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The current clinical role of optical coherence tomography angiography in neuro-ophthalmological diseases

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Abstract:

After the revolutionary effect of optical coherence tomography (OCT) on ophthalmology practice, recent OCT-based technology OCT angiography (OCT-A) also has rapidly gained a wide clinical acceptance. OCT-A is a noninvasive, depth-resolved imaging tool for the evaluation of retinal vascular changes. Since its introduction, the understanding of retinal vascular diseases, pachychoroid spectrum diseases, and other diseases have been enriched in many ways. More importantly, OCT-A provides depth-resolved information that has never before been available. The whole spectrum of neuro-ophthalmological diseases shows consistent peripapillary and macular capillary changes with structural and functional correlation. The superficial and deeper retinal and choroidal vasculatures are affected depending on the nature of the disease process. Therefore, OCT-A play an important role in the diagnosis and management of optic nerve-related diseases as well. In this review, we summarized existing literature on the use of OCT-A in neuro-ophthalmological diseases such as arteritic anterior ischemic neuropathy, nonarteritic anterior ischemic neuropathy, papillitis, papilledema, multiple sclerosis. Currently, OCT-A has an important position as a useful, noninvasive tool in the evaluation of neuro-ophthalmologic diseases; however, OCT-A has several limitations regarding its technical capabilities in challenging neuro-ophthalmic cases. With the improvement in the technical capacity of OCT-A, it will have a more important place in the diagnosis and follow-up of neuro-ophthalmological diseases in future.

Keywords:

Anterior ischemic optic neuropathy, multiple sclerosis, optic nerve head optical coherence tomography angiography, optical coherence tomography angiography, papilledema

Introduction

Early diagnosis is of great importance in neuro-ophthalmological diseases. Various imaging methods such as color fundus photography, multicolor retinal imaging, scanning laser ophthalmoscope, fundus fluorescein angiography (FFA), indocyanine green angiography, fundus autofluorescence, and optical coherence tomography (OCT) are used for the evaluation of the optic disc in the diagnosis of neuro-ophthalmological diseases.

FFA, which provides a qualitative assessment of the optic disc periphery,

retina, and choroid, remains the gold standard for demonstrating ischemia. However, FFA has some weak points in clinical evaluation. First of all, FFA requires intravenously applied dyes which takes a certain time and increases the workload for clinical practices. Second, images obtained from FFA are two-dimensional and therefore do not contain information about depth. Last but not least, hyperfluorescence due to leakage and staining also complicates the evaluation of deep vascular structures.

OCT, which is also widely used in the evaluation of the optic disc, provides high-resolution images similar to histological sections about the retina, choroid, and optic

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nerve head (ONH) by using low-coherence interferometry of near-infrared light.^[1]

Since 1991, the rapidly developing OCT technology has introduced the clinicians to Time Domain-OCT, Spectral domain-OCT, and Swept source OCT (SS-OCT), respectively, and these devices have gained an important place in clinical applications.^[2]

OCT angiography (OCT-A) is a new imaging method that provides detailed visualization of the retinal vascular network by obtaining the motion contrast of the erythrocytes in the vessel through sequential OCT scans of a specific retina or optic disc area without the use of any intravenous contrast agent (noninvasively, unlike FFA).^[3]

By OCT-A, three-dimensional images of vascular structures in various layers of the retina are obtained and quantitative measurement of blood flow in the vessels can also be made. Unlike FFA, OCT-A also provides detailed information about the deep capillary plexus.^[4] In contrast to FFA, it is not affected by conditions such as hyperfluorescence and can provide detailed information about the microvascular structures around the entire optic disc.

Retinal and choroidal vessels may be affected during the course of many neuro-ophthalmological diseases. Today, OCT-A is used in the diagnosis and follow-up of many neuro-ophthalmological diseases such as arteritic anterior ischemic neuropathy (AAION), non AAION (NAION), papillitis, papilledema, and multiple sclerosis (MS)...

