Review

Journal of INTERNATIONAL MEDICAL RESEARCH

Journal of International Medical Research
2023, Vol. 51(7) 1–16

DOI: 10.1177/03000605231187933
journals.sagepub.com/home/imr
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Optical coherence tomography angiography: a review of the current literature

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Abstract

This narrative review presents a comprehensive examination of optical coherence tomography angiography (OCTA), a non-invasive retinal vascular imaging technology, as reported in the existing literature. Building on the coherence tomography principles of standard OCT, OCTA further delineates the retinal vascular system, thus offering an advanced alternative to conventional dye-based imaging. OCTA provides high-resolution visualisation of both the superficial and deep capillary networks, an achievement previously unattainable. However, image quality may be compromised by factors such as motion artefacts or media opacities, potentially limiting the utility of OCTA in certain patient cohorts. Despite these limitations, OCTA has various potential clinical applications in managing retinal and choroidal vascular diseases. Still, given its considerable cost implications relative to current modalities, further research is warranted to justify its broader application in clinical practice.

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Keywords
Ophthalmic imaging, optical coherence tomography, age-related macular degeneration, glaucoma, retinal conditions, optical coherence tomography angiography, diabetic retinopathy, retinal vein occlusion

Date received: 3 March 2023; accepted: 9 June 2023

Introduction

Optical coherence tomography angiography (OCTA) is a non-invasive, rapid imaging modality that creates a cross-sectional in vivo image of the dynamic microvasculature of the choroid and retina.[1] More than two decades ago, the first phase-resolved OCT–optical Doppler tomography image of blood flow in blood vessels of human skin was produced with high velocity and sensitivity.[2] This progressed to development of a phase signal-based OCTA technique in 2006, which included methods to minimise sample movement in the axial direction and thus improve image quality.[3] Experimentation in ophthalmic OCTA began in 2006, and ophthalmic OCTA then took wider commercial effect in 2014. The software and scanning strategies used for OCTA are rapidly improving, and research is continuing to progress.[4] Several OCTA devices are available internationally, widely in the context of clinical research. The emerging use of OCTA as a tool in the diagnosis of ocular pathology is of growing importance, and potential clinical applications continue to be investigated through ongoing research.[5] The technological advances in OCTA imaging since its inception have allowed more detailed imaging of vascular structures and may herald an increase in its clinical utility in years to come.[6] In this narrative review, we present the detailed principles, limitations, and advantages of OCTA while also exploring its prospective future clinical applications.

Methods

We conducted a comprehensive search across multiple databases, including PubMed, EMBASE, and the Cochrane Library, to gather relevant studies for our narrative review on OCTA. Our search strategy combined terms such as 'optical coherence tomography angiography', 'OCTA', 'retinal imaging', 'retinal vasculature', and 'choroidal vasculature' along with conditions in which OCTA is used, including age-related macular degeneration (AMD), diabetic retinopathy (DR), and retinal vein occlusion (RVO). We limited the search to English publications only. To ensure all applicable articles were included in this study, we manually searched the reference lists of the selected articles. By employing this search strategy, we achieved an extensive overview of the available literature related to the benefits, limitations, and potential future clinical applications of OCTA.

Ethics approval was not required because of the nature of this study (review article).

Principles of coherence tomography

OCT utilises the optical principles of coherence and interferometry to produce a high-resolution cross-sectional image of anatomical structures. It is based on the application of 'wave-theory', in which light energy behaves as a wave (as opposed to a particle). Coherence refers to the physical property of light waves travelling exactly in

'phase', causing wave cycles to run in parallel.[1] The ability to measure the interference produced by superimposed waves produces images that are then captured.

In OCT, wave interference from the infrared (non-visible) wavelength (780–10,000 nm) of the electromagnetic spectrum is split and directed to an internal mirror and the object of interest; the phase difference is then collected and produces an image. Experiments have demonstrated that coherent infrared light targeted at different anatomical tissues can be utilised to produce high-quality in vivo images from the tissues of interest.[9] For ophthalmic purposes, the primary tissue of interest is the retina. The OCT device has a low-coherence infrared source that produces a beam of light, a beam splitter, a reference mirror, and a receiving source that can detect reflected light waves. First, an infrared beam generated by the light source travels towards the beam splitter, which produces two beams; one travels to a reference mirror, and the other travels toward the eye. Light passes through the eye tissues at varying speeds and is reflected by the retina toward the detector. Light waves are also returned from the reference mirror, and the differences between the combination of returning waves can be converted into computerised images to form a two-dimensional tomographic map based on the reflective properties of each individual tissue layer.

As for standard OCT images, the reflection of emitted infrared coherent (in-phase) light wave energy from eye tissues returning at varying speeds is what enables the computerised generation of OCTA images. Imaging of the retinal vasculature using OCTA facilitates identification of the movement pattern of erythrocytes within the retinal blood vessels, thus enabling real-time depiction of blood flow analogous to B-scan ultrasonography. Indeed, Doppler ultrasound scanning provided the initial foundation from which OCTA was developed to quantify the volume of blood flow within vessels.

Successive retinal images are taken in close sequence, depicting the movement of erythrocytes from one point to another within blood vessels. This series of images is compared with images of the static, non-moving retina for characterisation of areas of blood flow in different retinal layers, including the superficial, intermediate, and deep plexus; the inner retinal plexus; the outer retina; the choriocapillaris; and the choroid.[7]

OCTA further allows generation of en-face OCTA and cross-sectional B-scan images containing flow signals, facilitating a comprehensive view of the retinal and choroidal vasculature. En-face OCTA provides a top-down view of vascular layers, whereas a cross-sectional B-scan contains both structural and flow information, serving to localise the exact depth of vascular abnormalities.[8]

It is essential to assess images using multiple modalities because this brings together different pieces of the diagnostic puzzle to form a complete picture of the retinal and choroidal vasculature. Each imaging modality has its strengths and limitations and can result in incomplete diagnostic information when used in isolation. Combined assessment using en-face OCTA, cross-sectional B-scan, and other multimodal imaging techniques enhances the identification and interpretation of vascular abnormalities, thereby improving the diagnostic accuracy.[9] This integrated approach not only offers a more detailed understanding of the disease process but also facilitates tracking of disease progression and the response to therapy, thus playing a pivotal role in patient management.

