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Optical Coherence Tomography Angiography in Ischemic Retinal and Optic Nerve Diseases, with Emerging Applications in Athletes

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ABSTRACT

Background. Optical coherence tomography angiography (OCT-A) provides non-invasive, high-resolution assessment of retinal and optic nerve microvasculature. Ischemic disorders such as DR, DMI, RVO, RAO and NAION show characteristic microvascular deficits measurable with OCT-A biomarkers. Early data also demonstrate exercise-related modulation of retinal perfusion.

Aim. To review diagnostic, prognostic and emerging exercise-related applications of OCT-A in ischemic ocular disease.

Methods. Systematic overview of 30 studies evaluating OCT-A biomarkers, perfusion deficits, structure–function relationships and exercise-induced microvascular responses.

Results. OCT-A reliably detects early ischemic changes—reduced vessel density, deep plexus dropout, parafoveal non-perfusion and FAZ enlargement—correlating with functional loss. It differentiates ischemic from non-ischemic RVO, maps RAO perfusion deficits and identifies radial peripapillary capillary loss in NAION. Subclinical abnormalities appear in systemic conditions. In active individuals and endurance athletes, OCT-A captures transient and training-related perfusion changes. Limitations include artifacts, segmentation errors and lack of leakage detection.

Conclusions. OCT-A is essential for detecting and monitoring ischemic retinal and optic nerve disease. Key biomarkers (VD, PD, FAZ, NPA) reflect severity and prognosis. Early evidence suggests additional utility in assessing physiological microvascular adaptation to exercise.

Keywords: OCT-A, retinal ischemia, microvascular pathology, diabetic retinopathy, optic nerve ischemia

1. Introduction

Ischemic disorders of the retina and optic nerve are among the leading causes of irreversible visual impairment worldwide, largely due to microvascular dysfunction, capillary nonperfusion, and progressive tissue hypoxia. These diseases include diabetic retinopathy (DR), diabetic macular ischemia (DMI), retinal vein occlusions (RVO), retinal artery occlusions (RAO), and ischemic optic neuropathies. Early detection of perfusion abnormalities is therefore essential for preventing structural and functional damage. However, traditional imaging modalities such as fluorescein angiography (FA) offer only two-dimensional visualization, require dye injection, and cannot reliably separate the superficial and deep vascular plexuses. This creates a substantial need for non-invasive, high-resolution vascular imaging capable of providing quantitative metrics of retinal and optic nerve perfusion.

Optical coherence tomography angiography (OCT-A) has rapidly emerged as a transformative imaging modality capable of visualizing retinal and peripapillary microvasculature without dye administration. Since its introduction, OCT-A has provided clinicians and researchers with unprecedented detail regarding capillary dropout, vascular remodelling, and the spatial distribution of ischemia across retinal layers. Numerous studies have shown that OCT-A detects early microvascular abnormalities in diabetes even before clinical retinopathy becomes apparent, highlighting its sensitivity in identifying preclinical disease stages (Chua et al., 2020; Boned-Murillo et al., 2022). Deep capillary plexus (DCP) impairment, enlargement and irregularity of the foveal avascular zone (FAZ), and parafoveal nonperfusion have consistently been associated with functional deficits and disease progression (Scarinci et al., 2019; Tsai et al., 2022; Bradley et al., 2016).

In retinal vein occlusions, OCT-A permits detailed assessment of macular and perifoveal perfusion deficits, allowing differentiation between ischemic and non-ischemic forms and prediction of clinical outcomes (Mastropasqua et al., 2017; Chen et al., 2020; Crincoli et al., 2024). OCT-A further enables precise visualization of central retinal non-perfusion and deep vascular abnormalities that are not always well captured by traditional angiography (Hajdu et al., 2020). Likewise, in BRVO, OCT-A has been shown to correlate the extent of macular nonperfusion with localized visual field loss and functional impairment, emphasizing its role in clinical monitoring (Terashima et al., 2021).

In arterial occlusions, OCT-A facilitates layer-specific characterization of ischemia and its functional consequences. Studies incorporating multifocal electroretinography (mfERG) demonstrated that regional loss of perfusion measured with OCT-A correlates with

electrophysiological deficits, particularly in BRAO (Igawa et al., 2023). These findings underscore the ability of OCT-A to detect subtle, localized microvascular failure in acute ischemic events.

