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Ophthalmic Technology Assessment

OCT Angiography for the Diagnosis of Glaucoma

A Report by the American Academy of Ophthalmology

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Purpose: To review the current published literature on the use of OCT angiography (OCTA) to help detect changes associated with the diagnosis of primary open-angle glaucoma.

Methods: Searches of the peer-reviewed literature were conducted in March 2018, June 2018, April 2019, December 2019, and June 2020 in the PubMed and Cochrane Library databases. Abstracts of 459 articles were examined to exclude reviews and non-English articles. After inclusion and exclusion criteria were applied, 75 articles were selected and the panel methodologist rated them for strength of evidence. Three articles were rated level I and 57 articles were rated level II. The 15 level III articles were excluded.

Results: OCT angiography can detect decreased capillary vessel density within the peripapillary nerve fiber layer (level II) and macula (level I and II) in patients with suspected glaucoma, preperimetric glaucoma, and perimetric glaucoma. The degree of vessel density loss correlates significantly with glaucoma severity both overall and topographically (level II) as well as longitudinally (level I). For differentiating glaucomatous from healthy eyes, some studies found that peripapillary and macular vessel density measurements by OCTA show a diagnostic ability (area under the receiver operating characteristic curve) that is comparable with structural OCT retinal nerve fiber and ganglion cell thickness measurements, whereas other studies found that structural OCT measurements perform better. Choroidal or deep-layer microvasculature dropout as measured by OCTA is also associated with glaucoma damage (level I and II). Lower peripapillary and macular vessel density and choroidal microvasculature dropout are associated with faster rates of disease progression (level I and II).

Conclusions: Vessel density loss associated with glaucoma can be detected by OCTA. Peripapillary, macular, and choroidal vessel density parameters may complement visual field and structural OCT measurements in the diagnosis of glaucoma. *Ophthalmology 2021;128:1222-1235 © 2021 by the American Academy of Ophthalmology*

The American Academy of Ophthalmology prepares Ophthalmic Technology Assessments to evaluate new and existing procedures, drugs, and diagnostic and screening tests. The goal of an Ophthalmic Technology Assessment is to systematically review the available research for clinical efficacy and safety. After review by members of the Ophthalmic Technology Assessment Committee, other Academy committees, relevant subspecialty societies, and legal counsel, assessments are submitted to the Academy's Board of Trustees for consideration as official Academy statements. The purpose of this assessment was to evaluate the current published literature on the ability of OCT angiography (OCTA) to help the clinician diagnose glaucoma.

Background

OCT angiography is an emerging technology that provides noninvasive, high-resolution imaging of the vasculature of the retina, choroid, and optic disc region. Many studies have demonstrated an association between glaucoma and ocular blood flow. Epidemiologic studies have found that decreased ocular diastolic perfusion pressure, the difference between diastolic blood pressure and intraocular pressure (IOP), is associated with increased incidence, prevalence, and progression of glaucoma.[1–8] Studies of the optic nerve head have also shown that reduced blood flow is associated with glaucoma progression.[9–11] However, these earlier studies were limited to examining large blood vessels such as the central retinal artery or short posterior ciliary arteries. The first demonstration of using spectral-domain (SD) OCT to image small retinal vessels was based on optical Doppler tomography.[12] In 2012, Jia et al[13] demonstrated the ability of OCTA to image the large and small vessels of the optic nerve, and in 2015, Liu et al[14] first described the peripapillary vascular changes as imaged by OCTA in glaucoma. With its ability to detect flow through small vessels, including capillaries, OCTA holds the potential for diagnosing and monitoring glaucoma and

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complementing structural (SD OCT) and functional visual field (VF) measurements.

Compared with time-domain OCT, OCTA takes advantage of the faster acquisition speeds of SD OCT and swept-source OCT technology. OCT is fundamentally based on interferometry, by which 2 beams of coherent light are superimposed to create a distinct interference pattern based on the difference in their path lengths. In current SD OCT technology, laser light travels through a beam splitter to the eye and the reference mirror. Light reflecting back from tissues within the eye and from the reference mirror create an interference pattern based on the path length to the tissue and on the set path length to the reference mirror. Spectral-domain OCT provides ultrafast ultrahigh-resolution volumetric images by using a spectrometer to capture the interference pattern. For the purposes of this Ophthalmic Technology Assessment, structural OCT will refer to traditional OCT parameters, including retinal nerve fiber layer (RNFL) and macular or ganglion cell complex (GCC) thickness measurements.

OCT angiography detects the motion of blood within tissues by analyzing successive images of the same tissue. It detects the difference in signal between images separated in time. For the most part, the only element that changes over a short period is blood flowing through vessels. In the region of blood flow, the scattering of the light will vary depending on the position or absence of blood cells within that part of the vessel. By capturing multiple images over a brief period, a 3-dimensional construction of the motion contrast from flowing blood is generated.

Several OCTA instruments are available on the market. The various manufacturers use different techniques and algorithms to optimize scan duration and sensitivity while minimizing image artifacts from bulk motion, segmentation errors, signal processing, and other technical issues. The longer times required for OCTA image acquisition compared with structural OCT scan times require compromises in image quality, flow resolution, and speed. For example, manufacturers must balance the risk of motion blur from patient movement if the scan duration is too long with the inability to detect very low blood flow if the scan time is too brief. Thus, imaging results among different OCTA devices may not be directly comparable. It should also be noted that proprietary software, which was used in many of the early studies, may differ from what is now commercially available. Nonetheless, most of the findings are generalizable to current commercial instruments. When reporting findings, this Ophthalmic Technology Assessment does not distinguish between different instruments.

A major limitation of current OCTA technology in glaucoma diagnosis is the difficulty in imaging the deep optic nerve head microvasculature and the peripapillary choroid. Deeper retinal vessels may be obscured or shadowed by superficial blood vessels. The longer acquisition times may result in more artifacts resulting from eye movement. It is also important to realize that although current commercially available OCTA technology enables visualization of the structure of the vascular network, it does not provide a direct measurement of actual blood flow. As with structural OCT, image quality must be considered when interpreting OCTA output. Nonetheless, OCTA scans have been found to be repeatable and reproducible in the macular and peripapillary regions.[15–18]

Question for Assessment

The purpose of this assessment is to address the following question: Is OCTA of the peripapillary or macular regions able to help the clinician detect glaucomatous damage associated with the diagnosis of primary open-angle glaucoma?

Description of Evidence

Searches of the peer-reviewed literature were conducted in March 2018, June 2018, April 2019, December 2019, and June 2020 in the PubMed and Cochrane Library databases. The abstracts of 459 articles were examined to exclude reviews and articles not written in the English language. The full texts of the remaining articles were reviewed by the Glaucoma Panel to select only those that met the following inclusion criteria: (1) OCTA was the technology focus of the study; (2) the study reported on patients with primary open-angle glaucoma, normal-tension glaucoma, or both; (3) the study represented original research; (4) the study reported on the ability of OCTA to help detect changes associated with the diagnosis of glaucoma; (5) the study participants were adults; and (6) the study involved approximately 60 or more glaucoma eyes.

