Review Article

doi:10.5633/amm.2026.0321

Optical Coherence Tomography Angiography in Glaucoma: Novel Perspectives on Diagnostics and Future Directions

Maja Živković

University of Niš, Faculty of Medicine, Department of Ophthalmology, Niš, Serbia

Contact: Maja Živković

81 Dr Zorana Djindjića Blvd., 18000 Niš, Serbia

E-mail: drzivkovicmaja@gmail.com

Glaucoma remains the leading cause of irreversible blindness worldwide, and approximately half of affected individuals remain undiagnosed. Optical coherence tomography angiography (OCTA) has emerged as a noninvasive imaging modality that enables high-resolution visualization of the retinal and optic nerve head microvasculature, offering a fundamentally new perspective on the vascular contributions to glaucomatous damage. This review synthesizes current evidence on OCTA-derived biomarkers for glaucoma diagnostics, evaluates their utility across the disease spectrum from pre-perimetric to advanced stages, and discusses future research directions, including the integration of artificial intelligence and multimodal imaging approaches. A comprehensive literature search was conducted using the PubMed, ScienceDirect, and Web of Science databases, encompassing studies published through early 2025, with search terms combining OCTA, glaucoma, vessel density, optic nerve head, and artificial intelligence. OCTA-derived parameters, particularly peripapillary and macular vessel density, demonstrate significant diagnostic capability across the glaucoma continuum, showing particular promise for pre-perimetric glaucoma detection, monitoring advanced disease beyond the structural OCT floor effect, evaluating highly myopic eyes, and predicting disease progression. Ganglion cell–inner plexiform layer thickness provides complementary structural information that correlates strongly with visual field loss across disease stages, while artificial intelligence platforms analyzing OCTA data achieve area under the curve values exceeding 0.90 for glaucoma classification. OCTA thus represents a valuable complement to structural OCT in the diagnostic armamentarium for glaucoma. Although current limitations related to image artifacts, reproducibility, and standardization must be addressed, the integration of OCTA with deep learning algorithms and multimodal imaging platforms holds substantial potential to transform glaucoma management.

Keywords: *optical coherence tomography angiography, optical coherence tomography angiography, glaucoma, vessel density, retinal microvasculature, artificial intelligence, deep learning, diagnostics, disease progression, foveal avascular zone*

Pregledni rad

doi:10.5633/amm.2026.0321

Optička koherentna tomografska angiografija kod glaukoma: nove perspektive u dijagnostici i budući pravci

Maja Živković

Univerzitet u Nišu, Medicinski fakultet, Katedra Oftalmologija, Niš, Srbija

Kontakt: Maja Živković
Bulevar dr Zorana Đinđića 81, 18000 Niš, Srbija
E-mail: drzivkovicmaja@gmail.com

Glaukom je i dalje vodeći uzrok ireverzibilnog slepila u svetu, a približno polovina obolelih osoba ostaje nedijagnostikovana. Optička koherentna tomografska angiografija (OCTA) pojavila se kao neinvazivna slikovna metoda koja omogućava vizuelizaciju mikrovaskulature retine i glave optičkog nerva visoke rezolucije, pružajući suštinski nov uvid u vaskularne činioce glaukomskog oštećenja. Ovaj pregledni rad sintetizuje aktuelne dokaze o biomarkerima dobijenim OCTA metodom u dijagnostici glaukoma, procenjuje njihovu korisnost duž celog spektra bolesti — od preperimetrijskog do uznapredovalog stadijuma — i razmatra buduće pravce istraživanja, uključujući integraciju veštačke inteligencije i multimodalne slikovne pristupe. Sprovedena je sveobuhvatna pretraga literature u bazama PubMed, ScienceDirect i Web of Science, koja je obuhvatila studije objavljene zaključno sa početkom 2025. godine, uz ključne reči koje su kombinovale pojmove OCTA, glaukom, gustina krvnih sudova, glava optičkog nerva i veštačka inteligencija. Parametri dobijeni OCTA metodom, posebno peripapilarna i makularna gustina krvnih sudova, pokazuju značajnu dijagnostičku sposobnost duž celog kontinuuma glaukoma, a naročito su obećavajući u otkrivanju preperimetrijskog glaukoma, u praćenju uznapredovale bolesti izvan efekta „poda“ strukturnog OCT-a, u proceni izrazito miopnih očiju i u predviđanju progresije bolesti. Debljina sloja ganglijskih ćelija i unutrašnjeg pleksiformnog sloja pruža komplementarne strukturne informacije koje snažno koreliraju sa gubitkom vidnog polja u svim stadijumima bolesti, dok platforme zasnovane na veštačkoj inteligenciji koje analiziraju OCTA podatke postižu vrednosti površine ispod krive veće od 0,90 u klasifikaciji glaukoma. OCTA stoga predstavlja dragocenu dopunu strukturnom OCT-u u dijagnostičkom arsenalu za glaukom. Iako je neophodno prevazići aktuelna ograničenja vezana za artefakte snimka, ponovljivost i standardizaciju, integracija OCTA metode sa algoritmima dubokog učenja i multimodalnim slikovnim platformama ima znatan potencijal da transformiše lečenje glaukoma.

Ključne reči: *optička koherentna tomografska angiografija; optička koherentna tomografska angiografija; glaukom; gustina krvnih sudova; mikrovaskulatura retine; veštačka inteligencija; duboko učenje; dijagnostika; progresija bolesti; fovealna avaskularna zona*

1. Introduction

Glaucoma is a group of progressive optic neuropathies characterized by degeneration of retinal ganglion cells (RGCs) and their axons, resulting in characteristic optic nerve head (ONH) changes and corresponding visual field defects (1,2). It is the leading cause of irreversible blindness worldwide, with an estimated 111.8 million cases projected by 2040 (3). In 2020, glaucoma caused blindness in 3.6 million people aged 50 years and older, representing approximately 11% of all global blindness in this age group (4). Despite effective treatments that reduce intraocular pressure (IOP), the sole modifiable risk factor, the disease's insidious nature means that approximately half of glaucoma patients remain undiagnosed (5).

The pathophysiology of glaucoma involves a complex interplay of mechanical and vascular factors (1). The mechanical theory emphasizes IOP-mediated damage to the lamina cribrosa and retinal nerve fiber layer (RNFL), whereas the vascular theory posits that compromised blood flow to the optic nerve and surrounding tissues contributes significantly to RGC death (6,7). Normal-tension glaucoma (NTG), a subtype of primary open-angle glaucoma (POAG) in which IOP remains within the statistically normal range, provides compelling evidence for vascular involvement in glaucomatous pathogenesis (8). Multiple studies support the role of ocular blood flow in NTG, demonstrating altered hemodynamic profiles in the ophthalmic and retrobulbar circulation and associations with systemic vasospasm and cardiovascular dysregulation (8,9).

Traditional diagnostic approaches integrate clinical examination–including optic disc evaluation, gonioscopy, and IOP measurement–with ancillary testing such as standard automated perimetry (SAP) and structural optical coherence tomography (OCT) (1,10). While OCT has revolutionized the objective quantification of RNFL thickness, ganglion cell complex (GCC), and ganglion cell-inner plexiform layer (GCIPL) parameters, it fundamentally measures a static endpoint of neuronal damage (10). Studies have shown that GCIPL thickness is highly sensitive and specific for differentiating glaucomatous from healthy eyes, with areas under the receiver operating characteristic curve (AUROC) of 0.93–0.94. Each 1-micrometer decrease in average GCIPL thickness is associated with a 0.54 dB loss in mean visual field deviation (11). However, assessing the dynamic vascular component of glaucomatous damage has been limited by the availability of noninvasive imaging tools.