In this review, we tried to create a brief summary based on the existing literature on the use of OCT-A in neuro-ophthalmological diseases, which is becoming increasingly common in clinical practice due to its noninvasive and rapid application.

Comparison with Fundus Fluorescein Angiography

The main difference between FFA and OCT-A is intravenously applied contrast, fluorescein. With intravenous use of fluorescein in FFA, yellowish appearance on the skin that can last up to 36 h, local irritation/thrombophlebitis at the injection site and extravasation of the dye, nausea, vomiting, and severe allergic reactions can be observed. Since no intravenous contrast is applied in OCT-A, there is no such a risk of adverse reaction to fluorescein.^[5,6]

Na-fluorescein is eliminated by the liver and kidneys and is excreted in the urine within 24–36 h. This period

may be longer in renal dysfunction. Therefore, half-dose application and hydration support are recommended when administering FFA in patients with renal failure.

It is recommended not to perform FFA during pregnancy, especially in the first trimester.^[7] Since fluorescein can pass into breast milk, discontinuation of breast milk for 7 days or not performing angiography are among the limitations of FFA.

OCT-A is an ideal diagnostic method for the diagnosis of neuro-ophthalmological diseases in pregnancy, since it does not require pupillary dilation or intravenous dye injection.

OCT-A application and acquisition of images are very fast. It does not impose an extra burden on clinical practice in terms of time. It can be easily repeated many times during the day. It can also be easily used in follow-ups.

Images obtained by FFA are two-dimensional and do not provide information about which retinal layer is affected. On the other hand, three-dimensional images can be obtained in OCT-A, and sections can be taken from desired levels.

While all data are qualitative in FFA, some data can be obtained quantitatively in OCT-A. However, dynamic information such as perfusion, leakage, ponding, and staining in the vessels can be obtained in FFA, while this information cannot be obtained in OCT-A.

Limitations and Artifacts of Optical Coherence Tomography Angiography

Although the OCT-A is a newly introduced technology in ophthalmology, it has some similar limitations to its ancestor OCT. Due to patient incompatibility, false OCT-A signals may be received with eye, head, or body movement. However, recent developments in eye tracking systems used in new generation devices have significantly reduced these artifacts.

Low signal strength caused by smudges in the instrument's optical system can significantly affect the quality of OCT-A images. In such cases, dark areas with smooth edges may occur in the image. Similarly, media opacities such as cataract, corneal edema, vitreous hemorrhage, etc., can affect the OCT-A image quality. Ghost artifacts (black shadow cast), lens opacities, vitreous opacities, dense intraretinal solid pathologies can cause difficulties in visualizing deep vascular layers. SS-OCTA systems have partially overcome this limitation because the longer wavelength used limits attenuation from ambient

opacities and allows penetration into the deeper retinal and choroidal layers.

The blood flowing through the great vessels in the superficial layers can vibrate the scanning light that passes through it. In this case, an incorrect image may occur in OCT-A. Due to the quantitative analyzing system, OCT-A devices have a range for flow rate. If there is too low or too high flow in the lesion, OCT-A images may be misinterpreted.^[8,9]

Nonarteritic Anterior Ischemic Neuropathy and Optical Coherence Tomography Angiography

NAION, which is the most common cause of acute optic neuropathy in the population over 50 years of age, is a type of optic neuropathy that develops acutely due to vascular causes, except for reasons such as inflammation, demyelination, and compression. NAION, which can be detected in all age groups, most commonly affects the 55–65 years' age group.^[10]

Approximately 94% of ischemic optic neuropathies affect the anterior segment and 6% affect the posterior segment. 90% of anterior ischemic optic neuropathies and 66% of posterior optic neuropathies are nonarteritic ischemic optic neuropathy.^[11]

While posterior ciliary arteries generally play a role in the etiopathogenesis of NAION, posterior ischemic optic neuropathies are caused by the ophthalmic artery and the pial branches of the central retinal artery feeding the optic nerve. Hypoperfusion in the small diameter vessels feeding the anterior part of the ONH, which is seen in people with systemic diseases such as diabetes mellitus, hypertension, dyslipidemia, and hyperhomocysteinemia, may be responsible for the pathogenesis of NAION.