Application of these criteria yielded 75 articles, and the panel methodologist (J.A.R.) assigned each study a level of evidence based on the rating scale developed by the Oxford Centre for Evidence-Based Medicine and adopted by the American Academy of Ophthalmology.[19] A level I rating was assigned to well-designed and well-conducted longitudinal cohort studies; a level II rating was assigned to well-designed case-control studies and prospective cross-sectional studies; and a level III rating was assigned to case series, case reports, and poor-quality cohort and case-control studies. Three articles were rated level I and 57 articles were rated level II. The 15 level III articles were excluded.

Published Results

Optic Nerve Head and Peripapillary Microvasculature as Measured by OCT Angiography

Most OCTA studies of glaucoma have focused on the optic nerve head and superficial peripapillary microvasculature. Because the depth of imaging of the optic nerve head is currently limited with SD OCT, studies of the optic nerve usually included the surrounding peripapillary region. Peripapillary vessel measurements are generally confined to the superficial nerve fiber layer (i.e., internal limiting membrane to posterior RNFL boundary). Because the superficial peripapillary capillaries supply the local nerve fiber layer, some studies have examined the peripapillary microvasculature within an annulus around the optic disc in parallel with the OCT RNFL thickness measurements.

In essentially all studies to date, the peripapillary microcirculation, as measured by vessel density on OCTA, was decreased in glaucomatous eyes compared with healthy eyes.[20–48] Most studies detected a significant correlation between glaucoma severity and degree of vessel density

loss. Vessel density is generally defined as the proportion of the area occupied by vessels within the entire area of the measurement sector.

Association of Peripapillary Vessel Density and Visual Fields

Several studies have found moderate to strong correlations or associations between OCTA vessel density and VF defects (Table 1).[21–26,30,33,36,37,41,43,45,46,49] Sakaguchi et al[36] examined the correlation between VF sensitivity and vessel density or RNFL thickness in the 6 sectors around the optic disc and found that peripapillary vessel density showed the highest correlation with VF sensitivities in the corresponding sector for all 6 sectors (squared semipartial correlation: $sr^2 = 0.17–0.39$), whereas the sector RNFL thickness showed the highest correlation only with VF sensitivity in the corresponding sector for the temporal, inferotemporal, and superotemporal sectors ($sr^2 = 0.02–0.34$). Yarmohammadi et al[43] also found that in glaucoma patients with a VF defect in only 1 hemifield, circumpapillary vessel density showed as strong a correlation with VF mean sensitivity in each hemifield (affected hemifield: $r = 0.707$; intact hemifield: $r = 0.450$) as RNFL (affected hemifield: $r = 0.496$; intact hemifield: $r = 0.340$) and GCC (affected hemifield: $r = 0.482$; intact hemifield: $r = 0.290$) thickness measurements.

Some studies investigated the ability of OCTA to discriminate preperimetric glaucoma and glaucoma suspect eyes from healthy eyes. Kumar et al[26] found that OCTA of the superior and temporal sectors showed more vessel density loss in glaucoma eyes and showed comparable discriminant ability by area under the receiver operating characteristic curve (AUC) with SD OCT structural parameters between healthy and preperimetric glaucoma eyes (AUC, 0.70 [sensitivity, 69.2%; specificity, 72.9%] vs. AUC, 0.66 [sensitivity, 77.3%; specificity, 59.7%]). Lu et al[49] also found comparable ability between peripapillary vessel density and RNFL thickness in discriminating normal and preperimetric eyes (AUC, 0.880 vs. 0.906; $P = 0.448$). Yarmohammadi et al[44] also found that whole-image vessel density (AUC, 0.70) and circumpapillary vessel density (AUC, 0.65) were as good as RNFL thickness (AUC, 0.65) in differentiating healthy and glaucoma suspect eyes. In distinguishing glaucoma suspect eyes from healthy eyes, Triolo et al[41] found that annular peripapillary vessel density was no better than OCT RNFL thickness (AUC average, 0.506 vs. 0.649; AUC superior, 0.562 vs. 0.687; AUC inferior, 0.438 vs. 0.508; $P > 0.05$ for all). However, Chihara et al[22] found that whole-image peripapillary vessel density (AUC, 0.724; $P = 0.006$), unlike circumpapillary RNFL (AUC, 0.553; $P = 0.613$), could distinguish ocular hypertensive eyes from healthy eyes. Hou et al[50] found that intereye vessel density asymmetry, as measured by whole-image optic nerve head scans (4.5×4.5 mm^2 centered on disc), may differentiate glaucoma suspects from healthy persons (2.0% vs. 1.1%; $P = 0.014$), despite no difference in asymmetry of thickness parameters between these groups (RNFL: 3 μm vs. 4 μm; $P = 0.943$).

Association of Peripapillary Vessel Density and Structural OCT Parameters

Many studies found moderate correlation between the peripapillary OCTA parameters and structural OCT parameters, both overall[21,24,31,33,36,37,47,49,51,52] and in sectors,[30,36,47,52] in glaucomatous eyes (Table 1). Lee et al[29] found a very strong correlation between decreased vessel density and RNFL defects on red-free fundus photographs with regard to both location ($r = 0.997$; $P < 0.001$) and extent ($r = 0.988$; $P < 0.001$). Lommatzsch et al[30] found moderate to strong correlation between whole-image and peripapillary OCTA and OCT RNFL, GCC, and disc rim parameters ($r = 0.63–0.81$; $P < 0.0001$ for all).

Some studies compared the effectiveness of OCTA with that of structural SD OCT parameters in discriminating glaucoma patients from healthy persons (Table 2). Most of these studies found similar (nonsignificant difference) discriminatory ability (i.e., AUC) between peripapillary OCTA and OCT RNFL thickness.[21–24,27,32,35,41,47,49,53] For example, Geyman et al[24] also found comparable effectiveness of OCTA-measured peripapillary vessel density and peripapillary RNFL parameters in distinguishing mild glaucoma eyes from control eyes (AUC global, 0.907 vs. 0.934; AUC superior, 0.951 vs. 0.928; AUC inferior, 0.893 vs. 0.896). Similarly, for distinguishing mild to moderate glaucoma eyes from healthy eyes, Rao et al found similar AUCs between peripapillary vessel density (range, 0.48–0.88) and RNFL thickness (range, 0.51–0.90) for the 6 sectors and overall average ($P > 0.05$ for all).[32] Chung et al[23] found that peripapillary vessel density parameters generally showed similar glaucoma diagnostic abilities compared with peripapillary RNFL thickness, except in early glaucoma, for which RNFL thickness measurements in the temporal (AUC, 0.578 vs. 0.708; $P = 0.021$) and inferotemporal (AUC, 0.737 vs. 0.850; $P = 0.003$) sectors were significantly better. However, Yarmohammadi et al[45] found a stronger association between VF mean deviation (MD) with circumpapillary vessel density (coefficient of determination: $R^2 = 0.54$) and whole-image vessel density ($R^2 = 0.51$) than between VF MD with RNFL ($R^2 = 0.36$) and rim area ($R^2 = 0.19$; $P < 0.05$ for all).