Optical coherence tomography angiography (OCTA) addresses this gap by providing noninvasive, dye-free, three-dimensional visualization of retinal and ONH microvasculature (12,13). By detecting red blood cell motion through repeated B-scans at the same retinal location, OCTA generates high-resolution maps of blood flow across the retinal and choroidal layers (14). Since its clinical introduction, OCTA has been extensively studied to understand glaucoma pathophysiology, enhance early diagnosis, and monitor disease progression (15,16). Early systematic reviews established that OCTA demonstrates high repeatability and reproducibility, good discriminatory power between normal and glaucomatous eyes, a stronger correlation with visual function than conventional OCT, and a floor effect that occurs at a more advanced disease stage than with structural OCT (16).

The diagnostic evaluation of glaucoma has historically relied on the triad of IOP measurement, optic disc assessment, and visual field testing (1,10). Although IOP remains the only modifiable risk factor, it is increasingly recognized as an imperfect surrogate for disease activity because significant proportions of patients develop or progress at statistically normal pressures (6,8). Standard automated perimetry, though essential for functional assessment, is limited by high test-retest variability, patient learning effects, and the need for substantial RGC loss (estimated at 25–40% of total) before detectable visual field defects emerge (1). This temporal lag between structural damage and functional manifestation creates a critical diagnostic window during which disease-modifying intervention could be most effective.

Structural OCT has substantially improved our ability to detect early glaucomatous damage by providing objective, quantitative measurements of RNFL, GCC, and GCIPL thickness (10,11). However, because OCT measures tissue volume, it captures the cumulative result of neurodegeneration rather than the dynamic processes driving it. The vascular component of glaucomatous pathology–encompassing autoregulatory dysfunction, endothelial impairment, and microcirculatory compromise–has been difficult to assess noninvasively until the advent of OCTA (6,7,12). Prior to OCTA, technologies such as fluorescein angiography, indocyanine green angiography, laser Doppler flowmetry, and Doppler ultrasound demonstrated impaired blood flow in glaucoma but were limited by invasiveness, poor resolution, an inability to visualize specific vascular layers, or a lack of quantitative output (14).

The development of OCTA has thus filled a critical gap in our diagnostic capabilities, enabling, for the first time, routine, noninvasive, depth-resolved quantification of retinal and ONH microcirculation in clinical practice (12-14). Since Jia et al.'s 2014 demonstration of reduced optic disc perfusion in eyes with glaucoma using OCTA (12), the field has expanded rapidly, with hundreds of studies examining OCTA parameters across glaucoma subtypes, disease stages, and clinical contexts.

This review aims to provide a comprehensive synthesis of the current evidence on OCTA's role in glaucoma, with an emphasis on novel diagnostic perspectives, the integration of artificial intelligence (AI), and future research directions that may fundamentally alter clinical practice.

2. Principles and Technology of OCTA

2.1 Image Acquisition and Processing

OCTA images are generated using motion contrast, in which multiple OCT B-scans are acquired at the same retinal location over a defined period (12,14). The decorrelation signal from red blood cell motion within blood vessels is distinguished from that of static tissue, producing a map of the perfused vasculature. Various algorithms have been developed for this purpose, including split-spectrum amplitude-decorrelation angiography (SSADA), optical micro-angiography (OMAG), and full-spectrum amplitude-decorrelation (14). Phase-signal-based techniques measure the variance of the phase shift of light across successive B-scans, while intensity-signal-based techniques enhance flow signals by comparing reflectance amplitudes across serial scans. Complex-signal-based approaches combine both phase and intensity information to further improve flow sensitivity (14). Each algorithmic approach has specific advantages in terms of flow sensitivity and vulnerability to artifacts.

Current commercial OCTA platforms include the RTVue XR Avanti (Optovue, Inc., using SSADA), the Cirrus HD-OCT with AngioPlex (Carl Zeiss Meditec, using OMAG), the DRI OCT Triton (Topcon, using OCTA Ratio Analysis), and the Spectralis OCTA (Heidelberg Engineering) (14,15). Swept-source (SS) OCTA systems offer advantages over spectral-domain (SD) systems, including faster scan speeds, deeper tissue penetration, and reduced sensitivity roll-off, thereby improving visualization of the choroidal vasculature and the lamina cribrosa (14,15).

The choice of scan protocol significantly affects diagnostic performance. Standard scan sizes include 3×3 mm, 4.5×4.5 mm, and 6×6 mm, centered on either the optic disc or the macula (13,15-17). Each configuration captures different anatomical regions and involves distinct trade-offs between resolution and field of view. The 3×3 mm macular scan provides the highest resolution and best repeatability for FAZ and parafoveal VD measurements (17). The 4.5×4.5 mm optic disc scan is the most commonly used protocol for evaluating peripapillary vasculature (5,13).

The 6×6 mm macular scan, particularly its outer-sector measurements, has shown better diagnostic accuracy for mild glaucoma than the 3×3 mm scan, though with somewhat reduced repeatability (13,17).

An important technical consideration is how signal strength affects OCTA measurements. Lower signal strength index (SSI) values are associated with artifactually reduced VD values, which can mimic or exaggerate glaucomatous damage (15,18). Quality thresholds vary by platform: an SSI above 40 is recommended for Topcon devices, whereas a quality score of 6 or higher is standard for Zeiss instruments (5). Maintaining consistent image quality is essential for accurate longitudinal comparisons and for preserving the validity of AI-based analysis pipelines, which may be sensitive to variations in image quality (19).

2.2 Key Parameters in Glaucoma

The principal OCTA-derived parameters relevant to glaucoma assessment include several metrics (13,15,16). Peripapillary vessel density (VD) quantifies the proportion of the scanned area occupied by flowing blood vessels in the radial peripapillary capillary (RPC) network. Macular VD is assessed in the superficial capillary plexus (SCP) and deep capillary plexus (DCP), with the SCP the primary layer of interest in glaucoma because it directly supplies the RNFL and ganglion cell layer (15). The foveal avascular zone (FAZ) is evaluated by area, perimeter, and circularity, and an enlarged, irregular FAZ is associated with glaucomatous damage (8,20). Choroidal microvascular dropout (MvD), defined as focal sectoral capillary loss at the choroidal level within regions of parapapillary atrophy, has emerged as a significant biomarker (21). Additionally, the flux index (FI), which represents the average decorrelation signal intensity within detected vessels, provides information about blood flow velocity and density and has been shown to detect rates of glaucoma progression (22).

Contemporary OCTA machines provide automated segmentation of retinal layers, enabling quantitative assessment of vasculature at specific anatomical levels (13,15). Standard definitions include whole-image VD (measured across the entire scan), peripapillary VD (within a 750-µm-wide annulus from the optic disc boundary), parafoveal VD (between 1 mm and 3 mm centered on the fovea), and perifoveal VD (between 3 mm and 5 mm) (5). The 6×6 mm scan, particularly its outer-sector measurements, has demonstrated higher diagnostic accuracy for mild glaucoma than the 3×3 mm scan, although the smaller scan offers superior repeatability (13,17).

2.3 Comparison with Previous Vascular Assessment Techniques

Prior to OCTA, several technologies were available to assess ocular blood flow in glaucoma, though each had significant limitations (14). Fluorescein angiography (FA) provides a qualitative assessment of retinal vasculature but requires intravenous dye injection, carries the risk of allergic reactions, and lacks depth resolution–signals from different vascular plexuses are superimposed in a single image (14). Indocyanine green angiography (ICGA) offers better visualization of the choroidal circulation but shares FA's invasiveness and provides limited quantitative output. Both FA and ICGA require serial image capture and subjective interpretation, making standardized quantitative comparison difficult.