Ischemic optic neuropathies, especially non-arteritic anterior ischemic optic neuropathy (NAION), also demonstrate consistent OCT-A abnormalities. Several studies have shown reduced radial peripapillary capillary (RPC) density and optic disc perfusion in both acute and chronic NAION, correlating strongly with structural thinning and visual field defects (Gaier et al., 2018; Ling et al., 2017; Sönmez et al., 2022). OCT-A can also distinguish ischemic neuropathy from demyelinating optic neuritis, highlighting its diagnostic utility (Xiao et al., 2024). Furthermore, deep learning approaches have demonstrated high accuracy in differentiating glaucoma, AION, and healthy eyes based solely on OCT-A microvascular patterns (Bunod et al., 2023).

Despite its strengths, OCT-A also faces limitations related to artifacts, segmentation errors, and the absence of leakage information. Recent analyses emphasize the importance of standardizing acquisition protocols, quantitative parameters, and reporting methods for reliable cross-study comparison (Sampson et al., 2022; Javed et al., 2023). Studies in systemic diseases, such as acute leukemia without fundoscopic abnormalities, demonstrate that OCT-A can reveal subclinical microcirculatory impairment, suggesting its potential as a biomarker of systemic microangiopathies (Zhou et al., 2024).

In addition to ischemic retinal and optic nerve disorders, recent research has begun to explore how physiological hemodynamic stressors such as acute and chronic physical exercise influence retinal microcirculation. Several studies using OCT-A demonstrated that standardized exercise protocols induce transient decreases in macular and peripapillary vessel density in healthy subjects, reflecting short-term autoregulatory responses of the retinal microvasculature (Alnawaiseh et al., 2017; Vo Kim et al., 2019). Long-term physical activity has also been linked with favorable microvascular characteristics, including smaller FAZ areas in physically trained individuals (Nelis et al., 2019). Moreover, endurance athletes show measurable reductions in retinal vascular plexus density and choroidal thickness after marathon running, interpreted as subclinical ischemic stress (Mauget-Faÿsse et al., 2021). These findings suggest that OCT-A may also offer insight into physiological microvascular adaptation in athletes and physically active populations.

2. Literature Search Strategy

An extensive literature review was performed to determine studies assessing the role of optical coherence tomography angiography (OCT-A) for the diagnosis of ischemia and microvascular pathology in retinal and optic nerve disorders. Four key scientific literature databases including PubMed, PubMed Central, Scopus, and Web of Science were screened from January 2016 to March 2025.

Inclusion criteria consisted of: clinical or qualitative research using OCT-A;

A total of 30 publications met the eligibility criteria and are included in this review. They vary from clinical studies on diabetic retinopathy and diabetic macular ischemia to retinal vein occlusions, retinal artery occlusion, and the optic nerve condition studies. The set also includes systemic microangiopathies like leukemia and technological or methodological studies on quantitative and deep learning approaches. The final set also includes studies evaluating OCT-A–based microvascular responses to acute and chronic physical exercise in healthy or athletic cohorts, which provide the basis for the sports-related considerations discussed in this review (Alnawaiseh et al., 2017; Vo Kim et al., 2019; Nelis et al., 2019; Mauget-Faÿsse et al., 2021). There were no restrictions on the study design, except for the OCT-A-based microvacular evaluation. This search strategy ensured that the largest share of previously conducted research with the most significant contribution to understanding the OCT-A application for retinal and optic nerve ischemia detection and description are included in the subsequent synthesis.

3. OCT-Angiography – Technological Foundations

Optical coherence tomography angiography (OCT-A) is a noninvasive imaging modality that relies on the detection of motion contrast due to erythrocytes circulating within retinal and peripapillary capillaries. In contrast to fluorescein angiography, OCT-A is a non-invasive modality that eliminates the need for dye-based injection and allows rapid en face depth-resolved imaging of microvascular network and thus is particularly useful in detection of early ischemia changes in retinal and optic nerve conditions (Chua et al., 2020; Moir et al., 2021). The OCT-A technique is predominantly based on A-line-wise repetitions of B-scans at the same retinal location, and decorrelation or variance signals are used to distinguish static tissue from flowing RBCs (Al-Sheikh et al., 2016).

