# Optical Coherence Tomography Angiography in Glaucoma

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**ABSTRACT**

Optical coherence tomography angiography (OCTA) is a new device that provides noninvasive examination of the vascular structures in the optic disc, peripapillary area and macula. OCTA allows qualitative and quantitative examination of retinal vascular structures in layers and in three dimensions. It is now known that vascular damage progresses in both the peripapillary and macular superficial layers in patients with glaucoma as the disease stage progresses. This vascular damage is associated with structural tests in the early stages and functional tests in the late stages. Repeatability and reproducibility of OCTA is good, although it can be affected by subject-related, disease-related and eye-related factors. Recent studies have shown that OCTA can be used in the follow-up of progression in glaucoma patients.

**Keywords:** Glaucoma, Optical coherence tomography angiography, Diagnosis.

## INTRODUCTION

Glaucoma is an optic neuropathy characterized by progressive loss of retinal ganglion cells (RGCs).[1] Although its pathogenesis hasn't been fully elucidated, there are two major theories to explain loss of RGCs in glaucoma.[2] According to mechanical theory, RGC death is a result of elevated intraocular pressure (IOP). It has been proposed that elevated IOP blocks axoplasmic flow in RGCs within lamina cribrosa (LC). The neurotrophic growth factors are decreased, leading to RGC death.[3] The elevated IOP is the most important risk factor for glaucoma. However, there are situations where glaucoma progression occurs despite low IOP.[4]

The alternative theory is "vascular theory" to explain glaucoma pathogenesis. It is assumed that glaucoma is a consequence of decreased blood flow.[5] The impaired ocular blood flow leads ischemia causing damage optic nerve.[4]

Many techniques including fluorescein angiography (FA),[6] indocyanine green angiography (ICA),[7] scanner laser ophthalmoscopy,[8] laser Doppler flowmetry[9] and laser speckle flowgraphy[10] have been used to demonstrate changes in blood flow. However, these methods have some limitation in defining retinal micro-vascular changes in glaucoma and have had little success in elucidating the vascular role in glaucoma.[11] In addition, majority of these technologies failed to provide repeatable and quantitative measurements.[12]

Optical coherence tomography angiography (OCTA) is a non-invasive imaging technique. It provides 3-dimensional images of optic nerve head (ONH) and retinal blood vessels in vivo. In addition, it ensures better evaluation of ocular blood flow and retinal micro-vascularity in glaucoma.[13] It also allows qualitative and quantitative assessment of blood vessels.

Currently, various OCTA devices from different manufacturers are used in the clinical practice. There are four different algorithms and devices for evaluation ocular micro-vascularity: split-spectrum amplitude-decorrelation angiography (SSADA) used in Optovue (RTVue XR Avanti; Optovue, Inc. Fremont, CA, US); OCT based micro-angiography OMAG) used in Angioplex (Cirrus HD-5000; Zeiss Meditec, Dublin, CA, US); OCTA ratio analysis (OCTARA; swept-source OCT, Topcon, Japan) used in Topcon DRI OCT Triton; and full spectrum

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amplitude decorrelation angiography (FS-ADA) used in Spectralis OCT2 module (Heidelberg Engineering, Germany).[14]

Available OCTA devices can scan optic disc region and macula. Optic disc is generally scanned using volumetric scans involving a field of 4.5x4.5 mm$^2$ centered around optic disc (Figure 1). Optic disc scans are divided into quadrants for further analysis. The two sections found to be helpful in the glaucoma are radial peripapillary capillary (RPC) that defines the vessels within the retinal nerve fiber layer (RNFL) layer and choriocapillaris section that defines choroidal vessels within parapapillary region.

RPC layer extends to posterior margin of RNFL through inner limiting membrane (ILM). In glaucomatous eyes, reduced vascularity is observed in RPC.[15] Choroidal section is used to assess deep retinal and choroidal structures. In RTVue-XR SD-OCT, choroidal section begins from 75 µm under retinal pigment epithelium;[16] however, it may vary in different devices.

Macular OCTA scan is generally performed using a volumetric scan involving a field of 3×3 mm$^2$ or 6×6 mm$^2$ (Figure 2). The scans of 6×6 mm$^2$ (Figure 3) detect better glaucomatous changes compared to scans of 3×3 mm$^2$.[17] The macular assessment can be performed in superficial and deep retinal layers. In RTVue-XR SD-OCT device, superficial retinal layer extends from 3 µm below the ILM to 15 µm below the inner plexiform layer (IPL).[16] In glaucomatous eyes, vascular changes are more prominent in superficial retinal layers when compared to deep retinal layers.[18] In recent years, changes in deep retinal layers have also been examined; however, the diagnostic capacity was found to be better for superficial macular vascular structure then deep layers regardless of glaucoma stage.[19]

The OCTA quantitatively assess ocular circulation using 2 parameters: flow index and vascular density (VD). The flow index is defined as mean decorrelation value in the region of interest. The vascular density is more commonly used when evaluating OCTA data. The VD is defined as the percentage area occupied by vessels in the measured area.[20] In most devices, VD is calculated by device software in automated manner. However, VD measurements can vary among different devices due to different algorithms and segmentation techniques even among healthy individuals. The OCTA measurements cannot be used interchangeably.[21]

## REPEATABILITY AND REPRODUCIBILITY

Intra-visit repeatability and inter-visit reproducibility of OCTA have been evaluated in both peripapillary and superficial macular layers and OCTA had good repeatability and reproducibility. In studies using RTVue XR spectral-domain OCT, it was shown that intra-visit