Non-invasive techniques predating OCTA included laser Doppler flowmetry, scanning laser Doppler flowmetry (e.g., the Heidelberg Retina Flowmeter), and color Doppler imaging of the retrobulbar vessels (14). Although these methods provided valuable evidence supporting the vascular theory of glaucoma, they were limited by poor spatial resolution, an inability to measure capillary-level blood flow, high measurement variability, and a lack of depth-resolved information. Laser speckle flowgraphy, another non-invasive approach, measures relative blood flow velocity using the laser speckle phenomenon but does not provide the anatomical detail of capillary-level imaging.

OCTA represents a fundamental advance over these predecessor technologies by combining noninvasiveness with depth resolution, capillary-level spatial resolution, quantitative output, and rapid acquisition (12,14). The ability to separately visualize and quantify vasculature in the superficial plexus, deep plexus, outer retina, and choriocapillaris within a single examination provides an unprecedented window into the multilayered vascular supply of the retina and ONH. This depth-resolved capability is particularly important in glaucoma, where different vascular plexuses may be affected to varying degrees at different disease stages (5,13).

2.4 OCTA Metrics: Vessel Density, Perfusion Density, and Beyond

While vessel density (VD) is the most widely reported OCTA metric in glaucoma research, several additional parameters provide complementary information (5,9,13,22). Perfusion density (PD) quantifies the proportion of the scanned area with blood flow above a threshold and differs from VD in that it accounts for vessel caliber (20,22). Some studies suggest that PD may be more sensitive than VD in detecting early glaucomatous changes, though the evidence is inconsistent across platforms and populations (20).

Fractal dimension (FD) quantifies the branching complexity of the retinal vascular network, providing information about microvascular architecture that simple density metrics do not capture (9). In NTG, reduced FD has been observed in the peripapillary and macular regions, reflecting simplification of the vascular branching pattern associated with capillary dropout (9). The vessel diameter index (VDI), another morphometric parameter, provides information about the caliber of detected vessels and may help differentiate between loss of capillaries (which would reduce VD without changing VDI) and attenuation of larger vessels (9).

The choice of analytical metric can significantly influence diagnostic conclusions. While global (average) values of VD, PD, or FD are commonly reported, regional analyses at the hemispheric, quadrant, or sector levels often reveal diagnostic differences that are masked by averaging (17,23). This observation has led to an increasing emphasis on sector-based analysis protocols that align with the topographic distribution of glaucomatous nerve fiber loss, such as the Garway-Heath mapping scheme, which maps specific optic disc sectors to corresponding points on visual field tests (23,24) (Table 1).

Table 1. Key OCTA Parameters in Glaucoma Diagnostics

Parameter	Description	Clinical Relevance
Peripapillary VD	Fraction of flowing vessel area in the RPC region around the ONH (13,15)	Reduced in glaucoma; correlates with RNFL thinning and VF loss; useful for early detection and progression monitoring
Macular VD (SCP/DCP)	Proportion of perfused vasculature in the superficial and deep capillary plexuses (15,17)	Decreased in glaucoma; lower floor effect than structural OCT; valuable in advanced disease (MD < -14 dB) (25,26)
FAZ Metrics	Central avascular area assessed by area, perimeter, and circularity (8,20)	Enlarged/irregular in glaucoma; ROC analysis shows cut-off values with >90% sensitivity for XFG (20); AI shows associations with systemic factors
Choroidal MvD	Focal sectoral capillary dropout in the choroid within parapapillary atrophy (21)	Associated with disc hemorrhage, progressive RNFL thinning, and parafoveal VF defects (21,27)
Flux Index	Average decorrelation signal intensity reflecting blood flow velocity (22)	Detects rates of glaucoma progression; complements VD measurements (22)
GCL+IPL Thickness	Structural OCT measure of ganglion cell and inner plexiform layers (11)	AUROC 0.93–0.94 for glaucoma detection; progressive thinning across stages; 0.54 dB MD loss per µm decrease (11)

3. OCTA in Glaucoma Diagnosis

3.1 Pre-Perimetric Glaucoma

One of the most clinically significant applications of OCTA is detecting glaucomatous damage before measurable visual field loss occurs (15,16,28). Pre-perimetric glaucoma is a stage in which structural damage to the optic nerve and RNFL is evident, but standard perimetry has not yet detected functional deficits. In this population, superficial peripapillary vessel density is lower than in healthy controls, providing an additional biomarker for early detection (15).

Comparative studies have shown that OCTA is at least as effective as, and in some cases more effective than, structural OCT for diagnosing pre-perimetric glaucoma (16,28). Specifically, OCTA has outperformed GCC-based OCT measurements in certain study populations, whereas other studies report accuracy comparable to RNFL-based OCT (15). Circumpapillary capillary density (cpCD) measurements complement OCT-based RNFL thickness for early POAG diagnosis, with normalized cpCD loss exceeding corresponding RNFL thickness loss in pre-perimetric glaucoma across most regions analyzed (28). Combining OCT and OCTA parameters with artificial intelligence yields high diagnostic accuracy (AUROC = 0.93) in distinguishing healthy eyes from those with mild-to-moderate glaucoma (28).

The concept of neurovascular coupling–the relationship between neuronal activity and local blood flow–suggests that microvascular alterations may occur alongside or even precede structural RGC loss (6,7). This has important implications for the temporal sequence of glaucomatous damage and for OCTA’s potential to detect disease at its earliest stages. Whether vascular changes are a primary pathogenic mechanism or a secondary consequence of reduced metabolic demand from dying RGCs remains an active area of investigation, with evidence supporting both possibilities across disease subtypes (7,14).

3.2 Primary Open-Angle Glaucoma

In established POAG, OCTA consistently shows reduced peripapillary and macular VD compared with healthy eyes, and the magnitude of reduction correlates with disease severity as measured by visual field mean deviation and structural OCT parameters (5,13,15). The superficial vascular plexus shows more pronounced changes than the deep retinal layers, consistent with the anatomical distribution of the RPC network that supplies the RNFL (5,13). Meta-analyses have confirmed that VD is lower in eyes with glaucoma than in controls across all assessed macular and peripapillary regions, and that this reduction in perfusion is most pronounced in the superficial layers (5).

Regional analysis of OCTA parameters reveals patterns that mirror the characteristic sectoral nature of glaucomatous damage (23). The temporal superior and temporal inferior sectors, which correspond to the arcuate bundles most vulnerable to glaucomatous insult, typically show the greatest reductions in VD (23). Global and sector-based comparisons between OCTA and visual field defects have demonstrated significant correlations between RPC vessel density and visual field parameters, and region-specific analyses using Garway-Heath mapping have aligned with the results of location-based visual field examinations (23). Importantly, recent evidence suggests that global (average) VD values may mask regional hemodynamic deficits, underscoring the importance of sectoral and quadrant-level OCTA analysis in clinical practice (17).

The combined use of OCTA and structural OCT improves diagnostic accuracy beyond that of either modality alone (28,29). Studies incorporating circumpapillary microvasculature parameters alongside RNFL thickness and Bruch's membrane opening-minimum rim width (BMO-MRW) show improved prediction of the severity of paracentral visual field loss in POAG patients [29]. Furthermore, structural assessment using GCIPL thickness provides complementary information. Studies show progressive thinning across glaucoma stages–from 76.79 µm in early disease to 57.38 µm in severe disease, compared with 86.01 µm in controls–with high sensitivity (91.5%) and specificity (98.9%) (11).