It's suggested by Hayreh that axoplasmic stasis in the ONH causes axonal swelling and ultimately symptomatic disc edema in the pathogenesis of NAION.^[12] Levin and Danesh-Meyer also suggested that venous congestion in the optic nerve parenchyma due to central retinal vein occlusion causes vasoconstriction in small feeding vessels and secondary optic disc edema.^[13]

Optic disc edema, which is thought to occur with early axoplasmic stasis and axonal swelling, further deepens optic disc hypoperfusion. During the course of the disease, optic disc edema resolves, but optic atrophy occurs when the retinal nerve fiber layer (RNFL) and ganglion cells are severely affected.

At the clinical admission, patients present with decreased visual acuity within hours or days and haze in the

field of vision where they experience vision loss. In the early period, optic disc edema is expected to be seen in fundus examination in NAION patients. This edema may be diffuse or segmental. In general, the optic disc is hyperemic, unlike arteritic ischemic optic neuropathy. The retinal arteries narrow and the cup/disc ratio disappears, and the other eye may have a crowded disc appearance, which is predisposed to ischemic event, which is defined as a "disc at risk-crowded disc."^[11]

FFA may show disc hypoperfusion in NAION patients. In NAION patients, leakage from the disc (focal or generalized) and/or disc filling defects can be detected in FFA.^[14] FFA can give data about the superficial vessels of the optic disc, but not about the deeper blood vessels. However, fluorescein leakage in FFA may obscure the vascular network on the surface of the optic disc.^[14,15] FFA, which is the gold standard to diagnose retinal vascular diseases, is insufficient in the diagnosis of NAION because it fails to identify small vascular changes. Spade *et al.* revealed that in compare to FFA, OCT-A provides better visualization of the peripapillary microvasculature due to the absence of masking caused by vascular leakage.^[16]

There are various studies in the literature using OCT-A in NAION patients. In one of them, Ling *et al.* suggested that OCT-A can be used in both diagnosis and follow-up in NAION patients and showed that optical non-perfusion area percentages were significantly related to both visual acuity and visual field in chronic NAION patients.^[17]

Rougier *et al.* reported in the study includes four patients with NAION, 6 patients with papillitis and 13 patients with papilledema that morphological analysis of OCT-A is more beneficial than quantitative analysis in the acute phase of optic-disc edema. They also suggested that OCT-A may have a facilitating role in distinguishing between ischemic and inflammatory optic disc edema and papilledema by morphological and quantitative analyses. They described the global aspect of peripapillary regular pattern in OCT-A as severe disappearance in NAION, moderate alteration in papillitis and bushy aspect in papilledema and revealed that flux index is higher in inflammatory eyes. They also stated that at the acute phase, the morphological analysis appears to be more convenient than quantification because the edema itself may induce artifacts during the image acquisition affecting the quantification process.^[18]

Augstburger *et al.* compared 26 eyes of 24 patients with NAION and 24 healthy eyes and found a relationship between visual field and visual acuity loss and decreased peripapillary and macular retinal capillary density in OCT-A. They suggested that OCT-A could be a useful

tool for measuring and monitoring ischemia in NAION patients.^[19]

In the study of Al-Nashar and Hemed, in which they included 25 eyes of 25 patients with a diagnosis of unilateral acute NAION, axoplasmic stasis and vascular dilatation with tortuosity due to edema were detected in 17 eyes (68%). They also reported that peripapillary vessel density (VD) decreased significantly in these patients.^[20]

Higashiyama *et al.* showed a decrease in retinal perfusion in areas with loss of the RNFL and ganglion cell complex by OCT-A in a patient with NAION and suggested that OCT-A could be a helpful method in the diagnosis of NAION.^[21]