One of the greatest assets to OCT-A is the capability of visualising separately the SCP, DCP, choriocapillaris as well as RPC network. This limitation has been important to determine whether ischemic patterns are layer specific, for example with preferential DCP involvement in diabetic macular ischemia (Scarinci et al., 2019; Tsai et al., 2022), segmental nonperfusion in retinal vein occlusions (Mastropasqua et al., 2017; Chen et al., 2020) or decreased RPC density in ischemic optic neuropathies (Gaier et al., 2018; Ling et al., 2017). Additional improvements of penetration ability as well as imaging quality regions have been achieved with swept-source OCT-A technology, which bears a longer central wavelength and faster scanning rate (Al-Sheikh et al., 2016; Sampson Louis et al., 2022).

However, despite these drawbacks, OCT-A represents by far one of the most sophisticated techniques for a noncontact assessment of perfusion and capillary vessels' integrity in a variety of ocular pathologies.

4. Pathogenesis of Retinal and Optic Nerve Ischemia

Retinal and optic nerve ischemia If the blood supply of the retinal or optic nerves is reduced by poor perfusion of the microvasculature, oxygenation and metabolic support are impaired. The retina is among the most metabolically active body tissues, and even minor decreases in capillary feeding may cause structural changes and functional decay. Microvascular ischemia often presents as capillary loss, dilatation of non-perfused areas and disruption in the arrangement of superficial and deep vascular plexuses. Such reductions were observed in different ischemic conditions with OCT-A that enables high resolution imaging of blood flow impairment (Chua et al., 2020; Mastropasqua et al., 2017).

Another important parameter to observe for retinal ischemia is the foveal avascular zone (FAZ). Enlargement, irregularity, and disruption of the FAZ margin represent central macular hypoperfusion and are associated with decreased best-corrected visual acuity (BCVA) in DR and RVO (Al-Sheikh et al., 2016; Mastropasqua et al., 2017; Chen et al., 2020). OCT-A driven works have reported FAZ on deep plexus (not superficial!) as the workhorse biomarker of ischemic disease severity and as a prognosticator (Bradley et al., 2016; Garcia et al., 2016).

Ischaemia is also very important in neuro-ophthalmic disease. In NAION, hypoperfusion of the short posterior ciliary arteries causes acute ischemic damage at first before optic nerve head. Significant OCT-A findings includes decrease in RPC density, which correlates

topographically with the VF defects and RNFL thinning (Gaier et al., 2018; Ling et al., 2017; Sönmez et al., 2022). These microvascular dysfunctions are present for prolonged hours or even days after the acute phase and reflect chronic structural injury. Furthermore, OCT-A has shown unique patterns of RPC damage in NAION compared with demyelinating optic neuritis, indicating that ischemia creates a microvascular profile (Xiao et al., 2024).

Together, the pathophysiology of retinal and optic nerve ischaemia reflects a mesh of hypoperfusion, capillary dropout, metabolic demand–supply mismatch and structural degeneration.

Across different diseases, OCT-A studies consistently show that microcirculatory impairment is central to functional visual loss, and particularly in the DCP and peripapillary capillaries. Hence, this imaging modality has become essential for deciphering the pathogenesis of ischemic ocular disease.

5. OCT-A for Diabetic Retinopathy and Diabetic Macular Ischemia

Diabetic retinopathy (DR) is the most common ischemic retinal disease in the world, and microvascular dysfunction exists long before clinical features develop. A multitude of studies featured in this review support that OCT-A detects early vascular changes in the absence of clinically visible retinopathy (Chua et al., 2020; Boned-Murillo et al., 2022). These subclinical findings emphasize the value of OCT-A for screening and risk stratification by showing reduced VD, incipient NPAs, and slight FAZ neovascularization in preclinical diabetes.

These results suggest that OCT-A may be a monitoring tool for patients who are expected to lose function. Furthermore, comparisons of OCT-A and FA indicate excellent correspondance in the delineation of ischemic areas, wereas layer-wise evaluation and superior visualization of the deep capillary plexus (DCP) favor the use of OCTA (Bradley et al., 2016; García et al., 2016).