The structure-function relationship in glaucoma is a cornerstone of clinical decision-making, and OCTA adds a vascular dimension to this traditionally bimodal assessment (23,29). Studies have shown that OCTA vessel density is more strongly correlated with visual function than conventional OCT structural metrics in certain patient populations (16). Specifically, the correlation between peripapillary VD and visual field indices has been shown to be at least as strong as that between RNFL thickness and the same functional parameters (23). This observation suggests that vascular measurements may capture aspects of the disease process not fully captured by structural thinning, perhaps indicating ongoing metabolic compromise in still-surviving neurons.

A critical unresolved question in glaucoma pathophysiology is whether microvascular changes precede or follow neuronal loss. The neurovascular coupling hypothesis posits that reduced metabolic demand from dying RGCs leads to secondary capillary attrition (the “chicken” model), whereas the vascular insufficiency hypothesis suggests that primary perfusion deficits drive ischemia-mediated RGC death (the “egg” model) (6,7,14). Longitudinal OCTA studies have provided evidence for both mechanisms, depending on disease subtype and anatomical region. In POAG, peripapillary capillary density loss can precede RNFL thinning in some patients, supporting a primary vascular role, whereas in others, structural loss clearly precedes vascular changes (30,31). This heterogeneity suggests that glaucoma is a pathophysiologically diverse group of conditions with variable contributions from mechanical and vascular factors (1,6).

Compromised blood flow appears particularly relevant in patients with systemic vascular abnormalities, including hypotension, migraine, and Raynaud's phenomenon–conditions all associated with NTG and with paracentral visual field loss patterns (6,8,29). The superficial vascular plexus supplies the circumpapillary and parafoveal areas, so OCTA measurements of this layer may be particularly sensitive to the hemodynamic disturbances underlying these clinical phenotypes (29).

3.3 Normal-Tension Glaucoma

Normal-tension glaucoma is a particularly compelling clinical context for OCTA assessment, given the prominent role attributed to vascular dysfunction in its pathogenesis (6,8,9). Peripapillary perfusion analysis using OCTA in NTG patients reveals significant microvascular changes that may reflect the underlying hemodynamic compromise believed to contribute to optic nerve damage despite normal IOP (8,9).

Early OCTA studies in NTG showed significantly increased FAZ diameter and area and decreased vessel density compared with healthy controls (8). Using ZEISS AngioPlex with 3×3 mm macular scans, Zivkovic et al. found that vertical, horizontal, and maximum FAZ diameters, as well as FAZ area, were significantly enlarged in NTG eyes (all $p < 0.001$), whereas vessel density in the central and inner regions was significantly reduced (8). These findings provided objective, quantitative evidence of microcirculatory disturbances in NTG and supported the vascular theory of glaucomatous optic neuropathy.

Longitudinal OCTA studies have further strengthened OCTA's prognostic role in NTG. In a prospective cohort of 164 NTG patients (270 eyes) followed for a mean of 48.58 months, lower baseline superotemporal circumpapillary vessel density was independently associated with visual field deterioration (hazard ratio, 1.401 per 1-SD decrease) after adjustment for reported risk factors (9). These findings demonstrate that OCTA metrics can meaningfully improve risk stratification in NTG patients beyond traditional clinical parameters.

The role of systemic vascular dysregulation in NTG has been extensively studied using various hemodynamic assessment techniques (6,8). Color Doppler imaging has shown reduced ocular blood flow velocities in the ophthalmic artery, central retinal artery, and short posterior ciliary arteries in patients with NTG (8). OCTA complements this understanding by providing high-resolution mapping of the terminal capillary beds that directly supply retinal neurons and the ONH. The finding that FAZ parameters are significantly altered in NTG, even at early disease stages, suggests that macular microvascular compromise may be an early event in this disease subtype and could serve as a biomarker for the subclinical vascular insufficiency that characterizes NTG (8).

The relationship between blood pressure patterns and OCTA parameters in NTG is an active area of investigation. The concept of “dipping” (nocturnal blood pressure decrease) and its relationship to glaucomatous damage have been extensively studied, with evidence suggesting that excessive dipping may compromise optic nerve perfusion pressure, particularly in eyes with impaired autoregulatory capacity (6). OCTA provides a means to directly assess the microvascular consequences of these systemic hemodynamic patterns, potentially enabling more targeted therapeutic interventions that address both ocular and systemic vascular risk factors.

3.4 Exfoliation Glaucoma

Exfoliation glaucoma (XFG) is a secondary form of open-angle glaucoma characterized by the accumulation of exfoliation material in the anterior segment, associated with higher IOP and a more aggressive disease course than POAG (20). Vascular compromise is recognized as an important pathogenic factor in XFG, and OCTA provides a detailed, highly accurate, and reproducible map of the foveal microvascular architecture (20).

In a cross-sectional comparative study of 54 XFG patients and 94 healthy controls, the authors reported significantly lower VD, perfusion density (PD), and FAZ values in the XFG group (20). ROC analysis showed high discriminatory ability, with cut-off values demonstrating excellent diagnostic performance: VD total at 19.55 (sensitivity 92.3%, specificity 81.9%), VD parafoveal at 21.20 (sensitivity 100%, specificity 78.7%), PD total at 0.36 (sensitivity 98.1%, specificity 76.6%), and FAZ circularity index at 0.635 (sensitivity 79.3%, specificity 72%) (20). These findings establish quantitative OCTA-derived thresholds that may inform clinical decision-making for XFG patients.

3.5 Angle-Closure Glaucoma

Primary angle-closure glaucoma (PACG) accounts for a disproportionately high burden of glaucoma-related blindness, particularly in East and Southeast Asian populations (1,4). The pathogenesis of PACG involves both mechanical angle closure and potential vascular compromise, though the relative contributions of each mechanism remain debated. OCTA studies in PACG have shown reduced peripapillary and macular vessel density compared with healthy controls, and the extent of VD reduction correlates with visual field severity and RNFL thinning (13).

Choroidal microvascular dropout has been evaluated in PACG and found in approximately 35–47% of affected eyes, a prevalence lower than that in POAG eyes matched for disease severity (58–80%) (21). This difference may reflect distinct pathogenic mechanisms: whereas MvD in POAG appears related to chronic perfusion compromise potentially driven by IOP-mediated lamina cribrosa changes, the more acute pressure elevations in angle-closure disease may cause damage through different vascular pathways. In PACG eyes, MvD is associated with worse mean deviation on visual fields and with initial parafoveal scotoma patterns rather than nasal step defects, mirroring the topographic relationships observed in POAG (21).

The distinct vascular profiles of glaucoma subtypes, as revealed by OCTA, have important implications for understanding disease pathophysiology and may inform therapeutic tailoring. The observation that exfoliation glaucoma (20), POAG (13,15), NTG (8,9), and PACG (21) each show characteristic patterns of microvascular alteration supports the concept that glaucoma is a heterogeneous group of optic neuropathies with varying degrees of vascular involvement.

3.6 Choroidal Microvascular Dropout as a Distinct Biomarker

Choroidal microvascular dropout has emerged as one of the most clinically significant OCTA-derived biomarkers in glaucoma (21,27,32,33). MvD is defined as focal, sectoral capillary dropout with no visible microvascular network within the parapapillary atrophy region, as identified on en face choroidal slab images from OCTA (21,33). The choroidal slab typically extends from the retinal pigment epithelium to the outer scleral border, capturing signals from the choriocapillaris and deeper choroidal vessels (33). MvD area and angular circumference can be quantified using image analysis software such as ImageJ (32,33).

Multiple longitudinal studies have shown that MvD tends to enlarge over time in glaucomatous eyes, and the rate of enlargement is associated with several clinically relevant factors (32,33).