The ability of OCTA to produce high-resolution images is dependent on the

short interval between successive B-scan images. Shorter inter-scan times will lead to higher sensitivity thresholds and minimise the fastest distinguishable flow rate.[10] Advances in OCT technology have allowed the use of several different techniques that may be utilised to image the retinal vasculature, such as swept-source OCT (SS-OCT) and spectral domain OCT (SD-OCT). These techniques have been developed to capture images at faster speeds and with larger fields of view. SS-OCT is of particular use in the setting of choroidal vascular anomalies because it enables visualisation of choroidal blood flow by emitting light of a longer wavelength for enhanced tissue penetration. Furthermore, SS-OCT generates images at a faster rate to improve image resolution. SD-OCT operates at increased image speed, allowing direct comparison of the phase of A-scans. Both the Carl Zeiss and Optovue modalities use SD-OCT technology. Zeiss also has an SS-OCTA device that can be purchased in Europe and the United States, and Topcon Medical Systems has an SS-OCTA device that is available in England, Brazil, and Japan. It is expected that most manufacturers will develop OCTA platforms.[6]

Clinical uses of OCTA in current ophthalmic practice

Prior to the development of OCTA, imaging of the chorioretinal vasculature was predominately accomplished using fundus fluorescein angiography (FA) and indocyanine green angiography (ICGA). These modalities are essential tools for investigation of disorders of the fundus vasculature and remain the gold standard in current clinical practice. However, because FA is a moderately invasive procedure involving intravenous injection of sodium fluorescein dye, which has several important contraindications (e.g., dye allergy and pregnancy), the need for a less invasive imaging tool was a key impetus for the development of OCTA as an alternative imaging option.

OCTA has a few key advantages over FA. FA relies on the fluorescent properties of sodium fluorescein dye, which is injected intravascularly to observe blood flow within the retinal microvasculature. Because of the blocking effect of the retinal pigment epithelium (RPE), FA can only depict the more superficial layers of the retinal vasculature. This limits its potential diagnostic yield and necessitates the use of further invasive testing such as ICG dye studies to observe pathologies within deeper structures. OCTA is favourable because it is more time-efficient, taking approximately 6 s per image, and is technically easier to perform; there is no need for a skilled photographer, and the patient does not require a dye injection.[11]

The retina receives more blood flow per gram of tissue than any other structure within the body.[1] Thus, the health of the retinal tissue, a highly metabolically active structure, is inextricably linked to the viability of the retinal blood supply for the provision of nutrients and oxygen and the removal of metabolic waste products. Several retinal pathologies are characterised by an imbalance between the blood supply and nutrient demand. This may lead to growth of new vessels in response to tissue hypoxia, which is commonly mediated by upregulation of vascular endothelial growth factor (VEGF). This disease process may be seen in commonly encountered pathologies such as proliferative DR and neovascular AMD, which are primarily associated with choroidal neovascularisation (CNV). Relative tissue hypoxia may also be seen in association with retinal vascular occlusions, which require prompt identification to prevent irreversible vision loss. OCTA provides a rapid, non-invasive tool in the diagnosis of retinal vascular pathologies as well as subsequent long-term monitoring of chronic disease.

Wide-angle OCTA, which is an advanced form of OCTA imaging that enables the capture of a larger field of view of the retinal and choroidal vasculature, offers an unparalleled advantage in retinal imaging because it enables clinicians to capture a broader field of view than with conventional OCTA systems. This is immensely helpful for the diagnosis and monitoring of various retinal diseases such as DR and RVO, providing practitioners with insights into peripheral vascular abnormalities that would otherwise be inaccessible.[12] In fact, the integration of wide-angle imaging with OCTA has been shown to significantly improve our understanding of disease progression, leading to earlier detection rates as well more effective treatment planning.[13] This is also important because asymptomatic retinal pathology tends to be more peripheral and outside a patient's apparent visual field. Therefore, wide-angle OCTA may facilitate detection and monitoring of vascular abnormalities if they are picked up as incidental findings.

DR

Retinopathy secondary to diabetes mellitus is a well-characterised disease process that adversely affects the retinal vascular integrity through early loss of endothelial pericytes, microaneurysms, and ultimately growth of abnormal 'leaky' vessels. This process leads to haemorrhage with severe implications for visual function. Diabetic macular oedema is a complication of DR caused by the collection of tissue fluid that has leaked from abnormal vessels, and it may result in profound visual impairment. OCTA can quantify characteristic features such as microaneurysms, intraretinal microvascular abnormalities, and neovascularisation and may even detect the extent of the microvascular damage prior to any clinical signs.[14] The use of OCTA to monitor the progression of DR may guide clinical management in terms of offering therapeutics based on the disease severity as well as assessing treatment efficacy using anti-VEGF therapy.[4,15] Recent studies have shown that OCTA plays a significant role in identifying regression, reactivation, and resistance to treatment in patients with DR.[16]

In the RENOCTA study, OCTA was used as a prognostic tool in patients with proliferative DR who were treated with laser therapy.[17] The results showed that OCTA allowed for accurate prediction of the outcome of laser treatment in patients with proliferative DR, making it a reliable tool for the management of this condition.

In another study, Athwal et al.[18] evaluated the use of OCTA in imaging of the retinal vasculature in patients with DR. The use of registration and averaging techniques in OCTA improved the accuracy and detail of the retinal vasculature imaging in these patients. Thus, OCTA can provide valuable information for the diagnosis and management of DR.

Oliverio et al.[19] compared the retinal vasculature features of patients with type 1 and type 2 diabetes using OCTA. The authors found that patients with type 1 diabetes had a higher frequency of capillary dropout and a more irregular vasculature than patients with type 2 diabetes. This highlights the potential use of OCTA in distinguishing between different types of DR.