Ghasemi Falavarjani *et al.* reported that eyes with optic atrophy due to NAION had lower VD and thinner RNFL compared to normal eyes.^[22] Liu *et al.* also showed that peripapillary retinal perfusion decreased in optic atrophy in NAION patients and this finding was associated with RNFL thinning.^[23] Sharma *et al.* showed reductions in microvascular flow in the superficial and choroidal peripapillary regions in patients with NAION compared with the control group. In addition, partial recovery of peripapillary vascular flow with improvement in visual function has been reported, suggesting that OCT-A could be used as a possible follow-up tool to monitor visual improvement in NAION patients.^[24]

Wright Mayes *et al.* revealed OCT-A flow impairment of the retinal peripapillary capillaries, especially in the temporal sector, in patients with NAION. They also found that the flow impairment of the retinal peripapillary capillaries seen by OCT-A was compatible with RNFL and ganglion cell layer complex (GCC) pathologies in OCT and visual field defects.^[25]

In the study of Balducci *et al.*, four NAION patients and one AION patient were examined, and with OCT-A, they found a reduction in microvascular defects and vessel densities in cases of NAION and AION-induced acute optic disc edema. Balducci *et al.* revealed that the borders of non-perfusion areas of the ONH can be detected with OCT-A. They have shown that these areas are perfectly comparable to optic disc filling defects detectable in FFA. They also suggested that both ONH and peripapillary VD were decreased in NAION patients compared to controls, and that these parameters could be useful in differentiating ischemic forms from other causes of acute optic disc edema.^[26]

Song *et al.*, in their study in which 41 eyes of 30 NAION cases and 30 eyes of 30 healthy subjects were analyzed by OCT-A, found significantly reduced peripapillary

superficial retina and optic disc vessel densities in NAION patients compared to the control group. They also emphasized that the VD of the optic disc was significantly lower in chronic NAION patients compared to acute NAION patients.^[27]

Hata *et al.* included 15 NAION eyes and 19 normal eyes and found a significant decrease in peripapillary vascular density in NAION patients compared to other normal eyes.^[28] Similar to the study of Hata *et al.*, Rebolleda *et al.* showed a significant reduction in peripapillary capillary density, VD, and perfusion density in eyes with NAION compared to fellow unaffected eyes in both acute and chronic NAION patients.^[29] Gandhi *et al.* showed a significant decrease in peripapillary choroidal vascularity in OCT-A compared to healthy fellow eyes as the cause of ONH hypoperfusion in eyes with acute NAION.^[30]

Gaier *et al.* determined in OCT-A that a reduction in the signal from the major retinal vessels and dilation of patent superficial capillaries in the peripapillary area in the acute phase of NAION.^[31]

Anterior Arteritic Ischemic Optic Neuropathy and Optical Coherence Tomography Angiography

Almost all AAION develop due to giant cell (temporal) arteritis. Rarely, it may develop in association with other vasculitis.^[32] Giant cell arteritis is a vasculitis involving medium and large vessels. Embolism localized to the posterior ciliary artery due to coagulation triggered by inflammation is thought to play a role in the pathogenesis. In AAION the vasculopathy is located at the level of posterior ciliary arteries, proximal to their division into paraoptic and choroidal branches. Hayreh showed that there is occlusion in the posterior ciliary artery in early phase FFA performed in eyes with AAION involvement.^[33] However, it is also known that the FFA finding disappears as time progresses due to developing choroidal collaterals.

The classic systemic symptoms of temporal arteritis are headache, skin tenderness in the temporal region, and jaw fatigue. Headache is located especially in the temple area and is the most common symptom.^[34] Although sudden vision loss is the most important finding of giant cell arteritis, involvement of the fellow eye can usually occur days or weeks after the first eye is affected.^[35] In general, visual acuity is severely reduced and visual field defects are expected to be wider than in NAION patients.