Greater IOP fluctuation, higher peak IOP, worse baseline visual field mean deviation, and a greater number of IOP-lowering medications are significantly associated with faster MvD enlargement (33). In a four-year longitudinal study of 91 POAG eyes, more than three-quarters showed evidence of MvD at baseline or during follow-up, and the rate of MvD area change was significantly associated with the rate of cpRNFL thinning (32,33). These findings provide compelling evidence that choroidal perfusion deficits and structural nerve fiber damage are mechanistically linked in glaucoma.

Recent studies have further demonstrated that the topographic expansion of MvD toward the disc-fovea axis is specifically associated with the development of new central visual field defects (32). In glaucomatous eyes with significant macular RGC damage, group analyses showed that eyes developing new central VF defects exhibited significantly greater increases in MvD angular extent (17.8°) than eyes that remained stable (0.9°) or had baseline central defects (6.0°). OCT-based thickness changes did not differ between groups during the same period (32). This observation is particularly noteworthy because it suggests that OCTA-based MvD assessment may be more sensitive than structural OCT for detecting progression affecting the central visual field.

MvD is not limited to established glaucoma; it can also develop in glaucoma suspects, with axial length and baseline cup volume as risk factors in this population (33). The GCIPL thickness slope during follow-up was also associated with MvD development in glaucoma suspects, suggesting that early structural thinning may precede or coincide with choroidal vascular changes (33). These findings extend the clinical relevance of MvD from a marker of established disease to a potential early warning indicator.

3.7 Glaucoma in High Myopia

Diagnosing glaucoma in highly myopic eyes is challenging because structural artifacts compromise conventional OCT assessment (15,34). Disc torsion, rotation, tilt, and extensive peripapillary atrophy frequently cause RNFL segmentation errors and false-positive results (15). In this context, OCTA offers a distinct advantage: vessel density in healthy myopic eyes does not exhibit the same artifactual attenuation as structural OCT parameters (15,34).

The OCTA-PanoMap, an integrated widefield approach that combines SS-OCT and OCTA data across the peripapillary and macular regions, has demonstrated good diagnostic performance in distinguishing high myopia with glaucoma from high myopia alone (15). Longitudinal studies comparing macular and peripapillary VD changes with structural OCT thickness measurements in highly myopic glaucoma patients have shown that vessel density decline may be a more sensitive indicator of progression than structural parameters in this population (34). Specifically, in a study of 71 highly myopic glaucoma eyes followed for an average of 2.88 years, the progressive group showed a significantly greater decline in both macular and peripapillary VD than the stable group, whereas changes in GCIPL and RNFL thickness did not reach statistical significance between groups (34). Deep learning approaches using dual autoencoder models on SS-OCT texture en face images have achieved a diagnostic accuracy of 0.92 for detecting glaucoma in myopic eyes, outperforming conventional RNFL-based approaches (35).

3.8 Advanced Glaucoma

In advanced glaucoma, the utility of structural OCT is limited by the floor effect–a point at which RNFL and GCC thickness can no longer decrease despite ongoing disease progression (25,26). This structural floor varies widely across individuals and creates a significant blind spot in monitoring advanced disease. Studies using the Hodapp-Parrish-Anderson classification have shown that although GCIPL thickness decreases progressively with disease severity, the absolute difference between moderate and severe stages narrows, reflecting this floor limitation (11).

OCTA-derived macular vessel density does not show the same degree of floor limitation and continues to decline in eyes with severe visual field loss (25,26). Studies have shown that parafoveal VD remains a useful objective metric for detecting progression in eyes with MD worse than -14 dB, a range in which structural OCT measurements become unreliable (25,26). This extended dynamic range positions OCTA as a critical complementary tool for monitoring advanced glaucoma. Furthermore, OCTA has shown utility at both extremes of the disease spectrum, though it is important to recognize that despite OCTA parameters having a lower floor than structural OCT, the number of distinguishable steps within the dynamic range of RNFL may still be greater (15).

4. OCTA in Monitoring Disease Progression

4.1 Longitudinal Vessel Density Changes

Monitoring glaucoma progression is essential for optimizing treatment decisions (1,30). Longitudinal studies of OCTA changes in healthy, glaucoma-suspect, and glaucomatous eyes have revealed important patterns (30). In glaucomatous eyes, microvascular loss in the ONH region appears to occur earlier than in the macula, and ONH VD loss shows a slightly stronger association with baseline visual field status than macular VD changes (30). These findings suggest that peripapillary OCTA assessment may be particularly valuable for monitoring early disease progression.

Event-based progression analyses using OCTA show that both OCT and OCTA detect more progressors than standard visual field testing, yet the two imaging modalities show limited agreement on which specific eyes are classified as progressive (31). This discordance suggests that structural (OCT) and vascular (OCTA) measurements capture distinct, complementary aspects of glaucomatous damage, reinforcing the rationale for incorporating both modalities into clinical monitoring protocols (31). Machine learning models that combine baseline and longitudinal OCT and OCTA parameters at the global and hemifield levels achieve the best classification accuracy for detecting visual field progression (AUROC = 0.89), significantly outperforming models based on either modality alone (28).

Importantly, the rate of vessel density loss varies across disease stages and anatomical regions. In NTG patients, the superotemporal peripapillary region appears most vulnerable, and lower baseline VD in this sector predicts subsequent visual field deterioration (9). For highly myopic glaucoma patients, both macular and peripapillary VD decline more rapidly in progressive eyes than in stable eyes, even when structural parameters fail to distinguish between groups (34).

The temporal dynamics of vessel density loss also provide insights into disease mechanisms. Cross-sectional studies consistently show a gradient of VD reduction from glaucoma suspects through mild, moderate, and severe disease stages (5,22,28). Longitudinal analyses refine this picture by showing that the rate of VD decline varies across eyes, with some eyes exhibiting rapid microvascular deterioration and others maintaining relatively stable perfusion over years of follow-up (30,31). Understanding the determinants of this inter-individual variability–whether they relate to systemic vascular health, genetic factors, treatment responsiveness, or other mechanisms–is a priority for future research.

4.2 Predictive Value of Baseline OCTA

Beyond tracking ongoing changes, baseline OCTA measurements have predictive value for future disease progression (21,27,32,33,36). Baseline choroidal microvascular dropout is associated with subsequent disc hemorrhage and progressive RNFL thinning (21,27). Similarly, lower peripapillary vessel density at baseline predicts progressive thinning of both RNFL and GCC over time (36). The rate of initial loss of capillary density in the optic nerve head has been linked to the risk of subsequent visual field progression, providing clinicians with a potential biomarker to identify high-risk patients who may benefit from earlier or more aggressive treatment (36).

The predictive value of OCTA extends beyond simple vessel density to specific vascular parameters. Both VD and FI measured by OCTA can distinguish between normal and glaucomatous eyes, but their roles differ: VD is more sensitive for comparing eyes across disease stages, whereas FI appears better suited for detecting rates of ongoing progression (22). This complementary relationship among OCTA metrics suggests that a multiparametric approach may optimize the predictive utility of vascular imaging in glaucoma management.

The association between MvD enlargement and faster RNFL thinning is particularly important for prognosis (32,33). In the Diagnostic Innovations in Glaucoma Study (DIGS), a joint longitudinal model found that the rate of MvD area change was significantly associated with the rate of cpRNFL thinning in POAG eyes, even after adjusting for baseline disease severity and IOP metrics (33). Moreover, eyes that developed MvD during follow-up had greater IOP fluctuations than those without MvD, suggesting that unstable IOP control may contribute to choroidal vascular compromise and subsequent structural progression (33). These findings have direct clinical implications, underscoring the importance of achieving not only low mean IOP but also stable IOP in glaucoma management.