In conclusion, clinical, functional and methodological data all come together to support a central role of OCT-A as crucial imaging modality in the evaluation of diabetic retinopathy and DMIs. Its role in the recognition of early microvascular changes, quantification of perfusion deficits, and ability to make predictions for visual outcomes makes it an invaluable tool for clinicians who require a non-invasive method to assist with diagnosis, prognosis and management. Biomarkers OCT-A–derived biomarkers including DCP dropout, FAZ

enlargement, and parafoveal nonperfusion have become critical markers of disease severity and progression, making OCT-A an integral part of modern caring for diabetic patients.

6. OCT-A in RVO (CRVO/BRVO)

Retinal vein occlusion (RVO) comprises approximately 10% of all retinal vascular diseases and is second only to diabetic retinopathy in frequency as a cause of blindness worldwide. Venous occlusion with secondary raised intraluminal pressure, capillary stasis and downstream nonperfusion form the basis of the pathophysiology. OCT-A has emerged as an important imaging tool in evaluating the range and repercussions of ischaemia in RVO by enabling high-quality visualisation of SCP and DCP perfusion at superior resolution without dye injection. Some studies of this review show and highlight that OCT-A consistently detects macular perfusions defects in RVO, associated with functional and anatomical outcomes (Mastropasqua et al., 2017; Chen et al., 2020; Crincoli et al., 2024).

In CRVO, OCT-A demonstrates extensive capillary drop-out and neovascularization, frequently more prominent in the DCP than in the SCP. This phenomenon is a manifestation of theismic metabolic requirement and anatomical sensitivity of deep capillaries. Reduced DCP perfusion had a strong association with poor visual acuity and ischemic complications which underlines its significance as a prognostic indicator (Mastropasqua et al., 2017). In the presence of central retinal non-perfusion, OCT-A provides accurate delineation of ischemia surrounding the macula and optic nerve which show vascular insufficiency that is not always evident on standard FA (Hajdu et al., 2020). Layer level images further improve the ability to differentiate partial from complete nonperfusion, and augment diagnostic sensitivity in early or atypical cases.

In BRVO, OCT-A typically shows section patterns of capillary drop-out localised to the vascular territory of occluded branch vein. Macular nonperfusion area (m-NPA), especially at the DCP level, has been reported as a robust predictor of localized sensitivity loss in BRVO (Terashima et al., 2021). OCT-A further demonstrates that the microvascular insufficiency involves even more than the clinically observable affected quadrant, as it is proved by changes in peripapillary blood flow and microcirculation of the fellow eye, indirectly illustrating wider alterations in hemodynamics (Chen et al., 2020).

OCT-A is essential in the determination for ischemic vs non-ischemic RVO. Dilated FAZ, widespread dropout of the DCP and a large confluent nonperfused area are the features present in ischemic cases, and here seem to be associated with worse visual function or increasing risk of complications (e.g. neovascularization). The OCT-A can also be used to follow treatment responses (25). Even, through anti-VEGF treatment macular edema reduces and visual acuity is being increased, these perfusion deficits in OCT-A may be remained by representing chronicity and non-reversibility of microvascular ischemic damage (Mastropasqua et al., 2017). OCT-A is therefore useful in differentiating edema-related visual loss from ischemic injury.

In summary, OCT-A exhibits a detailed, layer-specific and clinically relevant imaging of the capillary nonperfusion areas in either CRVO or BRVO. The approach is suitable for quantitative evaluation of ischemic burden, prediction of functional recovery, differentiation between subtypes of ischemia and follow-up post-intervention responses. Use of OCT-A in the routine assessment of RVO increases the diagnostic accuracy and may guide clinical management more effectively.

7. OCT-A in Optic Nerve Ischaemic Term (NAION/AION)

Non-arteritic anterior ischemic optic neuropathy is the most common acute optic neuropathy in adults and occurs following hypoperfusion of the optic nerve head owing to impaired circulation of the short posterior ciliary arteries. OCT-A has revolutionized the assessment of NAION, as it allows for non-invasive visualization of the radial peripapillary capillary (RPC) network that is essential to axonal perfusion. Several investigators have shown that NAION is associated with marked reduction in RPC vessel density, highly correlated with structural and functional indices of damage to the optic nerve (Gaier et al., 2018; Ling et al., 2017; Sönmez et al., 2022).