In conclusion, the non-invasive nature of OCTA and its ability to provide detailed information about the retinal vasculature makes it a valuable tool in the diagnosis and monitoring of DR.

AMD

Aggregation of lipofuscin between Bruch's membrane and the RPE with advancing age is the primary mechanism thought to be responsible for AMD, which leads to subsequent macular photoreceptor degeneration due to loss of perfusion. AMD is the

leading cause of irreversible vision loss in older adults and represents a varied spectrum of retinal diseases. Its pathogenesis remains unclear but is believed to involve abnormal regulation of complement factors and the effects of environmental factors such as cigarette smoking. The retinal vasculature becomes compromised particularly in the late stages of the disease, during which new vessel proliferate; thus, OCTA may be key in the identification of potentially sight-threatening neovascularisation. CNV is a hypoxic tissue response in which new abnormal vessels infiltrate the retina. New vessels arise most commonly from two distinct sites: the sub-RPE (type 1 CNV) or the subretinal space (type 2 CNV). OCTA can detect CNV without the use of dye and, in some cases, shows superiority over FA and ICGA in terms of the detection of type 1 CNV.[7] Notably, OCTA can detect CNV flow prior to leakage of fluid from vessels, making it non-reliant on dye leakage patterns. No other imaging modalities (FA, ICGA) have been able to detect the direction and rate of flow before re-accumulation of fluid. OCTA can also be used to assess the effects of intravitreal therapy, which aims to reduce the CNV flow.[20] This can facilitate prediction of treatment patterns in high-risk patients.[21] Furthermore, OCTA facilitates precise delineation of the intraretinal neovascular complexes characteristic of retinal angiomatous proliferation (RAP) by enabling non-invasive visualisation of the retinal and choroidal vasculature.[22] OCTA assists in distinguishing RAP from other subtypes of neovascular AMD by displaying a distinctive tangled network of vessels within the neurosensory retina, which is often associated with retinal–choroidal anastomosis.[22] Moreover, OCTA can be used to monitor disease progression and the response to treatment by evaluating alterations in the size and flow signal within these neovascular complexes. As a non-invasive, repeatable imaging modality, OCTA significantly improves the clinical management of RAP by enabling early detection, accurate diagnosis, and effective monitoring of the treatment response.

For both neovascular (wet) and non-neovascular (dry) AMD, research has focused on investigating changes in choroidal blood flow to predict future disease progression. In patients with neovascular AMD, OCTA can be implemented before and after anti-VEGF therapy.[7] The early stages of dry AMD are characterised by patchy thinning and reduced density of the choriocapillaris, later progressing to geographic atrophy and flow impairment. These changes in the choriocapillaris may also be associated with displacement of the choroidal vessels into the choriocapillaris. Because of its deeper penetration, OCTA can detect loss or asymmetric alterations of the choriocapillaris layer in patients with dry AMD, which may lead to further research advances in disease monitoring and targeted therapy.[10]

Lauermann et al.[23] evaluated the impact of eye-tracking technology on the imaging quality of OCTA. They found that the use of eye-tracking technology improved the image quality and reduced image artefacts, resulting in more accurate and reliable images.

Lindner et al.[24] used OCTA to detect and quantify the neovascular network in patients with exudative AMD. The results showed that OCTA was effective in detecting and quantifying the neovascular network, providing valuable information for the diagnosis and monitoring of this disease.

Solecki et al.[25] investigated the predictive factors of exudation of quiescent CNV in the fellow eyes of patients treated for neovascular AMD. The study showed that the presence of certain risk factors, such as the size of the lesion and the presence of RPE

detachment, was associated with an increased risk of exudation.

Faatz et al.[26] examined the OCTA changes in patients with neovascular AMD who developed type 2 CNV during anti-VEGF treatment. The results showed that anti-VEGF treatment led to significant changes in the OCTA findings of type 2 CNV, including a reduction in the size of the neovascular network and improved perfusion.

Malamos et al.[27] evaluated the use of OCTA for monitoring and managing neovascular AMD. They found that OCTA was an effective tool for monitoring the progression of the disease and for guiding treatment decisions.

OCTA can also provide detailed, non-invasive imaging of CNV complexes, unveiling key features that can aid in determining the activity of CNV.[28] Active CNV is characterised by features such as dense vascular loops, anastomoses, tiny branching vessels, and glomeruli or medusa-like formations, all of which are indicative of ongoing vascular proliferation. Conversely, inactive CNV often presents a 'dead tree' sign characterised by attenuated, scarce vasculature.[29] Importantly, active CNV typically demonstrates a high flow signal in OCTA, whereas inactive CNV is characterised by a low or absent flow signal. Therefore, OCTA facilitates non-invasive, reliable determination of CNV activity, guiding clinicians in optimising treatment strategies and monitoring disease progression.

Furthermore, advancements in computerised analysis of CNV have been shown to enhance the precision of retinal imaging interpretations. An example of image optimisation is the use of 'image binarisation', which transforms grey-scale OCTA images into binary ones. The intent of this conversion is to distinctly segregate CNV lesions from the background, reducing noise and thereby increasing the accuracy of quantifying the area and vessel density of CNV.[30] This objective assessment is critical in determining CNV activity.

Another noteworthy computational approach is derivation of the choroidal vascularity index (CVI) from binarised OCT images. The CVI is a quantitative metric indicating the proportion of the choroidal region occupied by blood vessels. Variations in the CVI can shed light on choroidal alterations in conditions in which CNV is a hallmark feature, such as AMD.[31] Collectively, these computational methodologies provide standardised, reliable tools for investigating CNV and associated choroidal modifications, thereby enhancing ophthalmic patient care.

In summary, OCTA is a valuable tool for the diagnosis and monitoring of neovascular AMD. With its ability to detect and quantify the neovascular network, evaluate changes in the neovascular network during treatment, and monitor disease progression, OCTA has become an essential tool for the management of neovascular AMD. The predictive factors identified in the study by Solecki et al.[25] can provide valuable information for the management and treatment of the disease.

Representative cases of OCTA in patients with wet AMD are depicted in Figures 1, 2, and 3.