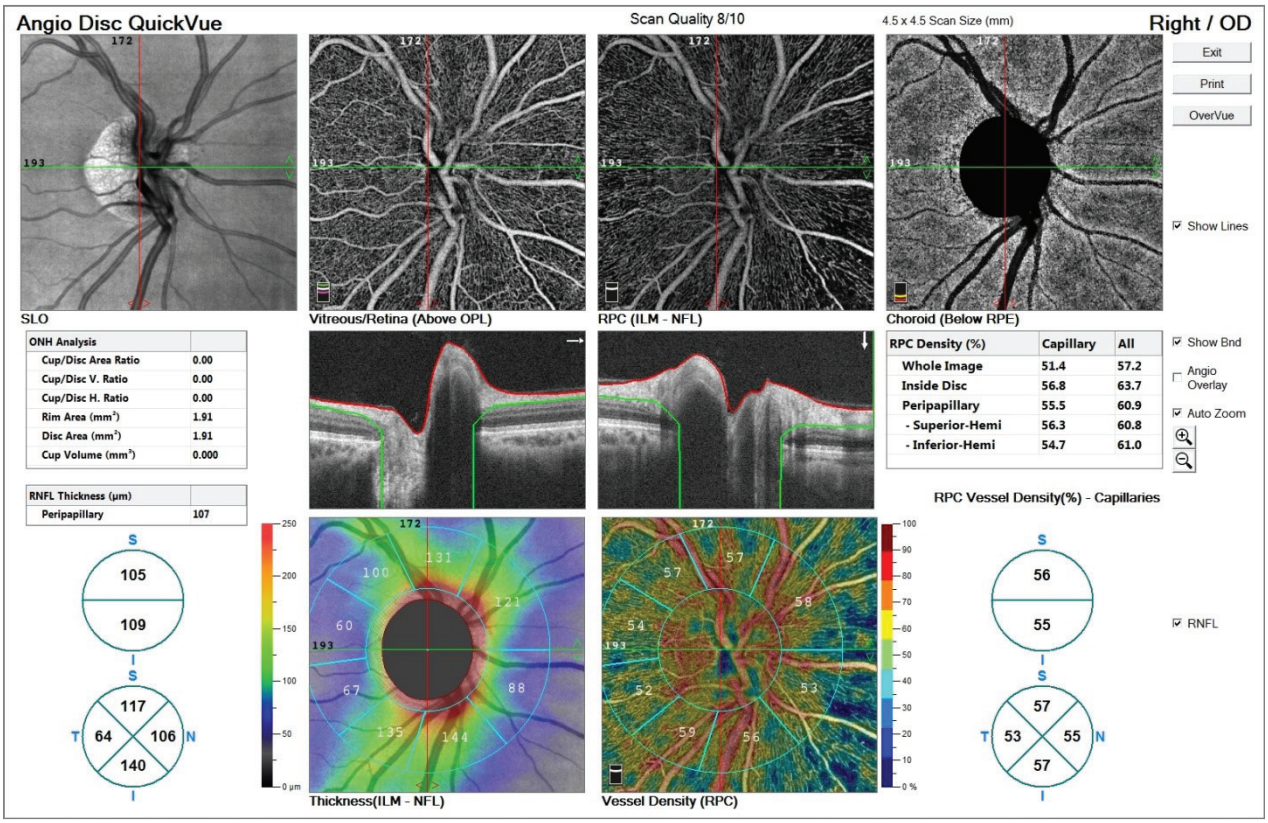


**Figure 1:** *Peripapillary OCTA image in a healthy individual.*

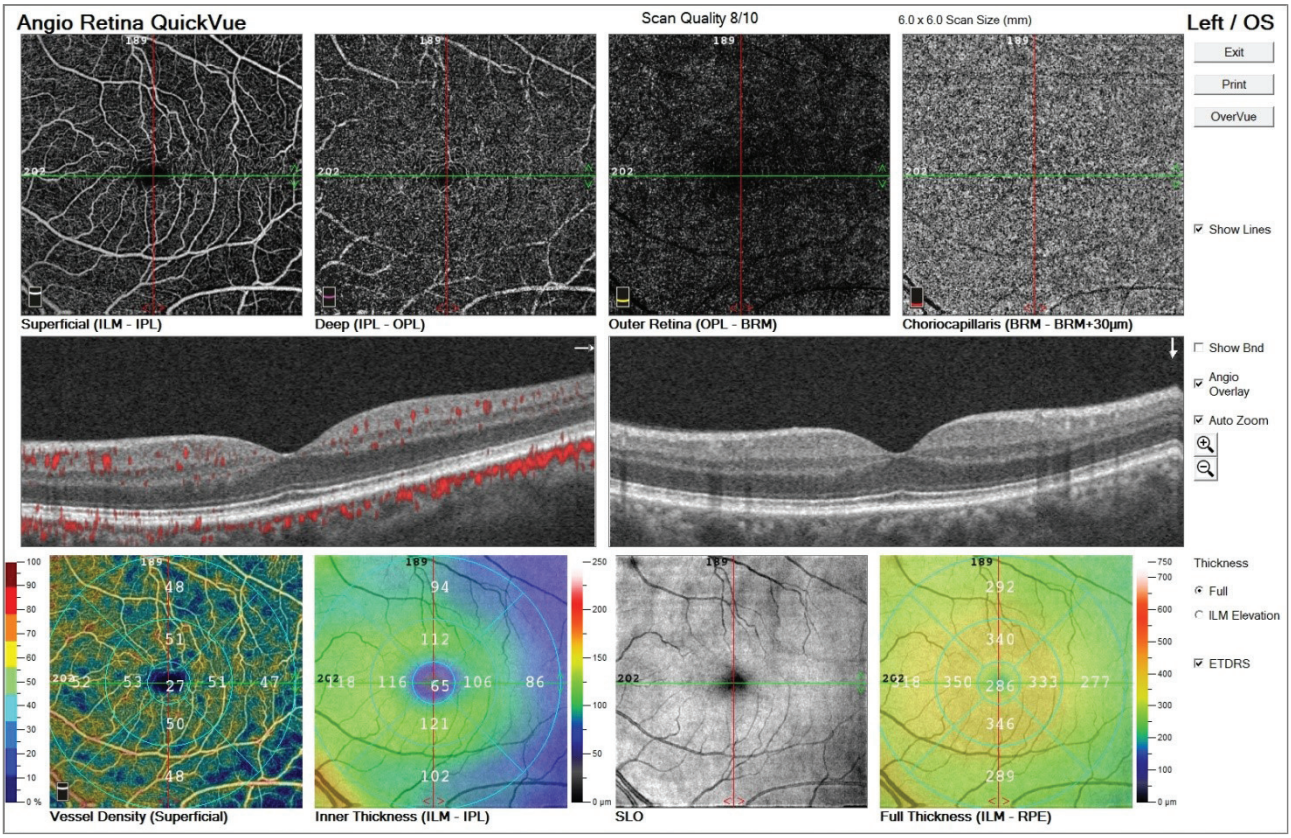


**Figure 2:** *Macular OCTA image in a healthy individual.*

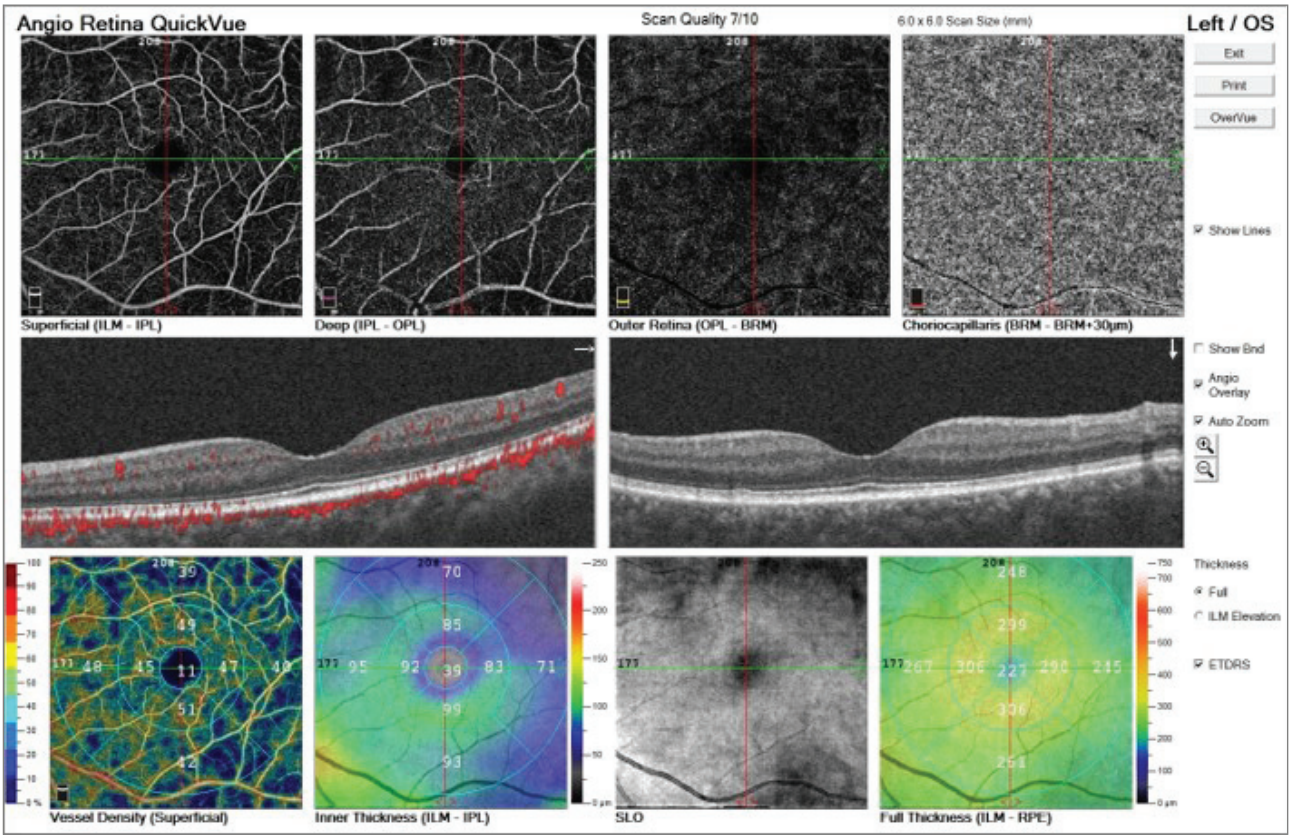


**Figure 3:** *Peripheral vascular damage are seen in OCTA image (6x6 mm$^2$) in a patient with early glaucoma.*

coefficient of variation (CV) ranged from 2.4% to 6.6%.[22] In healthy and glaucomatous eyes, repeatability coefficient ranged from 3.3% to 7.1% for macular and peripapillary OCTA parameters.[22] That is, the variability in peripapillary or parafoveal VD is less than 5% to 7%. It is clinically insignificant as test-retest variability.[14]

Intra-visit repeatability was found to be similar in healthy and glaucomatous eyes.[22-24] Based on global measurements, repeatability is poorer in peripapillary sectors. For OCTA measurements, signal power index values were found to be positively correlated with intra-visit repeatability.[22]

Inter-visit CV has been reported as 3.2-9.0% for macular and peripapillary OCTA parameters.[23, 24] As similar to repeatability, reproducibility was poorer in peripapillary sectors; in addition, it was also poorer in glaucomatous eyes than healthy eyes.[23]

It was observed that there are difference across measurements when repeatability of peripapillary measurements was assessed between OCTA devices. Again, OCTA measurements cannot be used interchangeably among the different devices.[21]

In a study comparing CVs of peripapillary and macular optical coherence tomography (OCT) ad OCTA, the CV was lower in OCT than OCTA.[23] In other words, OCTA repeatability is poorer than OCT. Mean intra-visit and inter-visit CV was found to be 4.0% for macular and peripapillary OCTA while it was 1.% for RNFL and ganglion cell complex (GCC), indicating a significant difference. This variability should be kept in mind in the follow-up of glaucoma progression.[23]

## DIAGNOSTIC CAPACITY OF OCTA IN PRIMARY OPEN-ANGLE GLAUCOMA

In previous studies, area under curve (AUC) was found to be high for peripapillary region in patients with glaucoma (>0.85 for both OCTA and OCT).[25-29] The asymmetrical VD measurements can be helpful in discrimination between suspected glaucoma and healthy eyes in early glaucoma; it provided higher AUC value when compared to asymmetrical RNFL thickness.[30]

There are contradictory results in studies on diagnostic performance of macular superficial OCTA parameters. High AUC values were reported for whole-image macular superficial VD in some studies while medium values were reported in others.[18, 29] In some studies, it was found that diagnostic value of GCC was found to be higher when compared to macular superficial VD.