In eyes with mild to moderate glaucoma (VF MD, > -12 dB), Moghimi et al[54] found a significant association between a faster rate of RNFL loss and both lower whole-image optic nerve vessel density (0.007 μm/year for each 1% decrease in vessel density; $P = 0.026$) and circumpapillary vessel density (0.006 μm/year for each 1% decrease in vessel density; $P = 0.018$).

Peripapillary Vessel Density in Normal-Tension Glaucoma

Rao et al[35] found that higher pretreatment IOP was associated with decreased optic disc vessel density compared with eyes with lower baseline eye pressures (multivariate ROC regression coefficient of pretreatment IOP: 0.08; $P < 0.05$), suggesting that poor ocular perfusion may not be the predominant pathogenic mechanism of normal-tension glaucoma. Moreover, Scripsema et al[37] found that peripapillary capillary density was reduced significantly in primary

Table 1. Association between Peripapillary OCT Angiography Vessel Density and Visual Field, OCT Retinal Nerve Fiber Layer Thickness, or Both

Study	Number of Participants	Whole-Image Vessel Density vs. Visual Field Mean Deviation	Peripapillary Vessel Density vs. Visual Field Mean Deviation	Superior or Superotemporal Vessel Density vs. Inferior or Inferotemporal Visual Field Mean Deviation	Inferior or Inferotemporal Vessel Density vs. Superior or Superotemporal Visual Field Mean Deviation	Whole-Image Vessel Density vs. Retinal Nerve Fiber Layer Thickness	Peripapillary Vessel Density vs. Retinal Nerve Fiber Layer Thickness	OCT Angiography Device*
Chen et al[21]	20 healthy, 26 suspect, 21 POAG, 21 NTG	$R^2 = 0.62$ ($P < 0.0001$)		$R^2 = 0.66$ ($P = 0.0001$)	$R^2 = 0.51$ ($P < 0.0001$)	$R^2 = 0.25$ ($P < 0.0008$)		Cirrus HD-OCT 5000
Chihara et al[22]	25 healthy, 66 POAG, 14 OHTN	$r = 0.346$ ($P = 0.002$)						AngioVue, RTVue XR
Chung et al[23]	113 healthy, 140 POAG	$r_s = 0.619$ ($P < 0.001$)	$r_s = 0.631$ ($P < 0.001$)					AngioVue RTVue XR
Geyman et al[24]	24 healthy, 60 POAG	$r = 0.49$ ($P < 0.05$)	$r = 0.56$ ($P < 0.05$)	$r = 0.46$ ($P < 0.05$)	$r = 0.60$ ($P < 0.05$)	$r = 0.62$ ($P < 0.05$)	$r = 0.68$ ($P < 0.05$)	AngioVue RTVue XR
Kiyota[25]	20 healthy, 82 POAG		$r = 0.43$ ($P < 0.001$)					DRI OCT Triton
Kumar et al[26]	74 healthy, 93 POAG	$r = 0.43$ ($P < 0.001$)		$r = 0.58^{\dagger}$ ($P < 0.001$)	$r = 0.64^{\dagger}$ ($P < 0.001$)			AngioVue, RTVue XR
Lommatzsch et al[30]	74 healthy, 41 POAG, 24 NTG	$r_s = 0.48$ ($P = 0.0004$)	$r_s = 0.50$ ($P = 0.0001$)			$r_s = 0.81$ ($P < 0.0001$)	$r_s = 0.76$ ($P < 0.0001$)	AngioVue RTVue XR
Lu et al[49]	41 healthy, 44 PP POAG, 42 early POAG		Preperimetric POAG: $r_s = -0.061$ ($P = 0.590$); early POAG: $r_s = 0.625$ ($P < 0.001$)				Preperimetric POAG: $r_s = 0.733$ ($P < 0.001$); early POAG: $r_s = 0.860$ ($P < 0.001$)	AngioVue RTVue OCT
Manalastas et al[31]	73 healthy, 41 suspect, 219 POAG						$r^2 = 0.404$ ($P < 0.001$)	AngioVue RTVue XR
Park et al[52]	30 healthy, 104 POAG		$R^2 = 0.19$ ($P < 0.001$)				$R^2 = 0.38$ ($P < 0.001$)	DRI OCT Triton
Rao et al[33]	44 healthy, 99 POAG		$R^2 = 0.39$ ($P < 0.001$)	$R^2 = 0.35$ ($P < 0.001$)	$R^2 = 0.49$ ($P < 0.001$)		$R^2 = 0.53$ ($P < 0.001$)	AngioVue RTVue XR
Sakaguchi et al[36]	18 healthy, 17 suspect, 94 POAG		$r_s = 0.68$ ($P < 0.001$)	sr = 0.628 ($P < 0.001$)	sr = 0.585 ($P < 0.001$)		$r_s = 0.74$ ($P < 0.001$)	AngioVue RTVue XR
Scripsema et al[37]	26 healthy, 40 POAG, 26 NTG		POAG: $r = 0.72$ ($P < 0.01$); NTG: $r = 0.50$ ($P = 0.01$)				POAG: $r = 0.69$ ($P < 0.01$); NTG: $r = 0.45$ ($P = 0.01$)	AngioVue RTVue XR
Triolo et al[41]	40 healthy, 40 suspect, 40 POAG		$r = 0.675$ ($P < 0.001$)	$r = 0.567$ ($P < 0.01$)	$r = 0.637$ ($P < 0.001$)			PLEX Elite 9000

(*Continued*)

Table 1. (Continued.)

Study	Number of Participants	Whole-Image Vessel Density vs. Visual Field Mean Deviation	Peripapillary Vessel Density vs. Visual Field Mean Deviation	Superior or Superotemporal Vessel Density vs. Inferior or Inferotemporal Visual Field Mean Deviation	Inferior or Inferotemporal Vessel Density vs. Superior or Superotemporal Visual Field Mean Deviation	Whole-Image Vessel Density vs. Retinal Nerve Fiber Layer Thickness	Peripapillary Vessel Density vs. Retinal Nerve Fiber Layer Thickness	OCT Angiography Device*
Wang et al[51]	111 healthy, 130 POAG					$r = 0.796$ ($P < 0.0001$)		RS-3000 Advance
Yarmohammadi et al[43]	28 healthy, 58 POAG		Affected hemifield: $r = 0.707$ ($P < 0.001$); intact hemifield: $r = 0.450$ ($P < 0.05$)					AngioVue RTVue XR
Yarmohammadi et al[45]	31 healthy, 48 suspect, 74 POAG	$R^2 = 0.51$ ($P < 0.001$)	$R^2 = 0.54$ ($P < 0.001$)					AngioVue RTVue XR
Kurysheva et al[46]	35 healthy, 90 POAG		$r_s = 0.435$ ($P = 0.001$)					AngioVue RTVue XR
Jesus et al[47]	40 healthy, 82 POAG						$r_s = 0.63$ ($P < 0.001$)	Cirrus HD-OCT 5000

NTG = normal-tension glaucoma; OHTN = ocular hypertension; POAG = primary open-angle glaucoma; PP = preperimetric; r = Pearson correlation coefficient; R^2 = coefficient of determination; r_s = Spearman rank correlation coefficient; sr = semipartial correlation using multiple linear regression model.