4.3 The Role of Anti-Glaucoma Medications on OCTA Parameters

An important consideration when interpreting longitudinal OCTA data is the potential influence of topical anti-glaucoma medications on retinal and choroidal blood flow (13,15). Prostaglandin analogs, the most commonly prescribed first-line agents, have been shown to increase ocular blood flow through mechanisms that may include increased production of endogenous vasodilators and reduced IOP-related changes in perfusion pressure (13). Conversely, beta-blockers may reduce ocular blood flow through systemic hypotension and direct vasoconstriction (15).

The clinical significance of medication-induced changes in OCTA parameters remains debated. Some studies suggest that the improvement in VD observed after initiating IOP-lowering therapy reflects genuine vascular recovery rather than a measurement artifact, supporting the concept that reducing IOP improves optic nerve perfusion (19). Others caution that medication effects may confound longitudinal monitoring by obscuring true disease progression or falsely suggesting improvement (13). Standardized protocols to control for medication effects in OCTA studies–for example, performing scans at consistent times relative to drug instillation–are needed to improve the reliability of longitudinal assessments.

4.4 OCTA Following Surgical Intervention

Emerging evidence suggests that OCTA can assess vascular changes after glaucoma surgery (5,19). Studies have reported changes in vessel density after procedures such as trabeculectomy, which may reflect vascular recovery associated with IOP reduction (19). Additionally, anterior segment OCTA offers a novel way to assess filtration bleb morphology and vascularity, with avascular blebs generally considered to be associated with successful surgical outcomes (5). The FAZ has also been proposed as an indicator of vascular reperfusion after surgery-induced IOP reduction (13). However, few studies have systematically recorded anti-glaucoma medication use in the postoperative period, and most have evaluated only trabeculectomy, limiting the generalizability of current findings (5).

5. Current Limitations and Technical Challenges

5.1 Image Quality and Artifacts

A major practical limitation of OCTA in clinical glaucoma assessment is its susceptibility to image artifacts (15,18). In a study of more than 5,000 OCTA images, approximately 34% were of poor quality, and among scans meeting quality thresholds, 23.4% still contained artifacts (15). Notably, 41% of glaucoma eyes exhibited artifacts. The most common artifact types include segmentation errors (particularly in eyes with advanced optic nerve damage), eye movement artifacts, blink artifacts, and Z-offset errors (15,18). Quality control is essential: images with a signal strength index below 40 (or 6 on Zeiss devices) should be excluded, as should those with significant motion artifacts, segmentation errors, or media opacities (5).

Factors associated with poor-quality scans include older age, male sex, worse visual field MD, lack of eye tracking, and macular scan area (15). Media opacities (such as cataracts) and concomitant retinal pathology further compromise image quality. High-definition imaging modes reduce artifacts but require longer acquisition times, which may be challenging for elderly or less cooperative patients (15,18).

5.2 Projection Artifacts and Segmentation

Projection artifacts occur when blood flow signals from superficial retinal vessels are erroneously attributed to deeper layers, creating false representations of vasculature in the deep capillary plexus, outer retina, and choriocapillaris (14). This well-known phenomenon results from the high variance associated with the strong blood flow in major vessels, which is projected onto the reflectance of deeper structures (13). Projection-resolved OCTA algorithms have been developed to mitigate this issue, but their effectiveness varies across platforms and clinical scenarios (14). Accurate segmentation of retinal layers is also critical, as segmentation errors can significantly alter VD measurements and lead to misclassification of disease status (13,14).

5.3 Reproducibility and Standardization

Inter-visit variability in OCTA measurements is a key limitation for longitudinal monitoring (16,37). Although reproducibility is generally acceptable for 3×3 mm macular scans, larger scan areas (6×6 mm) may improve diagnostic performance in mild glaucoma, albeit at the cost of somewhat reduced repeatability (13,17). Furthermore, VD measurements vary significantly across OCTA platforms because of differences in algorithms, scan protocols, and analysis software, precluding direct comparisons between devices and complicating multicenter research and clinical decision-making (16,37). Specialized software that provides more comprehensive analysis, including vessel-branching complexity metrics and fractal dimension, has been developed to address some of these limitations, but it requires further validation (9,13).

5.4 Confounding Factors

Age-related decline in retinal microvasculature is a significant confounding factor in OCTA-based glaucoma assessment (38). Systematic review data indicate that healthy aging is associated with a change in vessel density of approximately -0.33 ± 0.50 %/year on OCTA (38). Without appropriate correction for age-related physiological changes, the specificity of OCTA for detecting true glaucomatous progression may be compromised. Deep learning approaches have been developed to distinguish glaucoma progression from age-related changes in OCT scans, offering a promising computational solution to this clinical challenge (39). Additionally, systemic conditions such as hypertension, diabetes mellitus, and sleep apnea syndrome influence retinal microvascular parameters and must be considered during clinical interpretation (38).

Topical anti-glaucoma medications, particularly prostaglandin analogs and beta-blockers, have been shown to affect retinal and choroidal blood flow, introducing a potential treatment-related confounder in longitudinal OCTA studies (13). The relationship between FAZ characteristics and systemic factors has also been examined, with AI-enhanced OCTA analysis revealing associations between FAZ area enlargement and female gender, and between FAZ circularity loss and aging and sleep apnea syndrome (19).

The influence of axial length on OCTA measurements is another important confounding variable, particularly in highly myopic populations (34). Magnification effects from longer axial lengths can overestimate the scanned retinal area and underestimate vessel density if not properly corrected (15,34). Some OCTA platforms incorporate axial length correction into their analysis software, but standardization of this correction across devices remains inconsistent. Furthermore, the physiological differences in retinal microvasculature associated with high myopia–including elongated and stretched capillary networks–may independently affect VD measurements and must be distinguished from pathological changes due to coexisting glaucoma (15,34).

Ethnic and racial variations in OCTA parameters have been documented but remain incompletely characterized (38,40). Normative reference databases stratified by ethnicity, age, gender, and refractive error are essential for accurate clinical interpretation, yet most available databases are derived from relatively homogeneous populations (38). Developing inclusive normative datasets and training AI algorithms on diverse patient cohorts are prerequisites for the equitable global deployment of OCTA-based glaucoma diagnostics (40).

Finally, distinguishing cause from effect in OCTA findings remains a fundamental interpretive challenge. A measured reduction in vessel density may reflect primary vascular insufficiency driving neuronal death, secondary capillary attrition after RGC loss, medication-induced hemodynamic changes, or simple signal loss from tissue thinning, which reduces the volume of vasculature within the scanned layer (6,7,14). Disentangling these possibilities requires carefully designed longitudinal studies with comprehensive control for confounding variables, and the answer may ultimately vary across glaucoma subtypes and individual patients.

6. Artificial Intelligence and Deep Learning in OCTA-Based Glaucoma Assessment

6.1 Overview of AI Approaches

The integration of artificial intelligence, particularly deep learning (DL), with OCTA offers transformative potential for glaucoma diagnostics (19,39,41). DL models, especially convolutional neural networks (CNNs), are well-suited to image analysis because they can automatically learn spatial hierarchies of features that may be imperceptible to human observers (19). Various DL architectures–including CNNs, recurrent neural networks (RNNs), generative adversarial networks (GANs), autoencoders, and transformer models–have been applied to OCT and OCTA data for glaucoma classification, progression prediction, and structure-function mapping (19,41). These algorithms have been developed using various OCT image types, including conventional reports, cross-sections, 3D volumetric scans, anterior segment OCTs, and OCTA images, each providing unique information that enhances diagnostic accuracy (19).