Retinal vascular occlusion

Retinal artery occlusion (RAO) or RVO typically involves obstruction of either the central retinal vessels or subsequent larger branches. Atheroembolic disease is by far the most common cause of both pathologies, with RAO commonly leading to secondary RVO by compression at points of arteriovenous crossing.[32] Relative retinal ischaemia following vessel obstruction leads to photoreceptor death and upregulation of VEGF. OCTA can be utilised in this setting to detect non-perfusion within the superficial and deep choroidal plexuses caused by vascular occlusion.

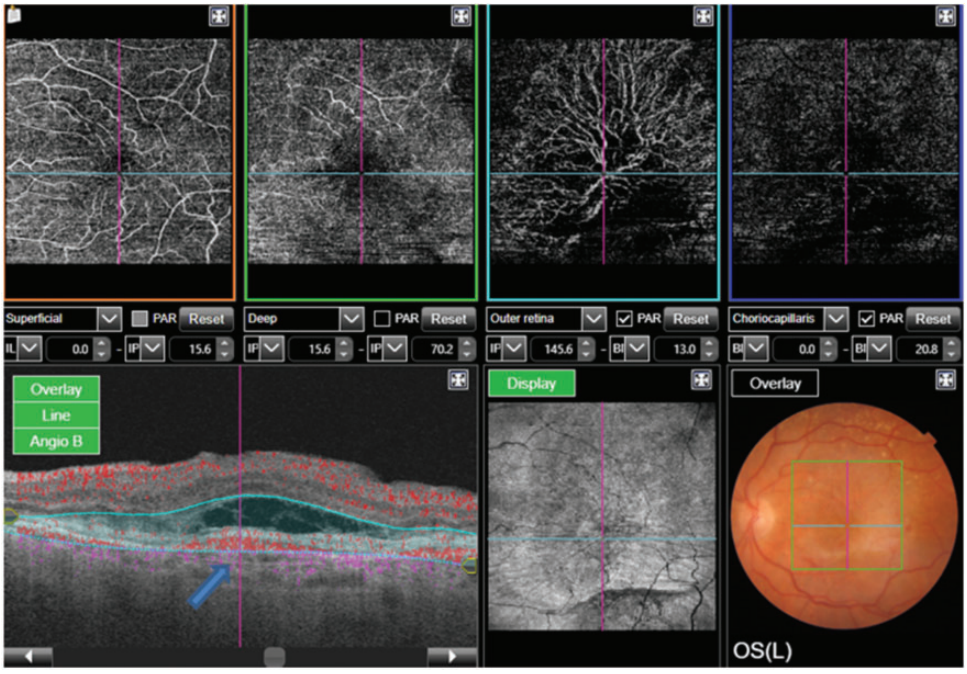

Figure 1. Left eye macular optical coherence tomography angiography. The outer retina slab (cyan) shows a large branching vascular network in the subretinal space (between the retinal pigment epithelium and the photoreceptor layer) with subretinal fluid suggestive of active type 2 choroidal neovascularisation. The Angio B mode (bottom left) shows blood flow through the vascular network (blue arrow), further confirming the activity of the choroidal neovascularisation.

Areas of non-perfusion in RVO were evaluated by Wakabayashi et al.,[33] who used OCTA to assess microvascular changes and disruption of the foveal avascular zone. Best-corrected visual acuity (BCVA) outcomes were measured and correlated to the OCTA findings in the vascular perfusion areas of the superficial and deep choroidal plexus within a defined area. Better BCVA outcomes were significantly correlated with preservation of larger vascular perfusion areas.[33] This indicates that preservation of the deep choroidal vasculature is crucial to improving visual outcomes in patients with branched RVO. Moreover, it indicates that OCTA is a useful imaging modality when evaluating and monitoring RVO as well as predicting visual outcomes following treatment.

In RVO, OCTA can detect characteristic findings such as venous dilation, cotton wool spots, and retinal haemorrhage. Kashani et al.[6] reviewed this topic and found that OCTA is useful for diagnosis and management of RAO and vascular complications of RVO in the macula. Evidence suggested that OCTA is as effective as FA for the clinical monitoring of RVO. Interestingly, the authors also found that a patient with branched RAO with insignificant symptoms, normal visual acuity, and unremarkable clinical examination findings had capillary and neurosensory loss of the superior macula on OCTA.[6] OCTA has been shown to precisely characterise macular ischaemia by demonstrating vascular remodelling of the capillary layer at the site of RAO over time; thus, OCTA

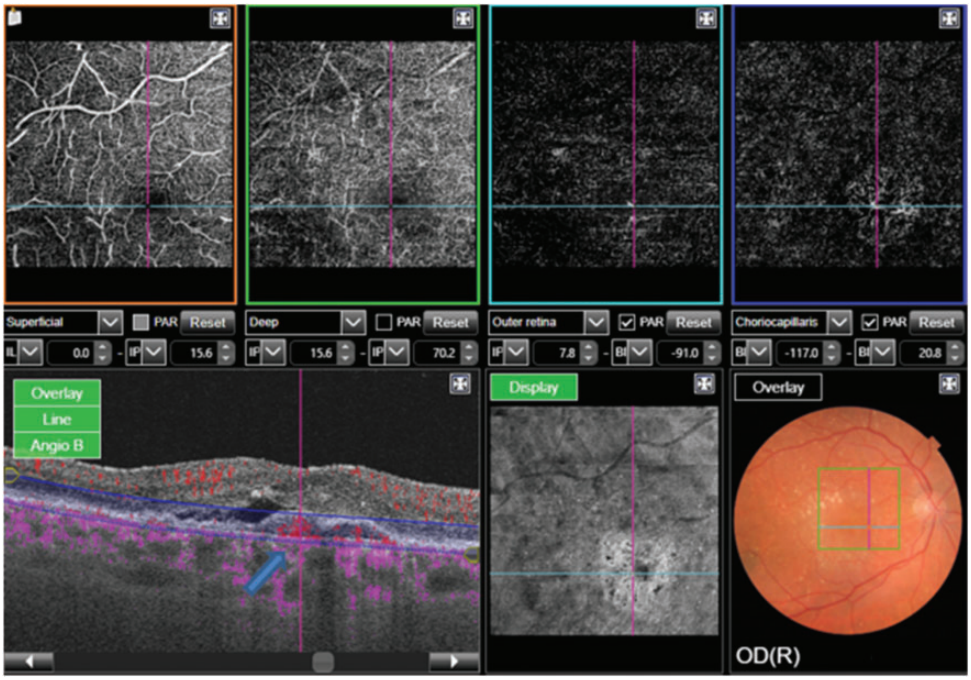

Figure 2. Right eye macular optical coherence tomography angiography. The choriocapillaris slab (blue) shows a well-circumscribed vascular network in the sub-retinal pigment epithelial space suggestive of type 1 choroidal neovascularisation. The Angio B mode confirms flow within the lesion (blue arrow).