Although combined elevation of erythrocyte sedimentation rate and C-reactive protein is highly sensitive for the diagnosis, temporal artery biopsy

is the gold standard for diagnosis.^[36] Techniques such as Doppler ultrasonography, positron emission scintigraphy, and magnetic resonance imaging (MRI) have been used for diagnosis, but to date they could not replace temporal artery biopsy.^[37,38]

Gaier *et al.* showed by OCT-A that AAION patients have focal nonperfusion areas in superficial and deep retinal capillaries. They suggested that focal nonperfusion finding with superficial peripapillary capillary dilatation may be useful in diagnosing AAION patients.^[39]

Chen *et al.* showed that peripapillary capillary dropout with OCT-A in chronic AAION patients and found a significant decrease in peripapillary VD in unaffected fellow eyes of a patient with chronic AAION disease.^[40]

In terms of distinction between NAION and AAION, Pierro *et al.* emphasized the presence of vascular tortuosity accompanied by decreased vessel densities, which was more severe in eyes with AAION than in eyes with NAION.^[41] It is also stated that the use of OCT-A is still limited in the differentiation of NAION/AAION in the acute period and that OCT-A can be used as supportive evidence rather than diagnostic of NAION.^[42] Balducci *et al.* similarly stated that no distinctly different vascular patterns except for the peripapillary watershed zone were found between them using OCT-A, despite the different pathogenesis of AAION and NAION.^[26] Ling *et al.* also reported that OCT-A is able to show a reduction in the blood flow of the ONH in both AAION and NAION, but it cannot differentiate between the two.^[17]

Multiple Sclerosis/Neuromyelitis Optica and Optical Coherence Tomography Angiography

MS is an autoimmune central nervous system disease characterized by inflammation, demyelination, and axon damage, the pathogenesis of which is still not completely explained. Visual symptoms such as diplopia and blurred vision are common symptoms in MS patients. After clinical findings, MRI is the most important parameter in the diagnosis of MS. In addition, tests such as cerebrospinal fluid analyzes and visual evoked potentials (VEP) test are also used to support the diagnosis.

The optic nerve is one of the most commonly affected regions in MS patients. Pathological changes can be seen in the VEP test even in the patient group without a clinical history of optic neuritis (ON) in MS patients. Tests such as OCT, visual acuity, visual field, contrast sensitivity, color vision examination can be used in follow-up.^[43] Various studies have shown thinning of

RNFL, ganglion cell and inner plexiform layer in patients with ON associated with MS.^[44,45]

OCT-A has been used in recent studies to evaluate microvascular damage, suggesting that microvascular changes accompany the retina in MS patients. Feucht *et al.* showed by OCT-A that MS-associated ON causes changes in the macular retinal vascular network. They found a decrease in superficial and deep retinal vessels in patients with MS with a history of ON compared to the control group, while there was no change in the vessel densities in the retinal vascular network in the eyes of MS patients without a previous diagnosis of ON.^[46] Similarly, Higashiyama *et al.* reported reduced retinal macular vessel densities in seven patients with MS/neuromyelitis optica associated ON. They suggested that treatment in people with ON may cause a decrease in retinal perfusion even after visual acuity has improved.^[47] In a study conducted by Lanzillo *et al.* in 2018, 50 MS patients were compared by OCT-A to 46 healthy individuals, and vessel densities of MS patients were found to be significantly lower in OCT-A than in the control group.^[48]

Cordon *et al.* stated in their study that OCT-A has the ability to detect subclinical vascular changes and may be a potential biomarker to diagnose the presence and progression of MS. They stated that lower VD was found in the superior, nasal and inferior parafoveal areas in patients diagnosed for more than 5 years compared to healthy people.^[49]

Balıkçı *et al.* revealed that there were significant differences in RNFL, GCC, and radial peripapillary capillary VD between the MS group and the control group, but no significant differences in superficial capillary plexus VD and deep capillary plexus VD, foveal avascular zone, non-flow area, and choriocapillary flow values. On the other hand, they found that the damage in eyes with ON was similar to that in eyes without ON.^[50]