*Device manufacturers are as follows: Cirrus HD-OCT 5000 (optical microangiography, AngioPlex; Carl Zeiss Meditec, Dublin, CA), AngioVue RTVue XR OCT (Optovue, Fremont, CA), DRI OCT Triton (Topcon, Tokyo, Japan), PLEX Elite 9000 SS-OCT (Carl Zeiss Meditec, Dublin, CA); RS-3000 Advance OCT (Nidek, Gamagori, Japan); and Spectralis OCT (Heidelberg Engineering GmbH, Heidelberg, Germany).

†Visual field pattern deviation compared instead of visual field mean deviation.

Table 2. Effectiveness of Peripapillary OCT Angiography versus Structural Spectral-Domain OCT Retinal Nerve Fiber Layer for Detecting Glaucomatous Eyes from Healthy Eyes

Study	No. of Participants	Comparison	Peripapillary OCT Angiography Area under the Receiver Operating Characteristic Curve (95% Confidence Interval)	Structural OCT Area under the Receiver Operating Characteristic Curve (95% Confidence Interval)	P Value	OCT Angiography Device*
Bowd et al[53]	180 healthy, 193 POAG	Normal vs. glaucoma	0.91 (0.86–0.94)	0.89 (0.84–0.93)	Not given	AngioVue
Chen et al[21]	20 healthy, 26 suspect, 21 POAG, 21 NTG	Normal vs. glaucoma,	0.82 (0.71–0.93)	0.97 (0.94–1.00)	0.009	Cirrus HD-OCT 5000
		normal vs. suspect	0.60 (0.43–0.77)	0.70 (0.54–0.85)	> 0.10	
Chihara et al[22]	25 healthy, 14 OHTN, 66 POAG	Healthy vs. glaucoma	0.832 ($P < 0.001$; 95% CI not given)	0.936 ($P < 0.001$; 95% CI not given)	0.055	AngioVue RTVue XR
		Healthy vs. OHTN	0.724 ($P = 0.006$; 95% CI not given)	0.553 ($P = 0.613$; 95% CI not given)	0.174	
Chung et al[23]	113 healthy, 140 POAG	Normal vs. glaucoma	0.807 (0.740–0.875)	0.868 (0.819–0.918)	Not given	AngioVue RTVue XR
Geyman et al[24]	24 healthy, 60 POAG	Normal vs. glaucoma	0.907 (0.816–0.998)	0.934 (0.869–0.999)	Not given	AngioVue RTVue-XR
Kwon et al[27]	45 healthy, 80 POAG	Healthy vs. glaucoma	0.87 (0.78–0.93)	0.90 (0.84–0.95)	0.33	AngioVue RTVue XR
Lu et al[49]	41 healthy, 44 PP POAG, 42 early POAG	Healthy vs. PP POAG	0.880 ($P < 0.001$; 95% CI not given)	0.906 ($P < 0.001$; 95% CI not given)	0.488	AngioVue RTVue OCT
		Healthy vs. early POAG	0.965 ($P < 0.001$; 95% CI not given)	0.942 ($P < 0,001$; 95% CI not given)	> 0.05	
Rao et al[32]	33 healthy, 39 POAG	Healthy vs. glaucoma	0.79 (0.66–0.91)	0.87 (0.74–0.94)	> 0.05	AngioVue RTVue XR
Rao et al[35]	50 healthy, 67 POAG	Healthy vs. glaucoma	0.85 (0.78–0.90)	0.95 (0.91–0.98)	0.002	AngioVue RTVue XR
Triolo et al[41]	40 healthy, 40 suspect, 40 POAG	Healthy vs. glaucoma	0.875 (95% CI not given)	0.927 (95% CI not given)	> 0.05	PLEX Elite 9000
		Healthy vs. suspect	0.506 (95% CI not given)	0.649 (95% CI not given)	> 0.05	
Jesus et al[47]	40 healthy, 82 POAG	Healthy vs. glaucoma	0.89 (0.83–0.94)	0.92 (0.87–0.97)	0.15	Cirrus HD-OCT 5000

CI = confidence interval; NTG = normal-tension glaucoma; OHTN = ocular hypertension; POAG = primary open-angle glaucoma; PP = preperimetric.
*Device manufacturers are as follows: Cirrus HD-OCT 5000 (optical microangiography, AngioPlex; Carl Zeiss Meditec, Dublin, CA), AngioVue RTVue XR OCT (Optovue, Fremont, CA), DRI OCT Triton (Topcon, Tokyo, Japan), PLEX Elite 9000 SS-OCT (Carl Zeiss Meditec, Dublin, CA); RS-3000 Advance OCT (Nidek, Gamagori, Japan); and Spectralis OCT (Heidelberg Engineering GmbH, Heidelberg, Germany).

open-angle glaucoma compared with normal-tension glaucoma (33.40% vs. 37.20%; $P < 0.05$), despite no differences in mean Humphrey VF MD, mean RNFL thickness, cup-to-disc ratio, or central corneal thickness ($P > 0.25$ for all). However, Xu et al[42] showed that the peripapillary vessel density was lower in the normal-tension glaucoma group compared with the high-tension glaucoma group of similar RNFL thickness and VF loss overall (49.78% vs. 55.57%; $P < 0.001$) and in all sectors ($P < 0.025$ for all) except the inferotemporal sector ($P = 0.68$). Looking at the optic disc only, Bojikian et al[20] found no difference between primary open-angle glaucoma and normal-tension glaucoma optic disc microvasculature measurements (vessel density, 0.68 vs. 0.70; $P = 0.32$).

Macular Microvasculature as Measured by OCT Angiography

The macular region is frequently abnormal in glaucoma, both structurally and functionally. Macular thickness, particularly of the GCC, is often thinner in glaucoma patients, and paracentral VF defects are common in glaucoma. Because the macular microvasculature supplies a significant portion of the ganglion cells, several groups of investigators have studied the macular microvasculature of glaucoma patients, particularly those with paracentral scotomas, macular thinning, or both on OCT.