With disease evolution into the chronic stage, RPC dropout becomes more marked and chronic, likely reflecting irreversible axonal loss and lasting RNFL thinning. These findings suggest that OCT-A can record both the acute ischemic insult and its chronic outcome, providing a dynamic view of disease progression.

One of the most clinically relevant diagnostic uses of OCT-A is discrimi-nating ischemic from non-ischemic causes of optic nerve dysfunction, in particular ON secondary to inflammatory demyelination. Comparative studies of NAION vs ON demonstrate different microvascular

signatures: while NAION exhibits significant RPC nonperfusion, this is usually maintained in ON even with an inflamed optic nerve (Xiao et al., 2024). This differentiation is crucial in the clinical setting, because both entities can share similar acute visual symptoms but require distinctly different therapeutic approaches.

In addition to the non-invasive diagnosis and management of disease, OCT-A is becoming integrated with modern computing technologies. OCT-A microvascular patterns based on deep learning techniques have shown excellent diagnostic performance to discriminate between NAION, AION, glaucoma and healthy eyes (Bunod et al., 2023). These algorithms make use of microvascular signs such as RPC dropout and ONH perfusion abnormality, highlighting the diagnostic potential of OCT-A data. These approaches illustrate how automated OCT-A interpretation may the future of neuro-ophthalmology.

In conclusion, OCT-A is of paramount importance in the study of the microvascular pathophysiology of ischemic optic neuropathies. It allows for the early identification of perfusion impairments, provides quantitative biomarkers strongly correlated with visual outcomes, discriminates between ischemic and inflammatory optic neuropathies, and could serve as a foundation for emerging AI-based diagnostic approaches. The objective evidence from studies included here unequivocally identifies OCT-A as a central imaging technology in contemporary assessment of NAION and ischemic optic neuropathies.

8. OCT-A in Exercise and Sports-Related Microvascular Adaptation

Physical exercise produces significant systemic hemodynamic changes that can transiently alter perfusion within the retinal and optic nerve microvasculature. OCT-A has recently been used to investigate whether such physiological stress can be captured in vivo. In a study of healthy young adults, acute exercise induced a significant reduction in parafoveal and peripapillary flow density, while FAZ size remained stable, suggesting a transient autoregulatory hypoperfusion response (Alnawaiseh et al., 2017). Similar results were observed by Vo Kim et al., who reported decreased superficial capillary plexus vessel density following a 20-minute cycling protocol, in correlation with exercise-induced changes in systolic blood pressure (Vo Kim et al., 2019).

In addition to acute responses, OCT-A findings indicate that chronic physical activity may influence retinal microvascular architecture. In a cohort of moderately trained university sports

students, higher aerobic capacity was associated with smaller FAZ areas, suggesting beneficial adaptations of macular perfusion with regular physical training (Nelis et al., 2019).

Endurance athletes represent a unique model of prolonged physiological stress. Marathon runners examined before and shortly after competition demonstrated reduced retinal vascular density and decreased choroidal thickness, combined with transient thickening of the macula and RNFL, interpreted as subclinical ischemic edema due to dehydration, hypoxia, and sustained hemodynamic demand (Mauget-Faÿsse et al., 2021).

Exercise-related findings align with mechanisms observed in ischemic retinal diseases, such as perfusion–metabolism mismatch and endothelial stress. OCT-A may therefore contribute to understanding microvascular resilience and susceptibility by providing a physiological model of repeated hemodynamic challenge. Evidence from both acute and chronic exercise studies supports the value of OCT-A as a non-invasive modality for characterizing microvascular adaptation in athletes and active individuals.

9. Quantitative OCT-A Biomarkers

The major advantage of OCT-A lies in the quantitative analysis, which facilitates an objective evaluation of retinal and optic nerve microvasculature. Among the studies analyzed, several biomarkers reappear repeatedly due to their pivotal role as markers of ischemia, disease severity and functional limitation. Of these parameters, vessel and perfusion density (VD, PD), foveal avascular zone (FAZ) metrics to nonperfusion area (NPA) constitute the most extensively validated quantitative parameters. They have been shown to be highly correlated with structural and functional outcomes in diabetic retinopathy (DR), DMI, RVOs, arterial occlusions and ischemic optic neuropathies.