Murphy *et al.* compared 201 eyes of 111 MS patients and 97 eyes of 50 control patients. They found that macular superficial vascular plexus (SVP) densities were decreased in MS patients compared to the control group. Furthermore, reduced SVP densities are associated with decreased visual function, longer disease duration, and higher global disability levels, suggesting that OCT-A may have additive value as a biomarker in MS in conjunction with routine OCT examinations.^[51]

Khader *et al.* conducted a study which includes 10 eyes with a history of ON, 10 eyes without a history of group ON, and normal patients. They found that the average, superficial, and deep vascular density indexes

were significantly reduced in MS patients compared to the control group.^[52]

Ulusoy *et al.* reported reductions in VD of retinal or peripapillary area of patients with MS in their study, which included 20 MS and 24 healthy subjects. They found a statistically significant decrease in optic disc OCT-A parameters, inferior and temporal quadrant vessel densities, in MS patients compared to the control group.^[53]

In a study by Spain *et al.*, 68 eyes of 45 MS patients (25 eyes had ON attack, 43 eyes had no ON attack) and 55 eyes of 32 normal control group were evaluated with OCT-A and ONH flow index (ONH-FI) were measured. It was shown that the ONH-FI was lower in the MS group than in the control group, regardless of the ON attack. They concluded that MS both causes retinal structural losses and impairs ONH perfusion, and suggested that ONH-FI may be useful in the detection and follow-up of optic nerve damage.^[54] Similarly, Wang *et al.* showed that ONH-FI values were lower in patients with MS with a history of ON compared to the control group and in patients with MS without a history of ON.^[55]

Liu *et al.* suggested that OCT-A has a good diagnostic value in comparing MS and neuromyelitis optica spectrum disorder (NMOSD) patients. They found that NMOSD patients had significantly smaller average thickness of peripapillary RNFL and ganglion cell-inner plexiform layer, and significantly smaller whole areas of VD and perfusion density than MS patients.^[56]

Lee *et al.* evaluated the superficial macular and radial peripapillary capillary plexus vessel densities in the eyes of patients with ON and reported that these vessel densities were lower in patients with NMOSD than in MS patients.^[57]

Papilledema/Pseudopapilledema and Optical Coherence Tomography Angiography

The most important causes of optic disc edema can be listed as high intracranial pressure (papilledema), ON (papillitis), diabetic or hypertensive papillitis, anterior ischemic optic neuropathy, neuroretinitis, uveitis, optic nerve compression or infiltration.^[58]

Papilledema is of critical diagnostic importance because it occurs as a result of high intracranial pressure. Therefore, it is important to diagnose conditions such as papilledema and pseudopapilledema.

Papilledema is swelling and edema of the optic disc due to an increase in intracranial pressure for any reason.

The term optic disc edema is preferred for ONH edema occurring with vascular, compressive, infiltrative, and infective pathologies.^[59]

One of the most important causes of papilledema is idiopathic intracranial hypertension (IIH-Pseudotumor cerebri), which is termed for high intracranial pressure in the absence of a structural lesion in the brain or abnormal findings in the cerebrospinal fluid.^[60]

Enlargement of the optic disc diameter, effacement of the optic disc margins, swelling of the optic disc, hyperemia, venous congestion and increased folds in the vessels, hemorrhages on and around the optic disc are expected in patients with papilledema. Based on the vascular changes seen in these patients, various studies have been conducted to evaluate the microvascular structures around the optic disc in patients with papilledema using OCT-A.