may be useful for monitoring these vascular flow changes during the management of this disease.[34] In a study by Ben Abdesslem et al.,[35] OCTA was used to analyse various parameters in eyes with RVO, including the extent of capillary dropout, presence of macular oedema, and presence of neovascularisation. OCTA was able to accurately detect the severity and extent of RVO, providing valuable information for the management of these cases.

In another study, Spooner et al.[36] evaluated the use of OCTA and ultrawide-field angiography in eyes with refractory macular oedema secondary to RVO that were switched to aflibercept treatment. The combination of these imaging techniques helped to assess the severity of macular oedema and the presence of neovascularisation, which are important factors in determining the best course of treatment for these patients.

In summary, OCTA has been shown to be a valuable tool for the evaluation and management of RVO. The non-invasive and high-resolution imaging provided by OCTA can help to accurately assess the extent of RVO and determine the most appropriate treatment for these patients.

A representative case of OCTA in a patient with RVO is depicted in Figure 4.

Glaucoma

An emerging use for OCTA is the evaluation of optic nerve disorders. Glaucoma refers to a spectrum of ocular conditions characterised by progressive optic neuropathy, and high intraocular pressure is a major risk factor. OCTA can be used to measure optic disc perfusion, which may be decreased in patients with glaucoma and can therefore contribute to the

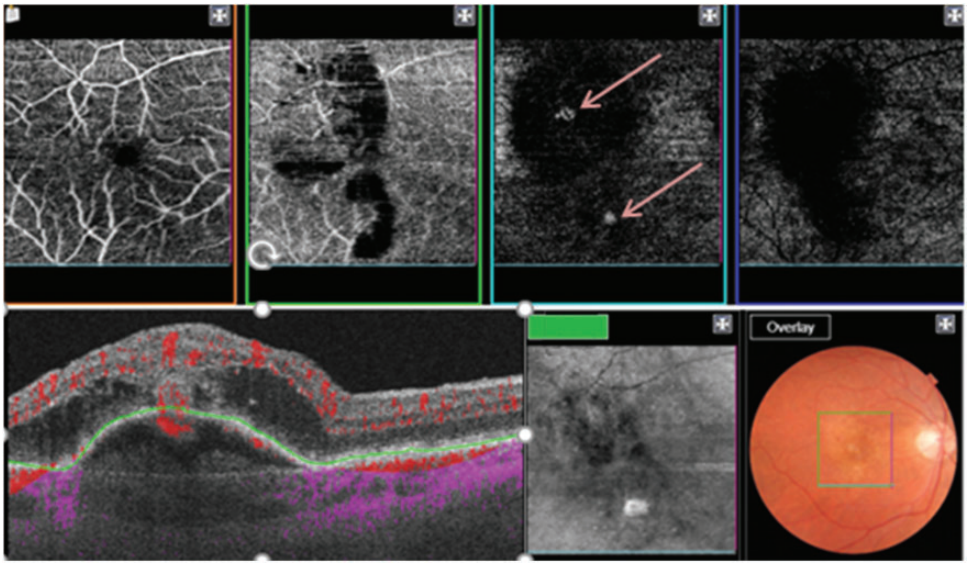

Figure 3. Right eye, type 3 choroidal neovascularisation (retinal angiomatous proliferation), two separate foci. Flow in the Angio B mode (upper lesion) shows communication with the sub-retinal pigment epithelial space.

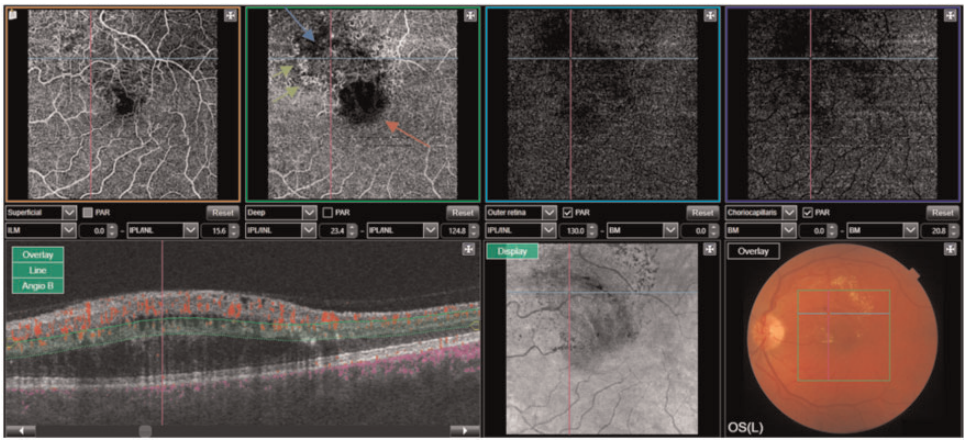

Figure 4. Left eye macular optical coherence tomography angiography in a patient with superior macular branch retinal vein occlusion. The deep vascular plexus slab (green) shows a widened, irregular foveal avascular zone (red arrow), capillary drop-out (blue arrow), and telangiectatic vessels at the borders (green arrow).

evaluation of disease progression.[37] OCTA can also be used to detect a reduction in the peripapillary vessel density before evidence of visual field loss has appeared. This could suggest earlier detection and therefore earlier diagnosis of glaucoma, leading to improved visual outcomes in patients with this condition.[38,39]

Miguel et al.[40] performed a systematic review of the ability of OCTA to detect longitudinal changes in the microvasculature in patients with glaucoma. OCTA was able to detect significant changes in the microvasculature in the eyes of these patients, including reductions in capillary density and changes in the flow of blood in the optic nerve head.