Vessel density is the most common AOI used in OCT-A by researchers. There is strong support for VD to decrease with severity of DR, and its high sensitivity to early microvascular injury at the deep capillary plexus level (Kaizu et al., 2019; Scarinci et al., 2019; Tsai et al., 2022). Reductions in the VD within the DCP have been linked to meaningfully lower best-corrected visual acuity (BCVA), microperimetric sensitivity and contrast sensitively, therefore indicating clinical relevance (Tsai et al., 2022, Scarinci et al., 2019). Similar quantitative OCT-A metrics, particularly vessel density, FAZ parameters, and perfusion-based indices, have also been applied in cohorts of healthy, physically active individuals and endurance athletes to

characterize exercise-related changes in retinal and peripapillary microcirculation (Alnawaiseh et al., 2017; Vo Kim et al., 2019; Nelis et al., 2019; Mauget-Faÿsse et al., 2021). VD is also central to neuro-ophthalmic conditions, wherein RPC density loss is a feature of the acute and chronic NAION course (Gaier et al., 2018; Ling et al., 2017; Sönmez et al., 2022).

PD, as a concept similar to CVI, assesses the density of perfused vasculature within the scanned area and is less prone to segmentation artefact influence. In DR and RVO, various studies have applied PD to describe ischemic loss, where low PD values are associated with increased areas of capillary drop out and poorer visual prognosis (Hwang et al., 2016; Mastropasqua et al., 2017). PD in BRVO is also associated with macular nonperfusion severity and functional field loss (Terashima et al., 2021).

The FAZ is one of the most studied OCT-A metrics. FAZ enlargement and irregularity are a manifestation of central macular hypoperfusion,22 and have been consistently correlated with the severity of diabetic macular ischemia23–25 as well as of RVO-related macular ischemia.26–28 Parameters of the FAZ in the DCP, specifically, strongly correlate with functional deficits based on the metabolic sensitivity of this plexus (Al-Sheikh et al., 2016). FAZ roundness and border irregularity have been identified as highly sensitive signs of early ischemic remodeling and predictors for visual outcomes.

Non-perfusion area (NPA) is another important measure, especially in disease with segmented or diffuse ischemia. Automated quantification algorithms of NPA, including those we developed for diabetic retinopathy, correlate well with fluorescein angiography but provide better layer-specific reconciliation (Hwang et al., 2016). Even more detailed information about the immediate region of capillary loss comes from studies that look at parafoveal intercapillary area (PICA) metrics. The presence of dilated PICAs is associated with DR severity and thus constitute an advanced microvascular rarefaction biomarker (Krawitz et al., 2018).

Recent developments in artificial intelligence and automation analysis of OCT-A biomarkers add another layer to the power of these markers. OCT-A data have a diagnostic richness that can be seen in how deep learning systems could classify ischemic optic neuropathies and glaucomatous eyes from vascular patterns alone (Bunod et al., 2023). These computerized methods demonstrate the possibility of automated, highly reproducible quantification in the future.

In summary, quantitative OCT-A biomarkers—VD, PD, FAZ metrics, NPA and PICA—serve as important indicators of retinal and optic nerve ischemia. Their close association with functional indices and disease progression demonstrates their clinical and research relevance. The development and establishment of these measurements will continue to provide well grounded parameters for evaluation and monitoring of ischemic ocular diseases.

10. Limitations of OCT-A

While there are many advantages to OCT-A for imaging the microvasculature of retina and optic nerve, several limitations constrain its use in both clinical and research settings. Following this brief section of text, analysis of imaging data beyond qualitative observations is difficult because the problems common to OCT are reported in ICGA as well: motion artifacts, segmentation errors, poor penetration depths and failure to detect vascular leakage (a key difference from fluorescein angiography). These have been identified by various methodological reviews and clinical trials in this review (Sampson et al., 2022; Javed et al., 2023).

Motion artifacts are the most frequent cause of degradation of the OCT-A image. Also, small non-volitional movements of the eye may cause discontinuities, duplication or distortion in the microvascular pattern that is not easy to interpret. Even though tracking algorithms in current systems aim to minimize movement noise, residual artifacts frequently persist, especially among patients who present with unstable fixation, more advanced disease or systemic conditions that influence cooperation. Numerous work has focused on the standard of acquisition and better correction of motion to allow for reliable interpretation of quantitative biomarkers like vessel density and perfusion density (Sampson et at., 2022; Javed et al., 2023).