Tüntaş Bilen and Atilla reported a significant decrease in mean peripapillary VD measured by OCT-A in IIH patients with papilledema compared to the control group.^[61]

In the study of Ghasemi Falavarjani *et al.*, patient groups diagnosed with optic disc edema, pseudopapilledema, and atrophy were compared. Prelaminar capillary network was dilated and tortuous in eyes with disc edema and decreased peripapillary capillary network was found in regions corresponding to RNFL thinning in patients with optic atrophy.^[22]

Optic disc drusen (ODD), one of the most common causes of pseudopapilledema, is formed by the accumulation of pathological mucoprotein debris in the hyaline structure in the optic disc due to disruption of axoplasmic flow. ODD is more common in patients with congenital optic nerve dysplasia or narrow scleral canal 66%–75% of ODD cases are bilateral, although some cases may be asymmetrical.^[62]

It is sometimes difficult to distinguish papilledema from pseudopapilledema. Patients with ODD or papilledema usually have normal visual acuity, while those with optic disc edema due to ON or anterior ischemic optic neuropathy typically have symptomatic vision loss. Venous occlusion and enlargement, peripapillary arteriolar irregularity or narrowing may be signs of ischemia.^[63]

Although B-scan ultrasound and ONH-OCT are used as adjunctive diagnostic tests for the diagnosis of ODD, they do not always give clear results. Because ODD is autofluorescent, it can be shown as round or oval hyperautofluorescent structures in the ONH, whereas

deeper-lying ODDs often cannot be reliably detected with this technique. FFA in pseudopapilledema, in contrast to the leakage that occurs in papilledema, early and late nodular staining at the ONH can be seen.^[59]

When the literature is evaluated, it is seen that there are studies that use OCT-A to distinguish papilledema from pseudopapilledema. Engelke *et al.* found a significant decrease in VD, especially in the peripapillary area, in their study of 25 patients diagnosed with ODD. In addition, while RNFL measurement is recommended as a useful screening and follow-up tool for patients with ODD, it has been stated that peripapillary capillary VD has a high correlation with other structural measurements such as RNFL and GCC.^[64] Lindberg *et al.* found a reduction in local peripapillary VD in peripapillary sections with a large volume of ODD in their study with five ODD patients.^[65] Cennamo *et al.*, in their study with 13 patients diagnosed with ODD, showed that both FI and VD were significantly lower than in the control group.^[66]

In 2017, Gaier *et al.* found in a patient with the diagnosis of ODD, which caused visual field loss, that the superficial capillary plexus of the optic disc revealed focal attenuation associated with the more prominent and superficial ODD.^[67] Flores-Reyes *et al.*, with OCT-A, found focal peripapillary microvascular attenuation in an ODD case.^[68] In the Leal-González *et al.* study, 42 eyes of 23 patients with ODD and 34 eyes of 17 control patients were included in the study. They showed that patients with ODD had significantly reduced peripapillary vascular flow and vascular density, and this decrease was associated with RNFL or GCC thickness.^[69]

Yan *et al.* compared 17 patients with ODD (29 eyes) and 35 age matched controls (53 eyes) in their study and found that ODD eyes with mild visual field loss (MD -2.0--5.0 dB) had high RNFL, GCC, and increased macular VD and flux while ODD eyes with moderate/severe visual field loss (MD < -5.0 dB) had decreased RNFL, GCC, peripapillary vessel area density, and increased macular VD and flux. They suggested that increased macular flow may be an early biomarker of visual field loss in ODD, while decreased peripapillary VD and RNFL thickness are late biomarkers of visual field loss in ODD.^[70]

Conclusion

The whole spectrum of neuro-ophthalmological diseases shows consistent peripapillary and macular capillary changes with structural and functional correlation. The superficial and deeper retinal and choroidal vasculatures are affected depending on the nature of the disease process. OCT-A is a noninvasive, depth-resolved

imaging tool for the evaluation of retinal vascular changes. Therefore, OCT-A play an important role in the diagnosis and management of optic nerve-related diseases as well. Currently, OCT-A has an important position as a useful, noninvasive tool in the evaluation of neuro-ophthalmologic diseases; however, OCT-A has several limitations regarding its technical capabilities in challenging neuro-ophthalmic cases. With the improvement in the technical capacity of OCT-A, it will have a more important place in the diagnosis and follow-up of neuro-ophthalmological diseases in the future.

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Conflicts of interest

The authors declare that there are no conflicts of interests of this paper.

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