radiation optic neuropathy by quantitatively measuring the peripapillary capillary density (PPCD) in eyes treated with plaque brachytherapy. We also demonstrated an inverse linear correlation between the calculated PPCD and the radiation dose to the optic nerve as well as the visual acuity (in logarithm of the minimum angle of resolution units) in the treated eye.

Methods

Study Participants

After institutional review board approval (Clinicaltrials.gov identifier, NCT01955941), participants were enrolled from an academic ocular oncology clinical practice. All participants had been diagnosed with ciliary body or choroidal melanoma in 1 eye and previously had undergone plaque brachytherapy or were scheduled to undergo this procedure for the treatment of the tumor. At the time of OCTA imaging after brachytherapy, all participants had clinically apparent radiation optic neuropathy, radiation retinopathy, or both.

Plaque Brachytherapy

Brachytherapy was performed using iodine 125 (I^{125}) seeds (IsoAid Model IAI-125A; IsoAid, LLC, Port Richey, FL) inserted in a silastic carrier and mounted in gold COMS-style plaques. Seed activity was calculated to deliver 85 Gy over 100 hours to a prescription depth dependent on tumor thickness. Starting with a minimum prescription depth of 3 mm, the depth was increased by multiples of 0.5 mm for thicker tumors to assure a margin of 0.5 mm or more but less than 1.0 mm, up to tumor thickness of 5 mm. For tumor thicknesses larger that 5 mm, the prescription depth was set to the tumor depth.

The planned seed activity was calculated using Plaque Simulator version 6.4.1 (Eye Physics LLC, Los Alamitos, CA). The software uses a superposition of a linear source model of all seeds as defined by the approved consensus data of American Association of Physics in Medicine with corrections for the presence of the plaque, carrier attenuation, and air interface.[23] Some of the plaques were modified in house with cut notches to allow implantation around or near the optic nerve. These were modeled specifically to account for the lack of a lip on the notched edge normally found on commercially available notched COMS plaques. The size and variation of the plaque were determined by the surgeon based on the limitations of surgical practicality. The dose to 50% of the optic nerve at the retinal surface (D50) was calculated with positioning based on fundus images loaded into the planning software.

OCT Angiography Data Acquisition and Analysis

A 70-kHz spectral-domain optical coherence tomography instrument (RTVue-XR; Optovue, Inc, Fremont, CA) obtained 4.5 × 4.5-mm optic disc scans for OCTA in tumor and fellow eyes. Two repeated B-scans, each consisting of 304 A-scans, were captured at each of 304 locations in 2.9 seconds. One x-fast and 1 y-fast scan were acquired, registered, and merged, minimizing motion artifacts. The split-spectrum amplitude-decorrelation angiography algorithm was applied to detect flow by calculating the decorrelation of the optical coherence tomography reflectance signal between 2 consecutive B-scans at the same location, as described previously.[24] The projection-resolution algorithm[25] was applied to remove the projection artifacts throughout the entire volume.

The merged volumetric OCTA images were exported for custom processing using the Center for Ophthalmic Optics & Lasers-Angiography Reading Toolkit software.[26] These custom