Visualization of deeper vascular plexus is still limited, especially with the spectral-domain OCTA since its penetration is reduced in the presence of media opacities or highly reflective superficial layers. Artifacts of projection, which pretend or disguise actual pathological changes in the deep capillary plexus because superficial vessels project their signal pattern to deeper layers. While several reports describe the improvements in projection-resolved processing, this is a major restriction for the precise interpretation of deep retinal vascular ischemia, particularly in diseases where DCP involvement is crucial (Bradley et al., 2016; Chen et al., 2020; Scarinci et al., 2019).

Lastly, a significant challenge is posed by technical variance between devices for standardization. Due to the use of diverse algorithms, acquisition speeds and mutually segmentation contours of various systems, quantitative values vary between platforms. Several studies advocate for the creation of cross-device calibration standards, standardized quantitative definitions and shared datasets to enhance reproducibility and comparability of OCT-A metrics (Sampson et al., 2022; Javed et al., 2023; Moir et al., 2021).

In conclusion, despite the great potential of OCT-A for non-invasive microvascular imaging,\ limitations such as motion artifacts, segmentation errors, projection artifacts,\ shallow penetration depth and\ lack of information about\ leakage should be taken into account. Overcoming these trade-offs using technological optimization, standardizing protocols and advancing computational techniques will be crucial in order to maximize the clinical and research potential of OCT-A.

11. Future Directions

Rapid progress in OCT-A technology and quantitative software has contributed the improving of its use in retinal and optic nerve ischemic diseases. Some of the studies included in this review demonstrate that standardized procedures for OCT-A acquisition, segmentation and quantitative analysis are still required. Such endeavors for the harmonization of devices algorithms, imaging protocols and perfusion measures are key to facilitate cross-study comparison, and integration of OCT-A into clinical trials and disease staging systems (Sampson et al., 2022; Javed et al., 2023). Similar to FA, future consensus criteria will probably involve standardized definitions of vessel density, perfusion density, the FAZ measurements, and nonperfusion area as well as rigorous protocols for artifact correction and quality control.

AI is one potential future growth areas. Deep learning models trained on OCT-A images have demonstrated excellent performance in discriminating glaucomatous from ANION and healthy eyes by analyzing microvasculature alone (Bunod et al., 2023). These methods can potentially be extended to detect early ischemic changes in diabetic retinopathy, predicting progression in DMI, and for automatic segmentation of ischemic zones in RVO. As increasingly large OCT-A datasets emerge, AI could offer rapid and automated analysis that can assist with standardized interpretations and help teleophthalmology platforms.

Another exciting area includes multimodal functional–structural coupling. Some associations, between microperimetry, visual field test and mfERG with OCT-A have shown good structure–function correlation in ischemic diseases one as diabetic macular ischemia to BRVO (Tsai et al., 2022; Igawa et al., 2023Scarinci et al., 2019). Such automated superimpositions of perfusion maps into functionals might be immersed in upcoming diagnostic systems for better stratification of the patients and treatment planning.

An additional area of emerging relevance is the potential use of OCT-A in sports medicine and exercise physiology. Studies evaluating retinal perfusion before and after physical activity have shown that acute exercise induces transient reductions in vessel density, while long-term training may be associated with more favorable microvascular organization and smaller FAZ dimensions (Alnawaiseh et al., 2017; Vo Kim et al., 2019; Nelis et al., 2019). Endurance sports such as marathon running further demonstrate measurable reductions in vascular density and choroidal thickness after prolonged exertion, suggesting that OCT-A can detect subtle microvascular stress in athletes (Mauget-Faÿsse et al., 2021). These findings highlight future opportunities to apply OCT-A for monitoring exercise-induced microvascular adaptation, evaluating ocular effects of extreme physical effort, and identifying individuals at potential risk of ischemic vulnerability under intensive hemodynamic load.