[31, 32] This variation may be due to use of different area (3x3 $mm^2$ and 6x6 $mm^2$) for macular measurements in different studies. In glaucoma, area outside of 3x3 $mm^2$ but inside of 6x6 $mm^2$ is more vulnerable to injury.[27] Thus, AUC value can be lower in studies using macular area of 3x3 $mm^2$ while it can be higher in studies using macular area of 6x6 $mm^2$. In other words, measurements using macular area of 6x6$mm^2$ have higher diagnostic value than those using 3x3$mm^2$.[18] In addition, OCTA measurements and OCT thickness measurements may not be overlap directly when macular area of 3x3 $mm^2$ is used.[31] In addition, test-retest variability was found to be lower in measurements using macular area of 3x3$mm^2$.[32] As a result, macular measurements using the area of 6x6$mm^2$ is recommended in glaucoma. As similar to peripapillary region, macular superficial VD has higher AUC value than GCC in discrimination between suspected glaucoma and healthy eyes.[31]

In most studies, AUC values of optic disc OCTA parameters were found to be lower than OCT parameters.[33, 34] This is due to individual variation of optic disc morphology. This leads to lower discriminative power of optic disc OCTA parameters in glaucoma. Another reason is challenges in identification of micro-vascularity due to presence of great vessels over optic disc.[35]

In conclusion, discriminative power for distinguishing glaucomatous eyes from healthy eyes is comparable between OCTA and OCT. The diagnostic capability of OCTA increases by progression of glaucoma.[28, 34] There are various results in studies using different devices due to differences in segmentation methods across devices. However, combined use of OCTA and OCT improves diagnostic value when compared to individual use of these modalities.[36]

In recent studies, it was shown that VD was decreased by increasing severity of glaucoma.[18, 37, 38] Also recently, there are studies on deep retinal microvascular drop-out (MvD) in patients with glaucoma. This denotes complete loss of choriocapillaris at the area of parapapillary atrophy (PPA).[39, 40] It was also shown that such drop-outs are true perfusion defect by ICA.[41]

## CORRELATION OF OCTA MEASUREMENTS WITH VISUAL FIELD AND OCT MEASUREMENTS

The OCTA measurements are correlated with visual field (VF) and OCT measurements. This relationship is not linear but it was found to be stronger than linear relationship.[42, 43] In addition, the correlation of VF parameters with OCTA measurement seems to be stronger than those with OCT measurements in glaucomatous eyes with high myopia[44] and in eyes with advanced glaucoma.[45,46] It has been reported that base effect is less in OCTA when compared to OCT.[47] Moreover, it seems that there is no detectable base effect for macular VD measurements. Given these

findings, OCTA can play an important role in the follow-up glaucoma progression in advanced disease.[47]