6.2 OCTA-Specific AI Applications

AI-based classification algorithms using OCTA data have demonstrated impressive diagnostic performance (41,42). Automated classification systems using support vector machines, random forests, and gradient boosting on OCTA scans have achieved AUROC values of 0.85-0.89 for glaucoma detection (42). Deep learning approaches using CNNs on en face vessel density images have further improved classification, achieving an adjusted area under the precision-recall curve of 0.97 for distinguishing healthy from glaucomatous eyes (41). A study using swept-source OCTA with superficial capillary plexus images achieved an AUROC of 0.946 for detecting glaucoma in highly myopic eyes, a performance comparable to that of macular OCT images and significantly superior to that of deep capillary plexus images (41).

A particularly innovative application uses deep learning to estimate 10-2 visual field maps from macular OCTA measurements, potentially reducing patient burden by deriving functional information from structural/vascular imaging (15). Furthermore, AI-enhanced OCTA analysis of FAZ parameters has identified FAZ metrics as promising biomarkers for early detection of open-angle glaucoma, with associations between FAZ characteristics and systemic risk factors that may not be apparent through conventional analysis (19). CNN-based algorithms have also been developed to analyze anterior segment OCT images, enabling automatic detection of the scleral spur, gonioscopic angle closure, and peripheral anterior syngchiae, which are essential for assessing angle-closure glaucoma risk (19).

6.3 Multimodal AI Fusion

Contemporary research increasingly emphasizes multimodal DL approaches that integrate data from multiple imaging sources (19,41,43). A notable CNN architecture (AI-GlauOCTA) that combines structural OCT and OCTA images of both the disc and macula found that, in certain configurations, OCTA alone showed superior sensitivity for detecting glaucomatous changes compared with combined OCT and OCTA (43). This finding suggests that DL can extract additional diagnostic information from vascular flow patterns that single-value metrics cannot capture, potentially because deep learning enables analysis of factors beyond a single vessel density value (43).

Multimodal CNN systems that integrate fundus photographs, OCT scans, and visual field data have achieved AUROCs of 0.86–0.95 for glaucoma detection, substantially outperforming single-modality models (19,41). Combining OCT and OCTA parameters with hemifield measurements significantly improves classification accuracy compared with global measurements alone (28). Incorporating longitudinal rates of change in OCT and OCTA parameters (AUROCs = 0.80–0.89) substantially increases classification accuracy compared with baseline measurements alone (AUROCs = 0.60–0.63), confirming the value of temporal information for AI-based progression detection (28).

6.4 Challenges in AI Implementation

Despite promising results, several significant challenges impede the clinical translation of AI-enhanced OCTA for glaucoma (19,39,40). Model interpretability remains a critical concern: most DL systems operate as “black boxes” without transparent reasoning, which reduces clinician trust (39,40). Explainable AI (XAI) frameworks are being developed to address this limitation, including tools that highlight image regions contributing to predictions, but these methods are not yet widely adopted (39). Furthermore, algorithmic fairness is increasingly recognized as essential, as studies have shown that DL models can produce unequal outcomes across demographic groups, with certain racial and ethnic minorities experiencing lower diagnostic performance (40).

The FairDist model, which uses knowledge distillation from an equity-aware detection model, represents an important advance in addressing these disparities, achieving the highest AUROC and equity-scaled AUROC for both gender and racial groups compared with methods with and without unfairness mitigation strategies (40). Data variability across OCTA platforms, inconsistent annotation practices, and the limited availability of large, longitudinal, multi-institutional datasets for training and validation further constrain AI development (19,39). Regulatory frameworks for AI-based medical devices continue to evolve, and integrating AI tools into existing clinical workflows requires careful attention to usability, interoperability, and adherence to standardized imaging quality-control guidelines (Table 2) (19).

Beyond classification and prediction, AI is increasingly used to improve the quality and interpretability of OCTA images (19,39,44). Deep learning algorithms have been developed to correct artifacts in RNFL thickness maps, potentially addressing a major practical barrier to reliable OCTA-based assessment (19). Automated neural network-based segmentation algorithms can correct layer boundary errors in eyes with advanced glaucomatous damage, media opacity, or high myopia, thereby improving the accuracy of downstream VD calculations (19,44). GAN-based super-resolution techniques can enhance the spatial resolution of OCTA images, potentially enabling detection of subtle capillary-level changes that would otherwise fall below the noise floor of conventional imaging (19).

Explainable AI is especially important in glaucoma management, where treatment decisions have lifelong implications (39). Occlusion analysis and attention mapping can identify the ONH regions that contribute most to a model's predictions, and these highlighted regions often align with clinical expectations about the topographic distribution of glaucomatous damage (19). Gradient-weighted class activation mapping (Grad-CAM) overlays provide visual explanations of CNN decision processes, enabling clinicians to assess whether an AI model's reasoning is consistent with known pathophysiology before incorporating its predictions into clinical decisions (39).

The integration of AI into clinical workflows also poses practical challenges for implementation science (19,39). Electronic health record (EHR) integration, real-time processing requirements, and the need for seamless embedding within existing imaging software platforms must all be addressed. Regulatory pathways for AI-based medical devices, including the FDA's 510(k) clearance process and the European CE marking requirements, impose additional requirements for clinical validation, post-market surveillance, and algorithm version control that must be factored into development timelines (19).

Table 2. Summary of AI Approaches Applied to OCTA in Glaucoma

AI Technique	Input Data	Application	Performance
SVM / RF / xGB [42]	OCTA scans	Glaucoma classification	AUROC 0.85–0.89
CNN [41]	En face VD images	Healthy vs. glaucoma	AUPRC 0.97
CNN (SS-OCTA) [41]	SCP macular images	High myopia glaucoma	AUROC 0.946
DL estimation [15]	Macular OCTA	10-2 VF map prediction	Structure-function mapping
Multimodal CNN [19]	OCT + OCTA + Fundus	Glaucoma detection (fusion)	AUROC 0.86–0.95
Dual Autoencoder [35]	SS-OCT en face images	Glaucoma in myopic eyes	AUROC 0.92
AI-GlauOCTA [43]	OCT-D + OCT-M + OCTA-D + OCTA-M	Intermediate fusion classification	OCTA > combined OCT+OCTA (sensitivity)
CNN + LSTM [41]	OCT + VF + Clinical	Progression prediction	Multimodal temporal prediction
FairDist [40]	Baseline OCT scans	Equity-aware progression	Highest equity-scaled AUROC

7. Emerging Technologies and Future Directions

7.1 Next-Generation OCT and OCTA Technologies

Several emerging OCT technologies promise to enhance OCTA capabilities for glaucoma assessment (10,19). Polarization-sensitive OCT (PS-OCT) provides additional contrast by leveraging the RNFL's birefringence, thereby improving detection of nerve fiber layer alterations that precede measurable thickness changes (10). Visible-light OCT offers improved axial resolution through shorter wavelengths, potentially enabling earlier detection of subtle structural damage in the ganglion cell layer (10).

Adaptive optics (AO) technology, which compensates for optical aberrations in the eye, enables visualization of individual retinal cells and capillaries (10). When combined with OCTA (AO-OCTA), it achieves cellular-level resolution of the retinal microvasculature, potentially enabling detection of single-capillary dropout events. Although currently limited to research settings, AO-OCTA represents the frontier of non-invasive retinal vascular imaging and may eventually provide unprecedented sensitivity for early glaucoma detection (10).

Widefield and ultra-widefield OCTA extend imaging beyond conventional 3×3 mm and 6×6 mm scan areas, enabling comprehensive assessment of peripheral retinal vasculature and broader peripapillary regions (15). Montage protocols that combine multiple scans can achieve field coverage comparable to that of fluorescein angiography. Advanced quantitative metrics, including fractal dimension, vessel diameter index, and branching complexity measures, are being developed using specialized software (such as custom MATLAB programs) to provide more nuanced characterization of microvascular changes beyond simple vessel density (9,13).