OCT angiography imaging of the macula typically involves the superficial vascular plexus within the inner layers of the retina (internal limiting membrane to inner plexiform layer). OCT angiography imaging of the deeper vascular plexus is prone to projection artifacts from the superficial plexus, so most studies have focused on the superficial plexus. Moreover, after removal of flow projection artifacts by a projection-resolved algorithm, the superficial plexus was found to be the primary level at which vessel density changes occur in glaucoma.[55]

Association of Macular Vessel Density and Structural OCT Parameters

Most studies found a significant correlation between macular or parafoveal vessel density and macular or GCC

Table 3. Association between Macular OCT Angiography Vessel Density and Visual Field Loss or Inner Macular Thickness

Study	No. of Participants	Macular Vessel Density vs. Visual Field Mean Sensitivity (in Corresponding Region as Appropriate)	Macular Vessel Density vs. Inner Macular or Ganglion Cell Complex Thickness	Inferior Macular Vessel Density vs. Inferior Macular Thickness	OCT Angiography Device*
Chung et al[23]	113 healthy, 140 POAG	$r_s = 0.544$ ($P < 0.001$)	$r_s = 0.624^{\dagger}$ ($P < 0.001$)		AngioVue RTVue XR
Manalastas et al[31]	73 healthy, 41 suspect, 219 POAG		$r^2 = 0.177^{\dagger}$ ($P < 0.001$)		AngioVue RTVue XR
Triolo et al[41]	40 healthy, 40 suspect, 40 POAG	$r = 0.139$ ($P > 0.05$)	$r = 0.395^{\ddagger}$ ($P < 0.05$)	$r = 0.343^{\ddagger}$ ($P > 0.05$)	PLEX Elite 9000
Yarmohammadi et al[43]	28 healthy, 58 POAG	affected hemifield: $r = 0.615$ ($P < 0.001$); intact hemifield: $r = 0.403$ ($P = 0.002$)			AngioVue RTVue XR
Kurysheva et al[46]	35 healthy, 90 POAG			$r = 0.323^{\dagger}$ ($P = 0.05$)	AngioVue RTVue XR
Lu et al[49]	41 healthy, 44 PP POAG, 42 early POAG	Preperimetric POAG: $r_s = -0.055$ ($P = 0.623$); early POAG: $r_s = 0.549$ ($P < 0.001$)	Preperimetric POAG: $r_s = 0.646$ ($P < 0.001$); early POAG: $r_s = 0.851$ ($P < 0.001$)		AngioVue RTVue-OCT
Penteado et al[57]	38 healthy, 31 suspect, 116 POAG	$R^2 = 0.269$ ($P < 0.001$)			AngioVue RTVue XR
Smith et al[62]	60 healthy, 91 POAG	$r = 0.36$ ($P < 0.01$)	$r = 0.19$ ($P = 0.07$)		Spectralis OCT2
Tao et al[66]	27 healthy, 58 POAG	inferior VD: $r_s = 0.433$ ($P < 0.001$); superior VD: $r_s = 0.339$ ($P = 0.002$); temporal VD: $r_s = 0.295$ ($P = 0.006$); nasal VD: $r_s = 0.327$ ($P = 0.002$)			AngioVue RTVue
Wan et al[59]	35 healthy, 115 POAG	$R^2 = 0.21$ ($P < 0.001$)			Triton SS-OCT Angio
Xu et al[60]	31 healthy, 68 POAG	$\beta = 0.52$ ($P < 0.001$)	$\lvert r \rvert = 0.69^{\ddagger}$ ($P < 0.001$)	$\lvert r \rvert = 0.72^{\ddagger}$ ($P < 0.001$)	AngioVue RTVue XR
Hou et al[61]	37 healthy, 121 POAG		$R^2 = 0.32^{\dagger}$ ($P < 0.0001$)		AngioVue RTVue XR
Wu et al[65]	21 healthy, 60 POAG	$r = 0.3$ ($P = 0.0028$)	$r = 0.3092^{\dagger}$ ($P = 0.0257$)		AngioVue RTVue XR

β = regression coefficient; GCC = ganglion cell complex; POAG = primary open-angle glaucoma; r = Pearson correlation coefficient; $\lvert r \rvert$ = Pearson partial correlation coefficient; r_s = Spearman rank correlation coefficient; R^2 = coefficient of determination; VD = vessel density.
*Device manufacturers are as follows: Cirrus HD-OCT 5000 (optical microangiography, AngioPlex; Carl Zeiss Meditec, Dublin, CA), AngioVue RTVue XR OCT (Optovue, Fremont, CA), DRI OCT Triton (Topcon, Tokyo, Japan), PLEX Elite 9000 SS-OCT (Carl Zeiss Meditec, Dublin, CA); RS-3000 Advance OCT (Nidek, Gamagori, Japan); and Spectralis OCT (Heidelberg Engineering GmbH, Heidelberg, Germany).
†Correlation with GCC.
‡Correlation with inner macular thickness.

thickness, particularly in the inferior hemimacula (Table 3). Most studies of macular OCTA found that macular vessel density is decreased in moderate and severe glaucoma compared with normal eyes.[23,31,42,56–60] For early-stage glaucoma, preperimetric glaucoma, and glaucoma suspect eyes, some studies have found significant reduction in macular vessel density,[46,49,57,60–62] whereas others have found no significant difference between early glaucoma and healthy control eyes.[23,27,41] In a short-term longitudinal study, Shoji et al[58] found that eyes with primary open-angle glaucoma showed significantly faster loss of OCTA macular vessel density (−2.23%/year) than either glaucoma suspect eyes (0.87%/year; $P = 0.001$) or healthy eyes (0.29%/year; $P = 0.004$; level I). In eyes with mild to moderate glaucoma (VF MD, > −12 dB), Moghini et al[54] found that each 1% decrease in macular vessel density was associated with a 0.09-μm/year faster rate of RNFL loss.

Many studies compared OCTA of the macular microvasculature with OCT of the macula GCC thickness in the ability to differentiate glaucoma eyes from healthy eyes. Most, but not all, studies found that macular vessel density has a lesser AUC than GCC thickness (Table 4).[23,27,34,35,41,46,49,53,57,59,61–63] However, Penteado et al[57] found that although superficial macular vessel density performed worse than GCC thickness in differentiating between glaucoma eyes and healthy eyes (AUC, 0.757 vs. 0.863; $P = 0.011$), it performed better in differentiating glaucoma suspect eyes from healthy eyes (AUC, 0.705 vs. 0.506; $P = 0.010$). Hou et al[61] found that macular vessel density performed as well as OCT GCC in distinguishing preperimetric glaucoma eyes from healthy control eyes (percent loss, 4.97% vs. 4.72%; $P = 0.856$) but worse in distinguishing early glaucoma eyes from healthy eyes (percent loss, 6.93% vs. 9.86%; $P = 0.001$). Hou et al[50]

Table 4. Effectiveness of Macular OCT Angiography versus Macular OCT Thickness for Detecting Glaucomatous from Healthy Eyes