In some studies, it was reported that there is a topographic relationship between localization of MvD and morphological parameters (RNFL thinning and LC defects) or functional parameters (VF loss) in eyes with POAG.[39, 48, 49]

In studies on eyes with perimetric glaucoma and VF defect limited to hemi-field, OCTA changes were evaluated in areas corresponding to healthy hemi-field. In these studies, it was found that peripapillary VD and RNFL thickness were decreased in the hemi-retina corresponding to perimetrically intact hemi-field when compared to healthy eyes.[50, 51] In a recent study on eyes with POAG and VF defect limited to hemi-field, it was shown that RNFL thickness and ganglion cell analysis (GCA) value were markedly low in the hemi-retina corresponding to perimetrically intact hemi-field in eyes with MvD when compared to those without.[52]

## FACTORS INFLUENCING ON OCTA MEASUREMENTS

Many disease-, patient-and eye-dependent factors may affect peripapillary and macular VD measurements. In clinical practice, these factors must be taken into consideration when analyzing OCTA data.

### Disease-dependent Factors

The variability in VD has been defined in different subgroup of patients with POAG. The eyes with POAG are not homogeneous regarding VD even in patients with similar stage. In addition, ocular characteristics of eyes with glaucoma can affect VD. The vascular damage on OCTA is increased by increasing functional and structural disease severity in glaucoma (Figure 4, 5).[18, 25]

The localization of global and local OCTA parameters are associated to VF parameters. Both peripapillary and macular VD were found to be associated with VF defects.[31,43,53,54]

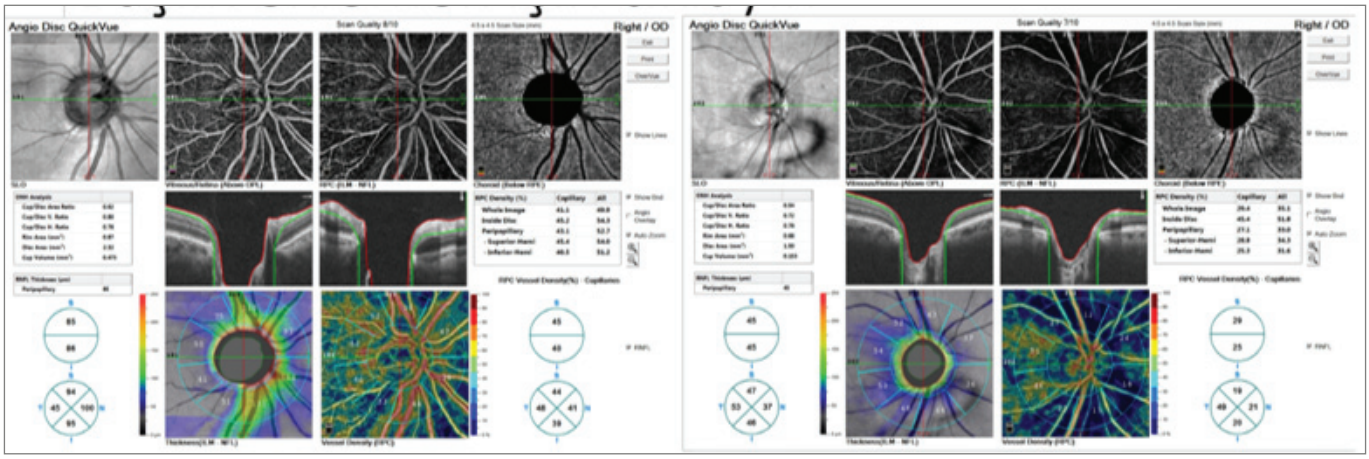


**Figure 4:** *Peripapillary OCTA image in patients with early* (left) *and advanced glaucoma* (right). *Marked decrease is seen in peripapillary vascularity in OCTA image* (right).

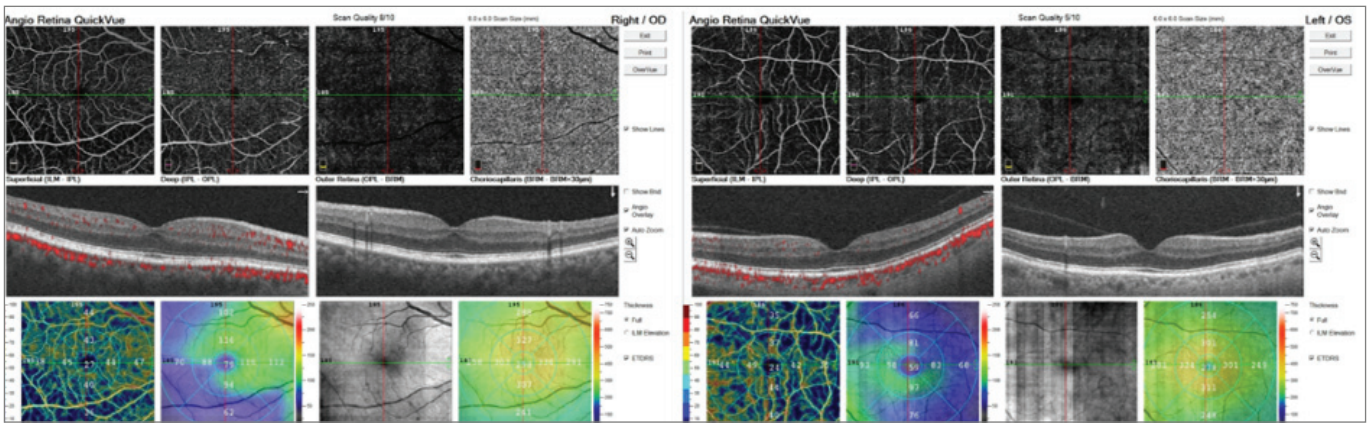


**Figure 5:** *Macular OCTA image in patients with early* (left) *and advanced glaucoma* (right). *Vascular loss is present at inferior hemi-field in a patients with early glaucoma* (left) *while marked decrease is seen in macular superficial vessels in OCTA image* (right).