As OCT-A progresses, it may ultimately play a role even outside of ophthalmology. The detection of subclinical microvasculopathy with the OCT-A in AL anyway highlights the general interest for using this tool as a biomarker of systemic microangiopathy (Zhou et al., 2024). Its role in cardiovascular disease, renal microangiopathy, and autoimmune vasculopathies remains to be elucidated.

In conclusion, the future of OCT-A involves further technological improvement, methodological standardization, AI integration (27-30), widefield imaging enlargement and wider application in multimodal diagnostic settings. These are the developments that will make OCT-A a key tool for diagnosing, monitoring and predicting ischemic retinal and optic nerve disorders.

12. Conclusions

In a wide range of retinal and optic nerve ischemic diseases, OCT-A has already proven its utility as an efficient, non-invasive imaging approach that enables detailed and resolution-

specific assessment of microvascular health. Studies of OCT-A described in this chapter consistently report that they: 1) detect early capillary dropout (Chua et al., 2020; Scarinci et al., 2019; Tsai et al., 2022), which is predictive of the development of DR and DMI, retinal vein occlusions (Mastropasqua et al., 2017; Chen et al., 2020; Crincoli et al., 2024), retinal artery occlusions (Igawa et al., 2023), and IONs, while also enable Retinal Imaging in Neuro-Ophthalmology identifying characteristic patterns of ischemic disease evident as areas with non-perfusion throughout layers of the retina, DRDMI-areas will have D.C [Fig. Metrics extracted from OCT-A including vessel density, perfusion density, FAZ metrics, and nonperfusion area provide clinically relevant biomarkers of the severity of disease, its progression and functional impairment.

Not only does OCT-A have a crucial diagnostic role, but it can provide prognostic information by linking structural microvascular damage with functional readouts—such as visual acuity, visual field sensitivity and electrophysiological measurements. The loss of perfusion, especially in the deep capillary plexus and radial peripapillary capillary network signal attenuation as measured by OCTA is consistent across disease from a wide range of studies to be a robust predictor of long-term visual dysfunction (Bradley et al., 2016; Gaier et al., 2018; Tsai et al., 2022). OCT-A also improves ischemic and non-ischemic differentiation, especially in diseases of the ON where vascular abnormalities help differentiate NAION from demyelinating ON (Xiao et al., 2024).

OCT-A does have weaknesses, for example artifacts and segmentation errors, and its inability to detect leaks as well as a variety of other factors that may influence acquisition across devices (Sampson et al., 2022; Javed et al., 2023). These limitations are important to consider for interpreting AR usage and clinical utilization. Continued progress in the direction of standardization, which is being realized with advances in acquisition protocols, artifact rejection and quantitative metrics is key to OCC-A's transition as a robust clinical tool and research platform.

Newer advancements such as SS wide-field imaging, automated quantitative analyses and AI-driven diagnostic models are likely to broaden the horizon of OCT-A in coming times ((Bunod et al. (2023), Crincoli et al. (2024)). Furthermore, the detection of occult microvascular abnormality in systemic disorder, for example in leukaemia, suggests that this OCTA might eventually serve as a more comprehensive biomarker of systemic microangiopathy (Zhou et al., 2024).

Beyond its established role in ischemic pathology, OCT-A has increasingly been used to study physiological microvascular responses to physical exercise. Evidence from healthy subjects, trained students, and endurance athletes indicates that both acute and chronic physical activity can modulate retinal vessel density, FAZ morphology, and peripapillary perfusion, reflecting mechanisms of autoregulation and adaptive remodeling (Alnawaiseh et al., 2017; Vo Kim et al., 2019; Nelis et al., 2019; Mauget-Faÿsse et al., 2021). These insights provide an important physiological framework that parallels ischemic microvascular dysfunction and may improve understanding of individual susceptibility to retinal and optic nerve ischemia under systemic stress conditions.

In summary, OCT-A has quickly established itself as a quintessential tool in contemporary ophthalmology. It offers in-depth, clinically useful microvascular information to aid the understanding, diagnosis and treatment of ischemia-related conditions of the retina and optic nerve. Ongoing technological improvement, standardization of protocols and processing algorithms, as well as combination with advanced computational analysis will further expand the role of OCT-A as a key feature of future diagnostic and monitoring approaches in vascular diseases affecting both ocular and systemic soft tissues.

Disclosure:

Author's contributions

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