Study	No. of Participants	Comparison	Macular OCT Angiography Area under the Receiver Operating Characteristic Curve (95% Confidence Interval)	Macular–Ganglion Cell Complex OCT Area under the Receiver Operating Characteristic Curve (95% Confidence Interval)	P Value	OCT Angiography Device*
Bowd et al[53]	180 normal, 193 POAG	Healthy vs. glaucoma	0.83 (0.78–0.88)	0.91 (0.86–0.94)	Not given	AngioVue
Chung et al[23]	113 healthy, 140 POAG	Healthy vs. glaucoma	0.729 (0.647–0.811)	0.856 (0.804–0.908)	< 0.01	AngioVue RTVue XR
Kwon et al[27]	45 healthy, 80 POAG	Healthy vs. glaucoma	0.52 (0.41–0.62)	0.88 (0.81–0.94)	Not given	AngioVue RTVue XR
Rao et al[34]	53 healthy, 39 POAG	Healthy vs. glaucoma	0.69 (0.56–0.79)			AngioVue RTVue XR
Rao et al[35]	50 healthy, 67 POAG	Healthy vs. glaucoma	0.73 (0.64–0.81)	0.93 (0.88–0.96)	< 0.001	AngioVue RTVue XR
Triolo et al[41]	40 healthy, 40 suspect, 40 POAG	Healthy vs. glaucoma	0.705 (95% CI not given)	0.946 (95% CI not given)	< 0.001	PLEX Elite 9000
		Healthy vs. suspect	0.559 (95% CI not given)	0.918 (95% CI not given)	< 0.001	
Kurysheva et al[46]	35 healthy, 90 POAG	Healthy vs. glaucoma	0.800 (SD, 0.06)	0.739 (SD, 0.09)	Not given	AngioVue RTVue XR
Lu et al[49]	41 healthy, 44 PP POAG, 42 early POAG	Healthy vs. PP POAG	0.770 ($P < 0.001$, 95% CI not given)	0.853 ($P < 0.001$, 95% CI not given)	Not given	AngioVue RTVue OCT
		Healthy vs. early POAG	0.920 ($P < 0.001$, 95% CI not given)	0.915 ($P < 0.001$, 95% CI not given)	> 0.05	
Pentreado et al[57]	38 healthy, 31 suspect, 116 POAG	Healthy vs. glaucoma	0.757 (95% CI not given)	0.863 (95% CI not given)	0.011	AngioVue RTVue XR
		Healthy vs. suspect	0.705 (95% CI not given)	0.506 (95% CI not given)	0.010	
Pentreado et al[63]	89 healthy, 190 POAG	Healthy vs. glaucoma	0.84 (0.76–0.90)	0.87 (0.78–0.93)	> 0.05	AngioVue RTVue XR
Smith et al[62]	60 healthy, 91 POAG	Healthy vs. glaucoma	0.76 (0.68–0.84)	0.90 (0.86–0.95)	< 0.01	Spectralis OCT2
Wan et al[59]	35 healthy, 115 POAG	Healthy vs. glaucoma	0.73 (0.60–0.85)	0.89 (0.79–0.97)	0.03	Triton SS-OCT Angio
Hou et al[61]	37 healthy, 55 PP POAG, 121 POAG	Healthy vs. glaucoma	0.74 (0.68–0.81)	0.79 (0.72–0.85)	0.215	AngioVue RTVue XR
		Healthy vs. PP glaucoma	0.71 (0.62–0.80)	0.65 (0.55–0.75)	0.190	

AUC = area under the receiver operating characteristic curve; CI = confidence interval; POAG = primary open-angle glaucoma; PP = preperimetric; SD = standard deviation.
*Device manufacturers are as follows: Cirrus HD-OCT 5000 (optical microangiography, AngioPlex; Carl Zeiss Meditec, Dublin, CA), AngioVue RTVue XR OCT (Optovue, Fremont, CA), DRI OCT Triton (Topcon, Tokyo, Japan), PLEX Elite 9000 SS-OCT (Carl Zeiss Meditec, Dublin, CA); RS-3000 Advance OCT (Nidek, Gamagori, Japan); and Spectralis OCT (Heidelberg Engineering GmbH, Heidelberg, Germany).

also found that intereye macular vessel density asymmetry was higher in glaucoma suspects compared with healthy persons (2.5 vs. 1.2; $P = 0.015$), despite no difference in asymmetry of thickness parameters ($P = 0.718$). For distinguishing early glaucoma eyes from healthy control eyes, Kurysheva et al[46] noted that superficial macular vessel density had a greater AUC than OCT GCC thickness (0.800 vs. 0.739).

Two longitudinal studies (level I) compared macular vessel density decrease and GCC thinning in glaucoma eyes. Shoji et al[58] found that over a period of 14 months or less, serial OCTA measurements detected glaucomatous change in macula vessel density (−2.23%/year; $P = 0.004$) in eyes without evidence of change in GCC thickness (−0.44%/year; $P = 0.609$). Hou et al found that compared with healthy eyes, glaucoma eyes with VF loss showed a faster rate of both macular vessel density loss (−0.76%/year vs. −1.35%/year; $P = 0.042$) and GCC thinning (−0.70 μm/year vs. −1.18 μm/year; $P = 0.045$).[64] However, compared with preperimetric glaucoma eyes, glaucoma eyes with VF loss showed a faster rate of macular vessel density loss (−0.93%/year vs. −1.35%/year; $P = 0.043$) but not of GCC thinning (−1.08 μm/year vs. −1.18 μm/year; $P = 0.562$).[64] Moreover, as a percentage of their dynamic range of values, the rate of macular vessel density loss was significantly greater than the rate of GCC thinning (7.12%/year vs. 2.13%/year; $P < 0.001$).[64]

Association of Macular Vessel Density and Visual Fields

Studies also found moderate correlation between macular vessel density and VF defects (Table 3).[23,43,49,57,59,60,62,65,66] The strongest correlation was found between the inferior

macular vessel density area and the severity of central VF loss.[43,60,66] Yarmohammadi et al[43] demonstrated that in glaucoma eyes with a single-hemifield defect on Humphrey 24-2 VF, macular vessel density was reduced in the intact hemiretinae compared with the hemiretinae of healthy eyes (51.1% vs. 53.8%; $P < 0.001$). In addition, the amount of structural damage and vessel density loss in both affected and intact hemiretinae were found to be associated with the extent of perimetric loss in the corresponding hemifields, and these associations were generally stronger for vascular measurements compared with structural measurements (affected hemifield: parafoveal vessel density, $r = 0.615$; RNFL, $r = 0.496$; GCC, $r = 0.482$ [$P < 0.001$ for all]; intact hemifield: parafoveal vessel density, $r = 0.403$; RNFL, $r = 0.340$; GCC, $r = 0.290$ [$P < 0.05$ for all]).[43] However, Wan et al[59] found a stronger structure−function association for mean inner macular thickness than for mean inner macular vessel density ($R^2 = 0.59$ vs. 0.21; $P < 0.001$). Wu et al[65] also found higher correlation between VF MD loss and structural OCT measures (RNFL, $r = 0.36$; GCC, $r = 0.6$) than between VF MD loss and macular vessel density ($r = 0.3$). Similarly, Tao et al[66] noted stronger correlations with VF MD for ganglion cell−inner plexiform layer (GCIPL) thickness sectors (Spearman correlation coefficient: $r_s = 0.404$−0.625) than for macular vessel density sectors ($r_s = 0.274$−0.415). Using an index that accounts for both global macular vessel density and asymmetric loss of perfusion, Smith et al[62] found that the index performed better than macular vessel density alone and may be comparable with ganglion cell layer thickness (AUC, 0.83 vs. 0.90; $P = 0.07$). Jeong et al[67] found moderate correlation between parafoveal vessel density and foveal threshold as measured during Humphrey VF 24-2 testing ($r = 0.431$; $P < 0.001$), and the correlation was stronger than the correlation between macular GCIPL thickness and foveal threshold ($r = 0.335$).