These findings suggest that OCTA has the potential to provide valuable information for the diagnosis and management of glaucoma. In addition, the ability of OCTA to detect microvascular changes in real time may allow for early detection of the disease and the initiation of appropriate treatment, potentially leading to better outcomes for patients.

Chemical eye injuries

Acute chemical injury to the eye is a sight-threatening emergency characterised by diffuse corneal epithelial erosion, limbal stem cell disruption, and conjunctival vessel infiltration, and the injury may progress to deeper ocular structures. The primary function of the limbal stem cells is to maintain the integrity of the corneal epithelium and prevent conjunctivalisation. Injury to this region is often catastrophic for visual outcomes. Ischaemia of limbal stem cells following acute chemical injury may be detected and monitored using anterior segment OCTA. This is performed by capturing blood flow in the corneal and limbal vessels. The degree of ischaemia can be quantified using different vessel-related parameters, among which the vessel density correlates with the severity of the injury. Clinical examination using slit-lamp biomicroscopy facilitates an accurate diagnosis of limbal stem cell injury but is unable to formally quantify the extent of ischaemia in the region. Although this is a new use of this technology and further evidence is needed to determine its utility, it holds potential for incorporation into the clinical setting for the management of chemical injuries. Opportunity lies in the ability to identify patients who will benefit from revascularisation therapies such as stem cell transplants.[41]

Uveitis

OCTA is a useful tool for identifying inflammation, vascular changes, and structural changes in the retina and choroid and for monitoring the disease activity and treatment response in patients with uveitis.[7] OCTA (together with wide-field OCT) allows for the identification of inflammation and vascular changes in the peripheral retina and choroid, which may not be visible on traditional imaging modalities. This is particularly important in uveitis because inflammation and vascular changes in the peripheral retina and choroid are often associated with poor visual outcomes.[42]

In a study by Dingerkus et al.,[43] OCTA was found to be a valuable diagnostic tool for uveitis because it was able to detect inflammation and vascular changes in the retina and choroid that were not visible using conventional imaging techniques. The study also showed that OCTA was able to detect inflammation in areas that were not visible on clinical examination, suggesting that it may be able to identify early stages of inflammation.[43]

It should be noted that a study by Herbort et al.[44] highlighted the limitations of OCTA in the diagnosis and follow-up of posterior intraocular inflammation, and the findings suggested that it should be used in combination with other imaging modalities and clinical examination. The study also suggested that the interpretation of OCTA images requires a high level of expertise and that false-positive and false-negative results can occur if the images are not properly interpreted.[44]

Clinical limitations of OCTA imaging

The primary difference between OCTA and other imaging modalities for the retinal circulation is the method used to detect vascular leakage. Following intravenous administration, fluorescein dye may be shed into retinal tissues and captured using a blue excitation filter. Unlike FA, OCTA is unable to image direct leakage from pathological blood vessels because it can only detect motion of erythrocytes within vessels. For patients in whom possible vascular leakage should be assessed, FA may be preferable in identifying leakage sites.[11]

Artefacts may hinder the image quality produced by OCTA and can arise from several sources. Because OCTA works by detecting motion, the quality of the images produced by OCTA is impacted by the patient's loss of fixation and eye movements. Adequate fixation may not be achieved in non-compliant patients, and this may contribute to motion artefact. Methods such as eye tracking and motion-correction techniques have been incorporated into some OCTA protocols to reduce the impact of patient-related movement artefact.[45]

Light scatter caused by superficial structures, including moving erythrocytes, can make the deeper retinal vascular layers more prone to projection artefact.[46] Software editing targets removal of projection artefact; however, these developments have not yet matured, and artefacts often remain.

Anterior segment opacities can create shadow artefacts often caused by corneal scarring, cataracts, or vitreous floaters, leading to signal attenuation. Anterior opacities may hide portions of the OCTA image and lead to diffuse reduction in image quality.[47] If a cataract is present or the pupils are poorly dilated, the image produced may show vignetting. In such an artefact, the centre of the image seems brighter than the area surrounding it, giving the appearance of irregular illumination. This poses difficulty when differentiating between the peripheral areas of the vignette artefact and areas of true low contrast from pathological vessels. Research is ongoing to develop algorithms to minimise artefact for improved use of OCTA.[48]

Other patient-related factors may also affect image quality. For example, patients with myopia may have conditions that disturb the image formed, such as RPE atrophy, retinoschisis, and lacquer cracks (a feature of pathologic myopia).[46]

OCTA is limited in its field of view because sequential B-scans are taken over a small area. This can be advantageous if the desired scan position is known; however, it may compromise the detection of peripheral vascular changes. To increase the field of view of OCTA, multiple images can be put together to produce a more inclusive image.[1]

Because OCTA imaging relies on the flow of erythrocytes through a vessel, a low-flow or diseased vessel may have a flow rate below the slowest detectable rate. This can occur in fibrotic neovascularisation, a condition in which the pathological blood vessels have become fibrosed and only leak slowly. In some OCTA systems, the slowest detectable flow can be customised to minimise this limitation and allow for better investigation of the vessel flow.[48] Increasing the time between consecutive OCT B-scans might allow for increased flow detection, but it would also increase the risk of movement artefacts.[7]

All these factors impact the quality of OCTA and can decrease the accuracy of detecting blood vessel abnormalities, potentially leading to misinterpretation of the image.

Conclusions

OCTA holds great promise in contributing to the clinical investigation and management

of retinal diseases.[11] The use of OCTA has improved our understanding of retinal and macular diseases in recent years.[4] Although the technology may not currently be easily accessible and may be of higher cost than FA or ICGA, it can provide clinical benefit to patients with poor vascular access or those for whom dye-based investigations are contraindicated, such as patients who are pregnant or breast feeding, patients with renal impairment, and patients with allergy to fluorescein sodium or indocyanine green dye.