Again, it was found that the width of foveal avascular zone was associated with central VF defect.[55] In particular, there is a strong correlation between superotemporal and inferotemporal peripapillary VD and corresponding VF sectors.[43, 53] There are many studies reported that the relationship between thickness and function is stronger than those between vascularity and function .[29, 38, 42, 53]

OCTA may be valuable in the follow-up of the patients with suspected glaucoma. Vascular injury can be detected even before presence of marked reduction in RNFL thickness in eyes with ganglion cell damage.[56] Reduction in structural parameters is directly related to VD decline.[26, 56, 57] In eyes with early, preperimetric open-angle glaucoma, it was shown that RNFL defects are correlated with localized peripapillary VD decline in terms of localization.[57]

The MvD prevalence and extent are increased by increasing disease severity. The MvD is more prominent in patients with VF defect at parafoveal region.[58-60]

In studies on patients with similar VF defects, it was shown that the extent of peripapillary VD decline was higher in patients with focal LC defect.[61] The decline in VD was correlated with localization at the side with LC defect.[61] However, no significant difference was found regarding macular VD in eyes with and without LC defect which showed similar glaucoma severity.[62] In addition, presence of MvD was found to be associated with LC defects.[39, 63]

In a study comparing POAG patients with and without disc hemorrhage, inferotemporal peripapillary VD was found to be lower in patients with disc hemorrhage.[14] The MvD is associated with disc hemorrhage. The MvD prevalence is higher in POAG patients with disc hemorrhage than those without.[58, 64]

In addition, presence of secondary etiology for glaucoma such as pseudoexfoliation (PEX) also affects peripapillary and macular VD values. The extend of decline in peripapillary VD is higher in PEX glaucoma than POAG. Similarly, there is a decline in peripapillary VD in eyes with PEX when compared to healthy population.[65] In the study we conducted in our clinic, a decrease in macular superficial VD was shown in eyes with PEX, which are structurally similar to healthy individuals.[66]

**Patient-dependent Factors**

Demographics

In previous studies, it has been shown that both peripapillary and macular VD are decreased by advancing age and the extent of the decrease is greater in male gender.[11, 67, 68] In a study comparing glaucomatous eyes from African and European descent, it was found that VD measurements were lower in individuals from European descent.[50, 69]

Diurnal variation

There is minimal, clinically irrelevant diurnal variation in OCTA measurements.[70]

Exercise and Systemic Diseases

The patient should have rest before OCTA examination since increased physical activity can lead alteration of perfusion in optic nerve and macula.[71] In addition, systemic blood pressure and diabetes mellitus can also affect OCTA.[72]

It was found that peripapillary VD was lower while macular VD was higher in hypertensive patients without retinopathy. Again, VD was lower in diabetic patients without retinopathy.[72] The decline in VD was correlated with duration diabetes mellitus.[73] In another study on diurnal variation, it was found that superficial macular and peripapillary VD was negatively correlated with heart rate while they were positively correlated with mean arterial pressure.[74]

Treatment

Topical β-blockers have influence on VD measurements.[18] It was reported that topical ß-blocker administration led 3.3% lower superficial macular VD when compared to alpha-agonists and carbonic anhydrase inhibitors.[18]

**Eye-dependent Factors**

Myopia

In studies comparing eyes with high myopia and emmetropic eyes, it was seen that VD measurements were lower in peripapillary region although there was no difference in macular region.[75] The peripapillary VD were lower in myopic eyes when compared to normal population while it was further declined in glaucomatous eyes with myopia.[76] In myopic eyes, one reason for lower VD values may be magnifier effect in quantitative measurement of retinal vascular network.[77] It was found that the relationship between regional VF and peripapillary VD was stronger than the relationship with RNFL thickness in POAG eyes with high myopia.[44]

Optic Disc Area

Optic disc area has no effect on VD measurements.[72]

Signal intensity

In many studies on OCTA, it was shown that low signal intensity is associated with low OCTA measurements.

Presumably, the software cannot clearly discriminate static structures from blood vessels at low signal intensities. In clinical practice, signal intensity should be taken into consideration when analyzing OCTA data.[11, 72]

Intraocular Pressure

In some studies, it was shown that peripapillary VD values, measured as low initially, were higher after reduction of IOP with treatment.[78, 79] However, there are studies reporting that IOP reduction did not alter DD values.[80, 81]

## MONITORING GLAUCOMA PROGRESSION AND RISK IDENTIFICATION USING OCTA

Although there is no long-term studies using OCTA, promising results have been reported regarding follow-up for glaucoma progression with VD monitorization.[68, 11, 82] However, it should kept in mind that VD can be affected by systemic perfusion, retinal oxygenation or hypercapnia when monitoring glaucoma progression using OCTA.

In a study including 2-years of follow-up in 20 patients with OHT and 24 patients with glaucoma, Holló et al. reported found a significant negative slope in RNFL thickness in one-third of patients but no decline in peripapillary VD.[83] In another study, same author reported negative slope in 17% of patients by removing great retinal vessels via software.[78] This decline in peripapillary VD was compatible with progression in corresponding RNFL region.

In a recent study, Shin et al. evaluated relationship between peripapillary VD, RNFL thickness and VF in 159 patients with varying stages of POAG over 2.66 years. Authors found that longitudinal peripapillary VD loss was associated with progressive VF loss regardless of glaucoma stage.[84]

The identification of patients at high risk for glaucoma development and progression is highly important in the management of glaucoma. The known risk factors include age, IOP, optic disc hemorrhage and decreased central corneal thickness.

In a follow-up study in patients with mild and moderate glaucoma, it was found that lower baseline macular and peripapillary VD is associated with faster RNFL progression.[68] Although follow-up duration was 2 years in the study, authors suggested the relationship is independent from baseline RNFL thickness and that OCTA can be used to predict risk for glaucoma progression.

In OCTA studies, it was reported that MvD can be used in the follow-up of progression and risk analysis.[85] The presence of MvD is associated with rapid thinning in RNFL and VF progression, particularly with central VF defect.[64, 86-88] In a recent study, it was found that MvD is more closely related with glaucoma progression if it is adjacent to optic disc margin.[89]

Above-mentioned studies suggest that peripapillary and macular VD can provide important, additional information regarding glaucoma progression. One of these factors can be that the decreased optic disc and retinal perfusion might have led to accelerated retinal ganglion cell death. Again, decreased perfusion in OCTA can be a biomarker for dysfunctional retinal ganglion cells which are viable and have decreased metabolic demands.[14] Future studies comparing OCTA parameters with structural and functional parameters will better elucidate role of OCTA in the follow-up of glaucoma progression.

## LIMITATIONS OF OCTA

The acquisition of OCTA images is a time-consuming procedure; thus, motion artifacts during procedure are common in OCTA imaging. To overcome poor scan quality, real-time eye-tracking technology and high-definition scanning mode are two recent improvements to control motion artifacts more effectively.[90] In the future, shortening acquisition time can improve image quality.

Medium opacity such as cataract or dry eye also impair scan quality, resulting in lower VD. Pupil dilatation enhances signal intensity and can allows better scan quality.

The OCTA technologies cannot deeper tissues at quality level comparable to those achieved in superficial layers. This is due to projection of signals from superficial retinal vessels to deep layers, resulting in projection artifacts.[13] It is thought that future technologies will allow better evaluation of deep retinal layers and choroidal vascularity.[91, 92]

Another important issue is that normal anatomic variation or pathological changes in retinal layers may lead segmentation errors. This should be taken into account when analyzing OCTA data.