Macular vessel density as measured by OCTA shows promise in monitoring advanced glaucoma. For moderate to advanced glaucoma, Shin et al[68] found a stronger association between macular vessel density and central VF sensitivity (central 12 points on Humphrey VF 24-2) than between macular GCIPL thickness and central VF sensitivity ($r = 0.625$ vs. $r = 0.437$; $P = 0.045$), although the opposite was true for early glaucoma ($r = 0.083$ vs. $r = 0.303$; $P = 0.049$). In contrast to structural OCT measurements, which reach a floor when the VF MD reaches approximately −14 dB (GCC thickness) and −17.5 dB (RNFL thickness), perifoveal vessel density does not show a measurement floor until the VF MD is less than −25 dB.[69] However, the number of measurement steps (dynamic range/test−retest variability) for macular vessel density was less than half the number of steps for structural OCT parameters, suggesting that macula vessel density may not be as sensitive as structural parameters for monitoring glaucoma progression until late-stage disease.[69]

Foveal Avascular Zone in Glaucoma

The foveal avascular zone (FAZ) has been evaluated in several studies for its usefulness in evaluating and monitoring glaucoma. The FAZ circularity index is a measure of compactness of a shape relative to a circle and is calculated as a function of the perimeter and the area of a shape (circularity index $= 4\pi \times$ area/perimeter^2). The circularity index of a circle is 1.0. Thus, an index closer to 0 indicates an irregular shape, and that closer to 1.0 indicates a circular shape. Compared with healthy eyes, eyes with glaucoma have been found to have an increased FAZ perimeter (2.32 mm vs. 2.64 mm; $P < 0.001$) and decreased FAZ circularity index (0.81 vs. 0.66; $P < 0.001$).[56] Indeed, the FAZ circularity index showed considerable diagnostic accuracy (AUC, 0.905) in discriminating glaucomatous eyes from healthy eyes.

The FAZ measurements may be superior to parafoveal vessel density in their diagnostic capability to differentiate glaucomatous eyes with central defects on 24-2 VF from healthy eyes. The FAZ perimeter showed a similar AUC value compared with the circumpapillary RNFL (0.88 vs. 0.96; $P = 0.24$) and macular GCIPL thickness (0.96) for differentiating eyes with central VF defects from healthy eyes.[27] The FAZ area was also significantly correlated with central VF function ($r = -0.347$; $P = 0.001$).[27,70] In contrast, parafoveal vessel density was less effective in differentiating normal eyes from eyes with central VF defects (parafoveal vessel density AUC, 0.53; FAZ area AUC, 0.78).[27] Not surprisingly, the FAZ parameters were less effective in differentiating eyes with peripheral VF loss from healthy eyes.[27] The FAZ area showed larger correlation with foveal vessel density ($r = -0.603$; $P < 0.001$) than with parafoveal vessel density ($r = -0.385$; $P < 0.001$) and weak, but still significant, correlation with circumpapillary vessel density ($r = -0.256$; $P = 0.003$).[70]

Peripapillary versus Macular OCT Angiography Diagnostic Performance

Peripapillary OCTA showed better discriminant ability (greater AUC) than macular OCTA in most studies that compared the 2 methods in differentiating glaucomatous and normal eyes.[34,35,41,49] For example, Rao et al[34] found that the AUC of peripapillary vessel density was significantly higher than that of parafoveal vessel density (0.83 vs. 0.63; $P = 0.005$). Lu et al[49] also showed better discriminant ability of peripapillary vessel density than of macular vessel density for distinguishing normal versus preperimetric glaucoma (AUC, 0.965 vs. 0.920; $P < 0.05$). However, Kurysheva et al[46] found a higher AUC to differentiate early glaucoma eyes from healthy eyes for the superficial macular vessel density (AUC, 0.80; $P = 0.001$) than for the vessel density of the combined disc and peripapillary area (AUC, 0.74; $P = 0.016$). Moghimi et al[69] found that perifoveal vessel density had a lower measurement floor (not reached until VF MD is less than −25 dB) than circumpapillary vessel density (reached when VF MD is less than −19 dB), although with fewer discriminating steps because of higher test−retest variability of measurements. Manalastas et al[31] found a stronger correlation between peripapillary vessel density and both RNFL ($r^2 = 0.404$) and macular thickness

($r^2 = 0.293$) than between macular vessel density and the structural parameters (RNFL, $r^2 = 0.237$; macular thickness, $r^2 = 0.141$).

Peripapillary Deep-Layer Microvasculature Dropout as Measured by OCT Angiography

Several studies examined the peripapillary deep-layer microvasculature by OCTA in glaucoma patients. The peripapillary choroid receives its blood supply primarily from the short posterior ciliary artery, which also supplies blood to deep optic nerve head structures, including the prelaminar and laminar tissues. Hence, the peripapillary choroidal network may be a surrogate marker for optic nerve head circulation, and abnormalities in the choroid microvasculature may correlate with glaucomatous optic nerve damage. Several groups investigated the peripapillary choroidal vasculature that can be visualized by OCTA in areas of β-zone peripapillary atrophy. The absence of retinal pigment epithelium in the region of peripapillary atrophy allows better OCT visualization of the deeper choroidal circulation. Other investigators imaged the deep-layer microvasculature using a 1050-nm swept-source OCT device that can image deeper than 840-nm SD OCT. Areas of regional choroidal or deep-layer microvasculature dropout (CMvD), defined as focal sectoral capillary dropout without any visible microvascular network, have been identified in up to half of patients with glaucoma but in no healthy control participants.[28,71–77] Most cases of CMvD occur in the inferior and inferotemporal sectors.[72]

The preponderance of eyes with CMvD have associated paracentral VF defects, whereas a much smaller portion of eyes with no CMvD have parafoveal VF defects (96% vs. 39%; $P < 0.001$).[28] Choroidal or deep-layer microvasculature dropout was associated significantly and correlated spatially with prior VF progression (multivariate logistic regression odds ratio, 5.04; $P = 0.018$), and the rate of prior VF progression was faster in eyes with CMvD than in those without microvascular dropout (visual field index, −2.23%/year vs. −0.05%/year; $P < 0.001$).[77] Moreover, the extent of CMvD, as measured by the angular circumference or arc width, and location of CMvD were associated significantly with severity ($r = -0.66$; $P < 0.001$) and the location ($\kappa = 0.34$; $P = 0.029$) of VF defects.[76] Glaucomatous eyes with localized CMvD were found to have more generalized peripapillary choroidal vessel density loss compared with glaucomatous eyes without localized CMvD ($P < 0.001$, multivariate logistic regression).[78] In addition, CMvD seems to affect the structure−function relationship. Compared with eyes of glaucoma patients without CMvD and matched for age and inferotemporal RNFL thickness, eyes with peripapillary CMvD showed worse VF total deviation (−7.66 dB vs. −4.89 dB; $P = 0.002$) and VF pattern deviation (−6.79 dB vs. −4.46 dB; $P = 0.007$).[74] In another study, lower baseline parapapillary choroidal vessel density was associated with progression of VF damage (multivariate logistic regression odds ratio for each % lower, 1.18; $P = 0.01$) but not with OCT RNFL thinning ($P = 0.21$).[79]