OCTA is an advancing technology that shows promise for use in clinical practice and research. It has the potential to involve artificial intelligence and deep learning to enhance the diagnosis and management of retinal diseases such as DR in upcoming years.[49] A recent study demonstrated the potential clinical applications of deep learning for early detection and assessment of the progression of DR.[50] Deep learning analysis has already demonstrated parity with human grading in several tasks using mostly small datasets. In the above-mentioned study, OCTA was used with deep learning principles, where avascular areas were segmented in diabetic eyes. This was successful in classifying the image findings and showed accuracy in decision-making.[50] With the growing implementation of OCTA in clinical practice and the corresponding increase in the amount of available OCTA data, artificial intelligence-based analysis is expected to expand and aid clinical decisions.[51]

Author contributions

All authors fulfil the International Committee of Medical Journal Editors (ICMJE) authorship criteria. All authors contributed significantly to the manuscript's conception, design, data acquisition or analysis, and drafting or critical revision. All authors approved the final version to be published and agreed to be accountable for all aspects of the work.

Declaration of conflicting interests

The authors declare that there is no conflict of interest.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

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References

1. Choi W, Mohler KJ, Potsaid B, et al. Choriocapillaris and choroidal microvasculature imaging with ultrahigh speed OCT angiography. *PLoS One* 2013; 8: e81499.
2. Zhao Y, Chen Z, Saxer C, et al. Phase-resolved optical coherence tomography and optical Doppler tomography for imaging blood flow in human skin with fast scanning speed and high velocity sensitivity. *Opt Lett* 2000; 25: 114–116.
3. Makita S, Hong Y, Yamanari M, et al. Optical coherence angiography. *Opt Express* 2006; 14: 7821–7840.
4. Spaide RF, Fujimoto JG and Waheed NK. Optical coherence tomography angiography. *Retina* 2015; 35: 2161–2162.
5. Wylegala A, Teper S, Dobrowolski D, et al. Optical coherence angiography: a review. *Medicine (Baltimore)* 2016; 95: e4907.
6. Kashani AH, Chen CL, Gahm JK, et al. Optical coherence tomography angiography: a comprehensive review of current methods and clinical applications. *Prog Retin Eye Res* 2017; 60: 66–100.
7. De Carlo TE, Romano A, Waheed NK, et al. A review of optical coherence tomography angiography (OCTA). *Int J Retina Vitreous* 2015; 1: 5.
8. Jia Y, Tan O, Tokayer J, et al. Split-spectrum amplitude-decorrelation angiography with optical coherence tomography. *Opt Express* 2012; 20: 4710–4725.
9. Drexler W and Fujimoto JG. State-of-the-art retinal optical coherence tomography. *Prog Retin Eye Res* 2008; 27: 45–88.

10. Waheed NK, Moult EM, Fujimoto JG, et al. Optical coherence tomography angiography of dry age-related macular degeneration. *Dev Ophthalmol* 2016; 56: 91–100.
11. Schwartz DM, Fingler J, Kim DY, et al. Phase-variance optical coherence tomography: a technique for noninvasive angiography. *Ophthalmology* 2014; 121: 180–187.
12. Sawada O, Ichiyama Y, Obata S, et al. Comparison between wide-angle OCT angiography and ultra-wide field fluorescein angiography for detecting non-perfusion areas and retinal neovascularization in eyes with diabetic retinopathy. *Graefes Arch Clin Exp Ophthalmol* 2018; 256: 1275–1280.
13. Lu ES, Cui Y, Le R, et al. Detection of neovascularisation in the vitreoretinal interface slab using widefield swept-source optical coherence tomography angiography in diabetic retinopathy. *Br J Ophthalmol* 2022; 106: 534–539.
14. Sun Z, Yang D, Tang Z, et al. Optical coherence tomography angiography in diabetic retinopathy: an updated review. *Eye (Lond)* 2021; 35: 149–161.
15. Pan J, Chen D, Yang X, et al. Characteristics of neovascularization in early stages of proliferative diabetic retinopathy by optical coherence tomography angiography. *Am J Ophthalmol* 2018; 192: 146–156.
16. Vaz-Pereira S, Morais-Sarmento T and Engelbert M. Update on optical coherence tomography and optical coherence tomography angiography imaging in proliferative diabetic retinopathy. *Diagnostics (Basel)* 2021; 11: 1869.
17. Lupidi M, Gujar R, Cerquaglia A, et al. OCT-angiography as a reliable prognostic tool in laser-treated proliferative diabetic retinopathy: The RENOCTA Study. *Eur J Ophthalmol* 2021; 31: 2511–2519.
18. Athwal A, Balaratnasingam C, Yu DY, et al. Optimizing 3D retinal vasculature imaging in diabetic retinopathy using registration and averaging of OCT-A. *Biomed Opt Express* 2021; 12: 553–570.
19. Oliverio GW, Meduri A, De Salvo G, et al. OCT angiography features in diabetes mellitus type 1 and 2. *Diagnostics (Basel)* 2022; 12: 2942.
20. McClintic SM, Jia Y, Huang D, et al. Optical coherence tomographic angiography of choroidal neovascularization associated with central serous chorioretinopathy. *JAMA Ophthalmol* 2015; 133: 1212–1214.
21. Huang D, Jia Y, Rispoli M, et al. Optical coherence tomography angiography of time course of choroidal neovascularization in response to anti-angiogenic treatment. *Retina* 2015; 35: 2260–2264.
22. Mao J, Cheng D, Lin J, et al. Evaluating retinal angiomatous proliferation with optical coherence tomography angiography. *Ophthalmic Surg Lasers Imaging Retina* 2020; 51: 136–144.
23. Lauermann JL, Treder M, Heiduschka P, et al. Impact of eye-tracking technology on OCT-angiography imaging quality in age-related macular degeneration. *Graefes Arch Clin Exp Ophthalmol* 2017; 255: 1535–1542.
24. Lindner M, Fang PP, Steinberg JS, et al. OCT angiography-based detection and quantification of the neovascular network in exudative AMD. *Invest Ophthalmol Vis Sci* 2016; 57: 6342–6348.
25. Solecki L, Loganadane P, Gauthier AS, et al. Predictive factors for exudation of quiescent choroidal neovessels detected by OCT angiography in the fellow eyes of eyes treated for a neovascular age-related macular degeneration. *Eye (Lond)* 2021; 35: 644–650.
26. Faatz H, Rothaus K, Gunnemann F, et al. [Changes in OCT angiography of type 2 CNV in neovascular AMD during anti-VEGF treatment]. *Klin Monbl Augenheilkd* 2017; 234: 1125–1131.
27. Malamos P, Tsolkas G, Kanakis M, et al. OCT-angiography for monitoring and managing neovascular age-related macular degeneration. *Curr Eye Res* 2017; 42: 1689–1697.
28. De Oliveira Dias JR, Zhang Q, Garcia JMB, et al. Natural history of subclinical neovascularization in nonexudative age-related macular degeneration using swept-source OCT angiography. *Ophthalmology* 2018; 125: 255–266.

