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Spectral-Domain Optical Coherence Tomography Angiography of Choroidal Neovascularization

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Purpose: To describe the characteristics as well as the sensitivity and specificity of detection of choroidal neovascularization (CNV) on optical coherence tomography angiography (OCTA) using spectral-domain optical coherence tomography.

Design: Observational, retrospective study.

Participants: Seventy-two eyes of 61 subjects (48 eyes of 43 subjects with CNV, 24 eyes of 18 subjects without CNV).

Methods: Patients imaged using the prototype AngioVue OCTA system (Optovue, Inc, Fremont, CA) between August 2014 and October 2014 at New England Eye Center were assessed. Patients in whom CNV was identified on OCTA were evaluated to define characteristics of CNV on OCTA: size using greatest linear dimension (small, <1 mm; medium, 1−2 mm; large, >2 mm), appearance (well-circumscribed, poorly circumscribed), and presence of subretinal and intraretinal fluid. Concurrently, an overlapping second cohort of patients who underwent same-day OCTA and fluorescein angiography (FA) for suspected CNV was evaluated to estimate sensitivity and specificity of OCTA in detecting CNV using FA as ground truth.

Main Outcome Measures: Choroidal neovascularization appearance, CNV size, and presence of subretinal and intraretinal fluid.

Results: In 48 eyes, CNV was visualized on OCTA. Thirty-one eyes had CNV associated with neovascular age-related macular degeneration. Size of CNV was small in 23% (7/31), medium in 42% (13/31), and large in 35% (11/31). Poorly circumscribed vessels, subretinal fluid, and intraretinal fluid each were seen in 71% (22/31). Seven eyes had CNV associated with central serous chorioretinopathy. Size of CNV was small in 71% (5/7) and large in 29% (2/7). Seventy-one percent (5/7) had well-circumscribed vessels, 86% (6/7) had subretinal fluid, and 14% (1/7) had intraretinal fluid. Thirty eyes with OCTA and same-day FA were evaluated to determine sensitivity and specificity of CNV detection on OCTA. Sensitivity was 50% (4/8) and specificity was 91% (20/22).

Conclusions: Using OCTA allows the clinician to visualize CNV noninvasively and may provide a method for identifying and guiding treatment of CNV. The specificity of CNV detection on OCTA compared with FA seems to be high. Future studies with larger sample sizes are needed to elaborate better on the sensitivity and specificity of CNV detection and to illustrate clinical usefulness. *Ophthalmology 2015;■:1−11 © 2015 by the American Academy of Ophthalmology.*

Choroidal neovascularization (CNV) can occur as a result of a variety of ophthalmologic diseases, such as neovascular age-related macular degeneration (AMD), high myopia, central serous chorioretinopathy (CSCR), multifocal choroiditis, and others. These abnormal blood vessels typically are derived from the choroidal vasculature and can penetrate Bruch's membrane into the space beneath the retinal pigment epithelium (RPE; type 1 CNV) or the subretinal space (type 2 CNV). In some eyes, neovascularization seems to begin from the retinal vasculature, eventually anastomosing with new vessels derived from the choroidal vasculature (retinal angiomatous proliferation, also called type 3 CNV).[1−3] Early diagnosis and visualization of CNV are crucial for initiating and guiding treatment, which in most cases is an intravitreal anti−vascular endothelial growth factor (VEGF) drug to prevent progressive, irreversible vision loss.[4]

The current gold standard for identifying CNV is fluorescein angiography (FA).[5−7] Fluorescein angiography uses intravenous dye injection to visualize CNV, and the patterns of hyperfluorescence that accompany the various kinds of CNV have been well characterized.[8−10] Although considered safe, intravenous dye has risks ranging from discomfort and nausea to, in rare cases, anaphylaxis. Fluorescein angiography is not considered an appropriate screening test for CNV detection in an asymptomatic population. In addition, the technique is expensive and time consuming, requiring up to 10 minutes of imaging time, which can limit its routine use in a busy clinical setting.[11,12]

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For these reasons, a noninvasive imaging technique to detect rapidly and to monitor CNV without the use of intravenous dye is desirable. Optical coherence tomography (OCT) has become an important noninvasive method for structural imaging of patients with suspected CNV. It enables visualization of subretinal fluid, intraretinal fluid, retinal pigment epithelial detachments (RPEDs), and retinal thickening using cross-sectional B-scans. Choroidal neovascularization may appear on structural OCT B-scans as subretinal or sub-RPE hyperreflective material, or both, often with breaks in Bruch's membrane and interruption of the RPE, but differentiation between fibrous and vascular tissue is limited using cross-sectional scans. In type 1 CNV, structural en face OCT images using enhanced depth imaging (EDI) may successfully visualize the branching CNV network below the RPE. However, this method is limited to use in fibrovascular RPEDs and therefore is not widely applicable to all types of CNV.[13] Thus, at the present time, there are no agreed-on standards for diagnosing CNV based strictly on cross-sectional OCT. Structural OCT cannot detect blood flow, nor can it reliably distinguish vasculature from fibrous and other surrounding tissue,[4] Therefore, OCT findings are used in conjunction with leakage on FA to diagnose CNV definitively.[14–16]