In a longitudinal study (level I) of normal-tension glaucoma patients (untreated IOP of less than 24 mmHg) followed up for at least 18 months, eyes with CMvD at baseline showed a significantly faster rate of RNFL loss than eyes without CMvD at baseline (−1.2 μm/year vs. −0.4 μm/year; $P = 0.036$), even after adjusting for age, mean follow-up IOP, axial length, central corneal thickness, and VF MD ($\beta = 0.85$; $P = 0.041$).[75]

Park et al[73] showed that the extent of CMvD is greater in eyes with recurrent disc hemorrhage (DH). Over at least 2 years, CMvD occurs more frequently in eyes with a prior DH (46.3% vs. 29.4%; $P = 0.025$) and often occurs at the hemorrhage site. Eyes with progressive RNFL thinning show more CMvD than stable eyes, with DH (77.3% vs. 10.5%; $P < 0.001$) or without DH (50.0% vs. 23.1%; $P < 0.001$).[73] Quadrant RNFL thinning is faster in eyes with both DH and CMvD compared with eyes with DH but without CMvD (−0.20 μm/year vs. −0.11 μm/year; $P = 0.004$). Progressive RNFL thinning is associated with recurrent DH and the presence of CMvD (multivariate logistic regression: DH, $\beta = 4.698$; $P = 0.008$; CMvD, $\beta = 11.473$; $P < 0.001$).[73] This suggests that CMvD, much like DH, may be useful as a biomarker for glaucoma progression.

Conclusions

OCT angiography provides remarkable detail of the microvasculature of the peripapillary and macular regions of the retina and choroid. Current technologies are able to segment the different vascular layers and allow users to visualize the superficial layers serving the RNFL and macular ganglion cell layer, both of keen interest in glaucoma disease diagnosis and management. Recent studies have shown significant correlation of the peripapillary (level II) and macular (levels I and II) microvasculature with RNFL and macular ganglion cell thickness OCT parameters, as well as with the location and severity of VF defects in glaucomatous eyes. In addition, deep-layer peripapillary microvascular dropout has been shown to correlate significantly with VF defects (level II) and progressive RNFL thinning (level I). These studies indicate that OCTA changes in glaucomatous eyes are consistent with glaucomatous pathophysiologic features and suggest that OCTA of the peripapillary and macular microvasculature can be useful in the diagnosis of primary open-angle glaucoma. OCT angiography provides complementary information to the traditional structural and functional parameters. It may be particularly helpful in the evaluation of patients who are glaucoma suspects and in the monitoring of advanced disease when structural OCT parameters have reached the floor of their dynamic range.

Future Research

Most published studies on the use of OCTA in glaucoma diagnosis and management have been cross-sectional. Additional studies should provide more information on key parameters of diagnostic discrimination, such as

sensitivity, specificity, and predictive value of positive or negative test results. Longitudinal investigations should evaluate OCTA parameters for their capability of predicting glaucoma onset and progression and for their usefulness in monitoring glaucoma progression. An important question that may be addressed is whether vascular changes lead to structural and functional loss or whether vascular changes result from functional loss resulting from decreased metabolic demand. Another important question is whether OCTA findings of vessel density loss are irreversible or whether vessel density increases with lowering of IOP.

As hardware and software technology advances, improvements can be expected in overcoming current limitations, such as projection artifacts, motion blur, difficulty in imaging deep optic nerve vasculature, and limited ability to quantitate blood flow through individual vessels. OCT angiography may improve our understanding of the mechanisms of glaucoma and thus lead to improved care for patients with glaucoma.

Footnotes and Disclosures

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Abbreviations and Acronyms:
AUC = area under the receiver operating characteristic curve; **CMvD** = choroidal or deep-layer microvasculature dropout; **DH** = disc hemorrhage; **FAZ** = foveal avascular zone; **GCC** = ganglion cell complex; **GCIPL** = ganglion cell−inner plexiform layer; **IOP** = intraocular pressure; **MD** = mean deviation; **OCTA** = OCT angiography; **RNFL** = retinal nerve fiber layer; **SD** = spectral-domain; **VF** = visual field.

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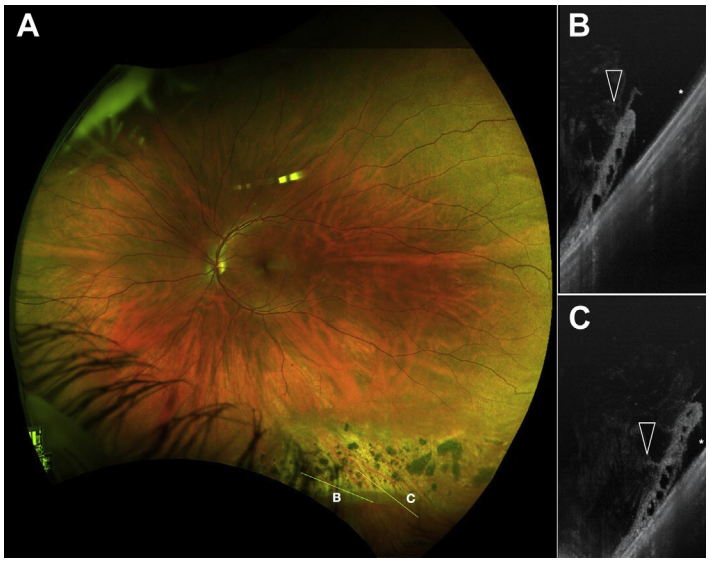
Pictures & Perspectives



Retinal Dialysis Revealed by Swept-Source OCT

We present a case of a peripheral retinal dialysis treated with laser photocoagulation imaged using far peripheral swept-source (SS)-OCT (Optos Silverstone, Optos). **A**, Ultra-widefield pseudocolor fundus photography of the left eye shows the inferotemporal retinal dialysis with the pigmented scars corresponding to the previous barricade laser treatment. Green lines (**B** and **C**) indicate the locations scanned by SS-OCT. B-scans (**B**) and (**C**) demonstrate vitreoretinal traction (*arrowhead*) with retinal elevation, the presence of intraretinal cystoid spaces and complete absence of the retina more distally (*asterisk*), consistent with a dialysis (Magnified version of Fig **A**-**C** is available online at www.aaojournal.org).

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Footnotes and Disclosures

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