## CONCLUSION

The OCTA is still a novel, non-invasive modality that allows monitoring vascular changes during glaucomatous process by providing 3-dimensional images of retinal vascular layers. Monitoring vascular changes will be beneficial in the follow-up of glaucoma progression and contribute our understanding about vascular etiopathogenesis. In order to detect early diagnosis and progression in patients with early glaucoma, additional examination methods may be needed when there is doubt in structural tests. Again, a base

effect is present in structural tests in advanced glaucoma and additional testing together with visual field testing will be helpful. OCTA will be more beneficial by introduction of devices allowing rapid acquisition, decreased motion artifacts, less affected by media opacities and better assessment of deep tissues. Further long-term studies will clarify whether OCTA detects vascular changes earlier than structural tests and its role in the follow-up glaucoma progression.

## REFERENCES


1. Weinreb RN, Aung T, Medeiros FA. The pathophysiology and treatment of glaucoma: a review. JAMA 2014;311:1901-11.
2. Fechtner RD, Weinreb RN. Mechanisms of optic nerve damage in primary open angle glaucoma. Surv Ophthalmol 1994;39:23-42.
3. Yan DB, Coloma FM, Metheetrairut A, et al. Deformation of the lamina cribrosa by elevated intraocular pressure. Br J Ophthalmol 1994;78:643-8.
4. Mansouri K. Optical coherence tomography angiography and glaucoma: searching for the missing link. Expert Rev Med Devices. 2016;13:879-80.
5. Flammer J. The vascular concept of glaucoma. Surv Ophthalmol 1994;38:3-6.
6. Arend O, Plange N, Sponsel WE, et al. Pathogenetic aspects of the glaucomatous optic neuropathy: fluorescein angiographic findings in patients with primary open angle glaucoma. Brain Res Bull 2004;62:517-24.
7. O'Brart DP, de Souza Lima M, Bartsch DU, et al. Indocyanine green angiography of the peripapillary region in glaucomatous eyes by confocal scanning laser ophthalmoscopy. Am J Ophthalmol 1997;123:657-66.
8. Rechtman E, Harris A, Kumar R, et al. An update on retinal circulation assessment technologies. Curr Eye Res 2003;27:329-43.
9. Nicolela MT, Hnik P, Drance SM. Scanning laser Doppler flowmeter study of retinal and optic disk blood flow in glaucomatous patients. Am J Ophthalmol 1996;122:775-83.
10. Yaoeda K, Shirakashi M, Funaki S, et al. Measurement of microcirculation in the optic nerve head by laser speckle flowgraphy and scanning laser Doppler flowmetry. Am J Ophthalmol 2000;129:734-9.
11. Shoji T, Zangwill LM, Akagi T, et al. Progressive Macula Vessel Density Loss in Primary Open-Angle Glaucoma: A Longitudinal Study. Am J Ophthalmol 2017;182:107-17.
12. Flammer J, Orgul S, Costa VP, et al. The impact of ocular blood flow in glaucoma. Prog Retin Eye Res 2002;21:359-93.
13. Jia Y, Tan O, Tokayer J, et al. Split-spectrum amplitude-decorrelation angiography with optical coherence tomography. Opt Express. 2012;20: 4710-25.
14. Moghimi S, Hou H, Rao H, et al. Optical Coherence Tomography Angiography and Glaucoma: A Brief Review. Asia Pac J Ophthalmol (Phila). 2019 Apr 4.
15. Liu L, Edmunds B, Takusagawa HL, et al. Projection-Resolved Optical Coherence Tomography Angiography of the Peripapillary Retina in Glaucoma. Am J Ophthalmol 2019;207:99-109.
16. Huang D, Jia Y, Gao SS, et al. Optical Coherence Tomography Angiography Using the Optovue Device. Dev Ophthalmol 2016;56:6-12.
17. Rao HL, Riyazuddin M, Dasari S, et al. Diagnostic Abilities of the Optical Microangiography Parameters of the 3×3 mm and 6×6 mm Macular Scans in Glaucoma. J Glaucoma 2018;27:496-503.
18. Takusagawa HL, Liu L, Ma KN, et al. Projection-Resolved Optical Coherence Tomography Angiography of Macular Retinal Circulation in Glaucoma. Ophthalmology 2017;124:1589-99.
19. Lee JY, Shin JW, Song MK, et al. Glaucoma diagnostic capabilities of macular vessel density on optical coherence tomography angiography: superficial versus deep layers. Br J Ophthalmol. 2021 Mar.
20. Jia Y, Morrison JC, Tokayer J, et al. Quantitative OCT angiography of optic nerve head blood flow. Biomed Opt Express 2012;3:3127-37.
21. Lei J, Pei C, Wen C, et al. Repeatability and Reproducibility of Quantification of Superficial Peri-papillary Capillaries by four Different Optical Coherence Tomography Angiography Devices. Sci Rep 2018;8:17866.
22. Venugopal JP, Rao HL, Weinreb RN, et al. Repeatability of vessel density measurements of optical coherence tomography angiography in normal and glaucoma eyes. Br J Ophthalmol. 2018;102:352-7.
23. Manalastas PIC, Zangwill LM, Saunders LJ, et al. Reproducibility of optical coherence tomography angiography macular and optic nerve head vascular density in glaucoma and healthy eyes. J Glaucoma. 2017;26:851-9.
24. Holló G. Intrasession and between-visit variability of sector peripapillary angioflow vessel density values measured with the angiovue optical coherence tomograph in different retinal layers in ocular hypertension and glaucoma. PLoS One. 2016;11:e0161631.
25. Geyman LS, Garg RA, Suwan Y, et al. Peripapillary perfused capillary density in primary open-angle glaucoma across disease stage: an optical coherence tomography angiography study. Br J Ophthalmol. 2017;101:1261-8.
26. Yarmohammadi A, Zangwill LM, Diniz-Filho A, et al. Optical coherence tomography angiography vessel density in healthy, glaucoma suspect, and glaucoma eyes. Invest Ophthalmol Vis Sci. 2016;57:OCT451-9.
27. Rao HL, Kadambi SV, Weinreb RN, et al. Diagnostic ability of peripapillary vessel density measurements of optical coherence tomography angiography in primary

open-angle and angle-closure glaucoma. Br J Ophthalmol. 2017;101:1066-70.