Optical coherence tomography angiography (OCTA) allows noninvasive visualization of retinal and choroidal vasculature via motion contrast imaging. This relatively new imaging technique maps erythrocyte movement over time by comparing sequential OCT B-scans at a given crosssection. Motion correction technology removes axial bulk motion from patient movement so that regions of motion between repeated OCT B-scans correspond to erythrocyte flow and, therefore, vasculature. Compared with structural OCT images, higher imaging speeds are required to obtain a densely sampled volume on OCTA. Conventional scanning speeds would result in decreased quality (because of undersampling), decreased field of view, increased acquisition time, or a combination thereof. Optical coherence tomography angiograms are coregistered with OCT B-scans from the same area, allowing for simultaneous visualization of structure and blood flow.[17–19] Jia et al[4] described a technique that uses a prototype swept-source (SS) OCT to visualize CNV noninvasively via OCTA, using the split-spectrum amplitude decorrelation angiography (SSADA) algorithm to improve flow detection and improve CNV visualization. To our knowledge, no group has studied CNV using a commercially available spectral-domain (SD) OCT. This study used an OCTA system based on a commercially available SD OCT device (Optovue, Inc., Fremont, CA), using a prototype OCTA SSADA algorithm to visualize CNV using noninvasive OCTA.

Methods

This study was approved by the institutional review board of Tufts Medical Center. Informed consent was obtained from patients in accordance with the Tufts Medical Center Institutional Review Board before examination. The research adhered to the tenets of the Declaration of Helsinki and complied with the Health Insurance Portability and Accountability Act of 1996. In this retrospective review, patients who underwent OCTA using the prototype AngioVue OCTA system on the commercially available Avanti SD OCT device (Optovue, Inc) between August 2014 and October 2014 at the Retina Service of the New England Eye Center at Tufts Medical Center were evaluated.

The AngioVue OCTA system used an SSADA software algorithm and operated at 70 000 A-scans per second to acquire OCTA volumes consisting of 304×304 A-scans in approximately 2.6 seconds. Orthogonal registration and merging of 2 consecutive scan volumes were used to obtain 3×3-mm and 6×6-mm OCTA volumes of both eyes of each patient. Both 3×3-mm and 6×6-mm OCTA volumes used a 304×304 scanning pattern. Optical coherence tomography angiograms were coregistered with the OCT B-scans obtained concurrently, allowing visualization of both retinal flow and structure in tandem. In addition, the SD OCT device was capable of acquiring the standard structural OCT scans typically used by commercially available devices in the evaluation of CNV (i.e., high-resolution line scans and cube scans).

The OCTA software was used to delineate a region of interest with an inner border at the level of the outer aspect of the inner nuclear layer (seen as a green line on the corresponding OCT B-scan) and an outer border at the level of Bruch's membrane (shown as a red line on the corresponding OCT B-scan). An artifact removal toggle function within the software was used to remove retinal vessel shadowing from the en face flow image. This function worked by automatically subtracting vessels that were seen above the inner border (vasculature of the inner retina) from the outer retina OCTA image. Therefore, only vessels truly within the outer retina segmentation boundary were shown. In healthy individuals, the outer retina is not expected to have blood vessels. Therefore, after accurate segmentation and retinal vessel shadowing removal, vessels identified in this region were presumed to be neovascularization. The levels of the inner and outer boundaries determining the thickness of the en face (C scan) section were fine-tuned manually to include all of the area suspicious for CNV as visualized on the corresponding OCT B-scan images. The inner boundary was adjusted to contain the innermost region suspicious of a CNV (characterized by disruption of the RPE, presence of subretinal fluid, RPED, or subretinal hyperreflective material). The outer boundary was adjusted to lie directly anterior to Bruch's membrane so minimal choroidal vasculature would be included in the region being imaged by OCTA. The prototype software did not allow the segmentation curve of the inner or outer limits to be adjusted; it only allowed movements up or down using the original automated segmentation line course, which was calculated automatically based on the contour of Bruch's membrane.

The 3×3-mm OCTA images were used primarily to evaluate each eye. If a 3×3-mm OCTA image did not show a CNV, the findings were confirmed by evaluating the 6×6-mm OCTA image to ensure that more peripheral CNVs were not missed. In cases where the 3×3-mm OCTA image showed a CNV that extended beyond the image border, a 6×6-mm OCTA image was used so that the entire CNV was evaluated.

All patients in whom CNV was identified on OCTA underwent further review of the medical records for patient characteristics and underlying diagnosis. The OCTAs were evaluated independently by 2 trained readers (T.E.D., M.A.B.F.) from the Boston Image Reading Center, Tufts Medical Center, to confirm the diagnosis and to define the characteristics of the CNV identified on the OCTA. The OCTA images and coregistered corresponding OCT B-scans were assessed for CNV size, CNV appearance, and presence of subretinal fluid, intraretinal fluid, and RPED. The CNV size was classified on the OCTA image as follows: small if the greatest linear dimension (GLD) was less than 1 mm, medium if GLD was between 1 and 2 mm, and