29. Al-Sheikh M, Iafe NA, Phasukkijwatana N, et al. Biomarkers of neovascular activity in age-related macular degeneration using optical coherence tomography angiography. *Retina* 2018; 38: 220–230.
30. Uji A, Balasubramanian S, Lei J, et al. Impact of multiple en face image averaging on quantitative assessment from optical coherence tomography angiography images. *Ophthalmology* 2017; 124: 944–952.
31. Agrawal R, Gupta P, Tan KA, et al. Choroidal vascularity index as a measure of vascular status of the choroid: measurements in healthy eyes from a population-based study. *Sci Rep* 2016; 6: 21090.
32. Fraser-Bell S, Symes R and Vaze A. Hypertensive eye disease: a review. *Clin Exp Ophthalmol* 2017; 45: 45–53.
33. Wakabayashi T, Sato T, Hara-Ueno C, et al. Retinal microvasculature and visual acuity in eyes with branch retinal vein occlusion: imaging analysis by optical coherence tomography angiography. *Invest Ophthalmol Vis Sci* 2017; 58: 2087–2094.
34. Bonini Filho MA, Adhi M, De Carlo TE, et al. Optical coherence tomography angiography in retinal artery occlusion. *Retina* 2015; 35: 2339–2346.
35. Ben Abdesslem N, Haddar S, Mahjoub A, et al. Retinal vein occlusions: an OCT-angiography analysis. *Tunis Med* 2021; 99: 538–543.
36. Spooner K, Fraser-Bell S, Hong T, et al. Optical-coherence tomography angiography and ultrawide-field angiography findings in eyes with refractory macular edema secondary to retinal vein occlusion switched to aflibercept: a subanalysis from a 48-week prospective study. *Taiwan J Ophthalmol* 2021; 11: 352–358.
37. Jia Y, Wei E, Wang X, et al. Optical coherence tomography angiography of optic disc perfusion in glaucoma. *Ophthalmology* 2014; 121: 1322–1332.
38. Yarmohammadi A, Zangwill LM, Diniz-Filho A, et al. Peripapillary and macular vessel density in patients with glaucoma and single-hemifield visual field defect. *Ophthalmology* 2017; 124: 709–719.
39. Koutropoulou N and Panos GD. The diagnostic value of optical coherence tomography angiography in glaucoma. *Curr Med Imaging* 2021; 17: 1179–1182.
40. Miguel A, Silva A, Barbosa-Breda J, et al. OCT-angiography detects longitudinal microvascular changes in glaucoma: a systematic review. *Br J Ophthalmol* 2022; 106: 667–675.
41. Kate A and Basu S. Role of anterior segment-optical coherence tomography angiography in acute ocular burns. *Diagnostics (Basel)* 2022; 12: 607.
42. Grewal DS, Agarwal M and Munk MR. Wide field optical coherence tomography and optical coherence tomography angiography in uveitis. *Ocul Immunol Inflamm* 2022: 1–11.
43. Dingerkus VLS, Munk MR, Brinkmann MP, et al. Optical coherence tomography angiography (OCTA) as a new diagnostic tool in uveitis. *J Ophthalmic Inflamm Infect* 2019; 9: 10.
44. Herbort CP Jr, Papasavvas I and Tugal-Tutkun I. Benefits and limitations of OCT-A in the diagnosis and follow-up of posterior intraocular inflammation in current clinical practice: a valuable tool or a deceiver? *Diagnostics (Basel)* 2022; 12: 2384.
45. Camino A, Zhang M, Gao SS, et al. Evaluation of artifact reduction in optical coherence tomography angiography with real-time tracking and motion correction technology. *Biomed Opt Express* 2016; 7: 3905–3915.
46. Chen FK, Viljoen RD and Bukowska DM. Classification of image artefacts in optical coherence tomography angiography of the choroid in macular diseases. *Clin Exp Ophthalmol* 2016; 44: 388–399.
47. Spaide RF, Klancnik JM Jr and Cooney MJ. Retinal vascular layers imaged by fluorescein angiography and optical coherence tomography angiography. *JAMA Ophthalmol* 2015; 133: 45–50.
48. Chua J, Sim R, Tan B, et al. Optical coherence tomography angiography in diabetes and diabetic retinopathy. *J Clin Med* 2020; 9: 1723.

49. Ting DSW, Pasquale LR, Peng L, et al. Artificial intelligence and deep learning in ophthalmology. *Br J Ophthalmol* 2019; 103: 167–175.
50. Guo Y, Camino A, Wang J, et al. MEDnet, a neural network for automated detection of avascular area in OCT angiography. *Biomed Opt Express* 2018; 9: 5147–5158.
51. Hormel TT, Hwang TS, Bailey ST, et al. Artificial intelligence in OCT angiography. *Prog Retin Eye Res* 2021; 85: 100965.