28. Rao HL, Pradhan ZS, Weinreb RN, et al. Regional comparisons of optical coherence tomography angiography vessel density in primary open-angle glaucoma. Am J Ophthalmol. 2016;171:75-83.
29. Chen HS, Liu CH, Wu WC, et al. Optical coherence tomography angiography of the superficial microvasculature in the macular and peripapillary areas in glaucomatous and healthy eyes. Invest Ophthalmol Vis Sci. 2017;58:3637-45.
30. Hou H, Moghimi S, Zangwill LM, et al. Inter-eye asymmetry of optical coherence tomography angiography vessel density in bilateral glaucoma, glaucoma suspect, and healthy eyes. Am J Ophthalmol. 2018;190:69-77.
31. Penteado RC, Zangwill LM, Daga FB, et al. Optical coherence tomography angiography macular vascular density measurements and the central 10-2 visual field in glaucoma. J Glaucoma. 2018;27:481-9.
32. Wan KH, Lam AKN, Leung CK. Optical coherence tomography angiography compared with optical coherence tomography macular measurements for detection of glaucoma. JAMA Ophthalmol. 2018;136: 866-74.
33. Chihara E, Dimitrova G, Amano H, et al. Discriminatory power of superficial vessel density and prelaminar vascular flow index in eyes with glaucoma and ocular hypertension and normal eyes. Invest Ophthalmol Vis Sci. 2017;58:690-7.
34. Rao HL, Pradhan ZS, Weinreb RN, et al. A comparison of the diagnostic ability of vessel density and structural measurements of optical coherence tomography in primary open angle glaucoma. PLoS One. 2017;12: e0173930.
35. Van Melkebeke L, Barbosa-Breda J, Huygens M, et al. Optical coherence tomography angiography in glaucoma: a review. Ophthalmic Res. 2018;60: 139-51.
36. Park K, Kim J, Lee J. Macular vessel density and ganglion cell/inner plexiform layer thickness and their combinational index using artificial intelligence. J Glaucoma. 2018;27:750-60.
37. Liu L, Jia Y, Takusagawa HL, et al. Optical Coherence Tomography Angiography of the Peripapillary Retina in Glaucoma. JAMA Ophthalmol 2015;133:1045-52.
38. Shin JW, Lee J, Kwon J, et al. Regional vascular density-visual field sensitivity relationship in glaucoma according to disease severity. Br J Ophthalmol 2017;101:1666-72.
39. Suh MH, Zangwill LM, Manalastas PI, et al. Deep Retinal Layer Microvasculature Dropout Detected by the Optical Coherence Tomography Angiography in Glaucoma. Ophthalmology 2016;123:2509-18.
40. Lee EJ, Kim TW, Lee SH, et al. Underlying Microstructure of Parapapillary Deep-Layer Capillary Dropout Identified by Optical Coherence Tomography Angiography. Invest Ophthalmol Vis Sci 2017;58:1621-7.
41. Lee EJ, Lee KM, Lee SH, et al. Parapapillary choroidal microvasculature dropout in glaucoma: a comparison between optical coherence tomography angiography and indocyanine green angiography. Ophthalmology. 2017; 124:1209-17.
42. Yarmohammadi A, Zangwill LM, Diniz-Filho A, et al. Relationship between Optical Coherence Tomography Angiography Vessel Density and Severity of Visual Field Loss in Glaucoma. Ophthalmology 2016;123:2498-508.
43. Rao HL, Pradhan ZS, Weinreb RN, et al. Relationship of Optic Nerve Structure and Function to Peripapillary Vessel Density Measurements of Optical Coherence Tomography Angiography in Glaucoma. J Glaucoma 2017;26:548-54.
44. Shin JW, Kwon J, Lee J, et al. Relationship between vessel density and visual field sensitivity in glaucomatous eyes with high myopia. Br J Ophthalmol 2018; 312085.
45. Ghahari E, Bowd C, Zangwill LM, et al. Association of Macular and Circumpapillary Microvasculature with Visual Field Sensitivity in Advanced Glaucoma. Am J Ophthalmol 2019;204:51-61.
46. Shin JW, Lee J, Kwon J, et al. Relationship between macular vessel density and central visual field sensitivity at different glaucoma stages. Br J Ophthalmol 2019;103:1827-33.
47. Moghimi S, Bowd C, Zangwill LM, et al. Measurement Floors and Dynamic Ranges of OCT and OCT Angiography in Glaucoma. Ophthalmology 2019;126:980-8.
48. Lee EJ, Lee SH, Kim JA, et al. Parapapillary Deep-Layer Microvasculature Dropout in Glaucoma: Topographic Association With Glaucomatous Damage. Invest Ophthalmol Vis Sci 2017;58:3004-10.
49. Suh MH, Park JW, Kim HR. Association Between the Deep-layer Microvasculature Dropout and the Visual Field Damage in Glaucoma. J Glaucoma 2018;27:543-51.
50. Yarmohammadi A, Zangwill LM, Diniz-Filho A, et al. Peripapillary and Macular Vessel Density in Patients with Glaucoma and Single-Hemifield Visual Field Defect. Ophthalmology 2017;124:709-19.
51. Pradhan ZS, Dixit S, Sreenivasaiah S, et al. A Sectoral Analysis of Vessel Density Measurements in Perimetrically Intact Regions of Glaucomatous Eyes: An Optical Coherence Tomography Angiography Study. J Glaucoma 2018;27:525-31.
52. Jo YH, Kwon J, Shon K, et al. Greater Severity of Glaucomatous Damage in Eyes With Than Without Choroidal Microvasculature Dropout in Open-Angle Glaucoma. Invest Ophthalmol Vis Sci 2019;60:901-12.
53. Holló G. Relationship between OCT angiography temporal peripapillary vessel-density and octopus perimeter paracentral cluster mean defect. J Glaucoma. 2017;26:397-402.
54. Yarmohammadi A, Zangwill LM, Diniz-Filho A, et al. Relationship between optical coherence tomography angiography vessel density and severity of visual field loss in glaucoma. Ophthalmology. 2016;123: 2498-508.
55. Kwon J, Choi J, Shin JW, et al. Alterations of the foveal avascular zone measured by optical coherence tomography angiography in glaucoma patients with central visual field defects. Invest Ophthalmol Vis Sci. 2017; 58:1637-45.

56. Jo YH, Sung KR, Yun SC. The relationship between peripapillary vascular density and visual field sensitivity in primary open-angle and angle-closure glaucoma. Invest Ophthalmol Vis Sci. 2018;59:5862-7.

57. Holló G. Vessel density calculated from OCT angiography in 3 peripapillary sectors in normal, ocular hypertensive, and glaucoma eyes. Eur J Ophthalmol. 2016;26:42-5.

58. Rao HL, Sreenivasaiah S, Dixit S, et al. Choroidal Microvascular Dropout in Primary Open-angle Glaucoma Eyes With Disc Hemorrhage. J Glaucoma 2019;28:181-7.

59. Lee EJ, Kim TW, Kim JA, et al. Central Visual Field Damage and Parapapillary Choroidal Microvasculature Dropout in Primary Open-Angle Glaucoma. Ophthalmology 2018;125:588-96.

60. Kwon J, Shin JW, Lee J, et al. Choroidal Microvasculature Dropout Is Associated With Parafoveal Visual Field Defects in Glaucoma. Am J Ophthalmol 2018;188:141-54.

61. Suh MH, Zangwill LM, Manalastas PI, et al. Optical coherence tomography angiography vessel density in glaucomatous eyes with focal lamina cribrosa defects. Ophthalmology. 2016;123:2309-17.