7.2 AI-Powered Predictive Models

The next generation of AI models for glaucoma aims to move beyond cross-sectional classification toward longitudinal prediction (19,41). DL frameworks that combine CNNs with long short-term memory (LSTM) networks can incorporate temporal sequences of imaging data to predict disease progression (41). Some approaches use generative algorithms to synthesize future imaging data from observed trends, enabling estimation of disease trajectory from baseline and early follow-up visits (41).

Foundation models–large-scale, pre-trained neural networks that can be adapted to multiple downstream tasks–represent the cutting edge of AI in ophthalmology (19). Models such as RETFound, trained on large collections of retinal images, demonstrate the potential of transfer learning, which requires only small task-specific datasets for fine-tuning (19). The development of multimodal foundation models that jointly process color fundus photography, OCT, and OCTA data represents the next frontier, with emerging research showing the potential for comprehensive retinal analysis from integrated imaging inputs (19). Large language models (LLMs) are also being explored to enhance the interpretability of ophthalmic diagnostics, including zero-shot studies for disease diagnosis (19).

7.3 Multimodal Integration and Precision Medicine

The convergence of OCTA with other diagnostic modalities–including continuous and at-home IOP monitoring devices, genetic risk profiling, and systemic vascular health assessment–signals an era of precision medicine in glaucoma (10,19). Hybrid AI models that integrate imaging data with clinical parameters (IOP history, central corneal thickness, family history, and systemic comorbidities) are being developed to provide personalized risk assessments and treatment recommendations (10,19).

Multimodal approaches that integrate imaging data across modalities with clinical and demographic information are expected to yield the most clinically impactful AI systems (39,41).

The concept of a “digital twin” of the glaucomatous eye–a computational model that integrates structural, vascular, and functional data to simulate disease progression under different treatment scenarios–is a longer-term aspiration for which OCTA data will be essential. Such models could enable truly individualized treatment optimization by predicting responses to IOP-lowering interventions or neuroprotective therapies, based on a comprehensive characterization of each patient’s disease phenotype (19).

7.4 Standardization and Clinical Integration

To realize its potential in routine glaucoma management, OCTA must overcome several practical obstacles (5,16,37). Standardizing acquisition protocols, analysis algorithms, and quality metrics across platforms is essential for meaningful cross-platform comparisons and multicenter clinical trials (16,37). Developing normative databases that account for age, ethnicity, axial length, and other relevant covariates will improve the clinical interpretability of OCTA measurements (38). Recently proposed systematic guidelines for imaging classification, annotation, and quality control, specifically designed for AI applications in glaucoma, mark an important step toward harmonizing data practices (19).

The introduction of dedicated Current Procedural Terminology (CPT) codes for OCTA (e.g., CPT 92137 in 2025) is an important step toward broader adoption by addressing reimbursement barriers (10). Clinical guidelines that integrate OCTA into standard glaucoma diagnostic and monitoring protocols are needed to guide appropriate utilization and ensure the technology is deployed where it adds the most clinical value. The American Academy of Ophthalmology technology assessment confirms that OCTA can detect vessel density loss associated with glaucoma, though it notes that the technology’s role relative to existing structural OCT remains to be fully defined in clinical practice guidelines (37).

7.5 Telemedicine and Global Health Applications

The global burden of glaucoma disproportionately affects low- and middle-income countries, where access to specialist ophthalmological care is limited (3,4). Portable, lower-cost OCTA devices, paired with cloud-based AI analysis, could enable screening and monitoring programs in settings without experienced glaucoma specialists. The non-invasive nature of OCTA, which requires no pupil dilation for many protocols and no dye injection, makes it particularly suitable for community-based screening, where minimizing procedural complexity is essential (5,10).

Telemedicine platforms that incorporate remote OCTA image analysis can extend specialist-level glaucoma assessment to underserved populations (10,19). AI-driven automated quality control can ensure that only images meeting diagnostic standards are forwarded for analysis, while automated classification algorithms can flag high-risk cases for priority review by remote specialists. Although still in early stages, the development of smartphone-based OCT prototypes points toward a future in which retinal vascular imaging may become accessible even in resource-limited settings.

Cost-effectiveness analyses of integrating OCTA into glaucoma care pathways are needed to inform health policy decisions about adoption and reimbursement (10). Although the additional hardware cost of OCTA-capable devices compared with standard OCT is declining, the incremental diagnostic and prognostic value must be demonstrated through rigorous health economic studies that account for potential savings from earlier disease detection, more efficient monitoring, and the prevention of irreversible vision loss.

8. Conclusions

OCTA has emerged as a transformative imaging modality in glaucoma, providing noninvasive assessment of retinal and optic nerve head microvasculature that complements established structural OCT parameters (1,5,13,15,16). The evidence reviewed herein demonstrates the clinical utility of OCTA across the entire glaucoma spectrum: from detecting pre-perimetric microvascular changes (15,28), through diagnosing and staging established disease, including POAG (13,23), NTG (8,9), exfoliation glaucoma (20), and angle-closure glaucoma (21), to monitoring advanced glaucoma beyond structural measurement floors (25,26). Particular strengths include evaluating glaucoma in highly myopic eyes (15,34) and predicting future disease progression from baseline vascular assessments (9,21,36).

Choroidal microvascular dropout has emerged as a particularly important OCTA-derived biomarker. Longitudinal evidence indicates that MvD enlargement is associated with IOP fluctuations, loss of nerve fibers, and the development of central visual field defects (32,33). The ability of MvD assessment to capture aspects of disease progression not reflected in OCT thickness measurements further underscores the complementary nature of vascular and structural imaging (32).

Structural parameters, such as GCIPL thickness, remain indispensable for comprehensive glaucoma evaluation and provide complementary diagnostic information across disease stages

(11). Integrating structural OCT and OCTA parameters, particularly when analyzed using multivariate approaches or machine learning algorithms, consistently yields superior diagnostic and predictive performance compared with either modality alone (28,31,41).

The integration of AI and deep learning with OCTA data is the most promising near-term frontier, with multimodal fusion models demonstrating diagnostic accuracy that approaches or even exceeds that of expert clinicians (19,28,41,43). However, the responsible deployment of these technologies requires addressing challenges in algorithmic fairness (40), model interpretability (39), and data standardization (19,37). Equity-aware models such as FairDist are important steps toward ensuring that AI-enhanced diagnostics benefit all patient populations equitably (40).

Several key priorities for future research and clinical development emerge. First, large-scale, multicenter longitudinal studies using standardized OCTA protocols are needed to establish definitive evidence for the independent prognostic value of OCTA parameters beyond structural OCT and visual field testing. Second, developing platform-independent normative databases that incorporate demographic and biometric covariates is essential for clinical interpretation. Third, prospective studies evaluating the impact of OCTA-guided treatment decisions on patient outcomes are needed to move beyond association and demonstrate clinical utility. Fourth, integrating OCTA with other emerging technologies–including adaptive optics, polarization-sensitive OCT, and home-based IOP monitoring–promises to create comprehensive disease-monitoring systems that could fundamentally transform glaucoma care.

In conclusion, OCTA is poised to become an indispensable component of the modern glaucoma diagnostic and management paradigm. As imaging technologies advance, AI algorithms mature, and clinical guidelines evolve to incorporate vascular biomarkers, integrating OCTA into the glaucoma clinician’s toolkit has the potential to improve early detection, enable more precise monitoring, facilitate personalized treatment strategies, and ultimately preserve vision for patients worldwide.

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