62. Ghahari E, Bowd C, Zangwill LM, et al. Macular Vessel Density in Glaucomatous Eyes With Focal Lamina Cribrosa Defects. J Glaucoma 2018;27:342-9.

63. Han JC, Choi JH, Park DY, et al. Border Tissue Morphology Is Spatially Associated with Focal Lamina Cribrosa Defect and Deep-Layer Microvasculature Dropout in Open-Angle Glaucoma. Am J Ophthalmol 2019;203:89-102.

64. Park HL, Kim JW, Park CK. Choroidal Microvasculature Dropout Is Associated with Progressive Retinal Nerve Fiber Layer Thinning in Glaucoma with Disc Hemorrhage. Ophthalmology 2018;125:1003-13.

65. Suwan Y, Geyman LS, Fard MA et al. Peripapillary Perfused Capillary Density in Exfoliation Syndrome and Exfoliation Glaucoma versus POAG and Healthy Controls: An OCTA Study. Asia Pac J Ophthalmol (Phila) 2018; 7(2): 84-9.

66. Gür Güngör S, Sarigül Sezenöz A, Öztürk C, et al. Peripapillary and Macular Vessel Density Measurement With Optical Coherence Tomography Angiography in Exfoliation Syndrome. J Glaucoma. 2021;30:71-7.

67. Yu J, Jiang C, Wang X, et al. Macular perfusion in healthy Chinese: an optical coherence tomography angiogram study. Invest Ophthalmol Vis Sci. 2015;56:3212-7.

68. Moghimi S, Zangwill LM, Penteado RC, et al. Macular and optic nerve head vessel density and progressive retinal nerve fiber layer loss in glaucoma. Ophthalmology. 2018;125:1720-8.

69. Hou H, Moghimi S, Zangwill LM, et al. Macula vessel density and thickness in early primary open angle glaucoma. Am J Ophthalmol. 2019; 199:120-32.

70. Mansouri K, Rao HL, Hoskens K, et al. Diurnal variations of peripapillary and macular vessel density in glaucomatous eyes using optical coherence tomography angiography. J Glaucoma. 2018;27:336-41.

71. Alnawaiseh M, Lahme L, Treder M, et al. Short-term effects of exercise on optic nerve and macular perfusion measured by optical coherence tomography angiography. Retina. 2017;37:1642-6.

72. Rao HL, Pradhan ZS, Weinreb RN, et al. Determinants of peripapillary and macular vessel densities measured by optical coherence tomography angiography in normal eyes. J Glaucoma. 2017;26:491-7.

73. Chang R, Nelson AJ, LeTran V, et al. Systemic Determinants of Peripapillary Vessel Density in Healthy African Americans: The African American Eye Disease Study. Am J Ophthalmol 2019;207:240-7.

74. Muller VC, Storp JJ, Kerschke L, et al. Diurnal variations in flow density measured using optical coherence tomography angiography and the impact of heart rate, mean arterial pressure and intraocular pressure on flow density in primary open-angle glaucoma patients. Acta Ophthalmol 2019;97:844-9.

75. Wang X, Kong X, Jiang C, et al. Is the peripapillary retinal perfusion related to myopia in healthy eyes? A prospective comparative study. BMJ Open. 2016;6:010791.

76. Suwan Y, Fard MA, Geyman LS, et al. Association of myopia with peripapillary perfused capillary density in patients with glaucoma: an optical coherence tomography angiography study. JAMA Ophthalmol. 2018;136: 507-13.

77. Sampson DM, Gong P, An D, et al. Axial length variation impacts on superficial retinal vessel density and foveal avascular zone area measurements using optical coherence tomography angiography. Invest Ophthalmol Vis Sci. 2017;58:3065-72.

78. Holló G. Influence of large intraocular pressure reduction on peripapillary oct vessel density in ocular hypertensive and glaucoma eyes. J Glaucoma. 2017;26:7-10.

79. Shin JW, Sung KR, Uhm KB, et al. Peripapillary microvascular improvement and lamina cribrosa depth reduction after trabeculectomy in primary open-angle glaucoma. Invest Ophthalmol Vis Sci. 2017;58: 5993-9.

80. Zeboulon P, Leveque PM, Brasnu E, et al. Effect of Surgical Intraocular Pressure Lowering on Peripapillary and Macular Vessel Density in Glaucoma Patients: An Optical Coherence Tomography Angiography Study. J Glaucoma 2017;26:466-72.

81. Zhang Q, Jonas JB, Wang Q, et al. Optical Coherence Tomography Angiography Vessel Density Changes after Acute Intraocular Pressure Elevation. Sci Rep 2018;8:6024.

82. Hou H, Moghimi S, Zangwill LM, et al. Macula Vessel Density and Thickness in Early Primary Open Angle Glaucoma. Am J Ophthalmol 2019;199:120-32.

83. Holló G. Comparison of peripapillary OCT angiography vessel density and retinal nerve fiber layer thickness measurements for their ability to detect progression in glaucoma. J Glaucoma. 2018;27:302-5.

84. Shin JW, Song M, Kook MS. Association Between Progressive Retinal Capillary Density Loss and Visual Field

Progression in Open-Angle Glaucoma Patients According to Disease Stage. Am J Ophthalmol . 2021;226:137-47.

85. Kim JA, Lee EJ, Kim TW. Evaluation of Parapapillary Choroidal Microvasculature Dropout and Progressive Retinal Nerve Fiber Layer Thinning in Patients With Glaucoma. JAMA Ophthalmol 2019;137:810-6.
86. Lin S, Cheng H, Zhang S, et al. Parapapillary Choroidal Microvasculature Dropout Is Associated With the Decrease in Retinal Nerve Fiber Layer Thickness: A Prospective Study. Invest Ophthalmol Vis Sci 2019;60:838-42.
87. Kwon JM, Weinreb RN, Zangwill LM, et al. Parapapillary Deep-Layer Microvasculature Dropout and Visual Field Progression in Glaucoma. Am J Ophthalmol 2019;200:65-75.
88. Jo YH, Kwon J, Jeong D, et al. Rapid Central Visual Field Progression Rate in Eyes with Open-Angle Glaucoma and Choroidal Microvasculature Dropout. Sci Rep 2019;9:8525.
89. Kwon JM, Weinreb RN, Zangwill LM, et al. Juxtapapillary Deep-Layer Microvasculature Dropout and Retinal Nerve Fiber Layer Thinning in Glaucoma. Am J Ophthalmol. 2021 Jul;227:154-65.
90. Camino A, Zhang M, Gao SS, et al. Evaluation of artifact reduction in optical coherence tomography angiography with real-time tracking and motion correction technology. Biomed Opt Express 2016;7:3905-15.
91. Campbell JP, Zhang M, Hwang TS, et al. Detailed Vascular Anatomy of the Human Retina by Projection-Resolved Optical Coherence Tomography Angiography. Sci Rep 2017;7:42201.
92. Rao HL, Pradhan ZS, Suh MH, et al. Optical coherence tomography angiography in glaucoma. J Glaucoma. 2020; 29(4): 312-21.