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Advancements in the Use of OCTA for Studying Intraocular Pressure and Retinal Perfusion

Chaoxuan Li, Weiguo Zhang*

Department of Ophthalmology, Wuhai City People's Hospital, Wuhai 016000, Inner Mongolia, China

**Corresponding author: Weiguo Zhang, 449233160@qq.com*

Abstract: Optical coherence tomography angiography (OCTA) is a non-invasive imaging technique that analyzes the microvascular system of the eye. By capturing high-speed, repeated scans to detect the movement of red blood cells, OCTA visualizes the vascular network, revealing ischemia and reperfusion patterns in retinal vascular diseases. It has become a primary tool for assessing changes in the multilayer microvascular structure of the retina, applicable in conditions such as diabetic retinopathy, age-related macular degeneration, central serous chorioretinopathy, vascular occlusions, and glaucomatous optic neuropathy, among others. Moreover, OCTA is useful in the assessment of central nervous system diseases and is increasingly utilized in routine health examinations and scientific research. Its main advantages include high resolution, rapid, non-invasive scanning, and the ability to analyze microcirculation by observing different vascular layers through tomographic imaging. However, its sensitivity to blood flow velocity and susceptibility to artifacts, such as slow blood flow appearing as non-perfusion, are notable limitations. Overall, OCTA provides a visually intuitive approach for observing retinal blood flow and has significant clinical implications for ocular conditions.

Keywords: Retinal perfusion; Optical coherence tomography angiography; Blood flow density; Perfusion density

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1. Introduction

The OCTA application scope is quite broad. Currently, it is most widely used in neurology and ophthalmology clinics. This non-invasive blood flow monitoring is becoming a powerful tool and assistant for clinical doctors in their diagnosis and treatment, and its clinical value is also increasing. Especially in the preoperative assessment and postoperative follow-up of retinal diseases in ophthalmology, as well as in the prevention and control of myopia, the clinical non-invasive nature of OCTA makes its practical significance increasingly important.

2. Application of OCTA in normal eyes

Traditionally, normal ocular perfusion is primarily determined by the difference between local arterial blood pressure and intraocular pressure (IOP). The autoregulation of microvessels generally follows Laplace's law (vessel wall tension = transmural pressure × vessel radius). As transmural pressure increases, the vessel diameter decreases, maintaining relatively constant wall tension, which helps stabilize blood flow. Retinal arterioles can maintain relatively consistent tissue perfusion despite moderate changes in perfusion pressure, attributed to the intrinsic autoregulation of retinal vessels. This autoregulation might be influenced by neural control or local metabolic products. OCTA-based studies have shown that most superficial and deep microvascular perfusion in the retina does not exhibit significant changes during the day, even with increased activity [1].

Several OCTA studies have indicated that age and gender significantly impact macular and choroidal perfusion in healthy adults [2]. With aging, macular blood flow density tends to decrease, and there are gender differences in the perfusion across various retinal layers. OCTA assessments reveal that the foveal avascular zone (FAZ) in Caucasian children closely resembles that of adults, but the FAZ area across deep, middle, and superficial retinal layers exhibits gender differences [3]. Thus, evaluating standardized ratios of macular avascular volume to surface area may provide more accurate assessments. Some OCTA perfusion parameters might serve as biomarkers for health evaluations, with variations in blood flow density or perfusion density in the FAZ potentially predicting changes in adult vision [4]. Furthermore, repeated and continuous monitoring of microvascular structure through wide-field OCTA can quantify changes over time, potentially acting as biomarkers for neural aging [5].

Research on retinal superficial and deep capillary perfusion density using OCTA has found a linear relationship in oxygen concentration responses across different retinal layers in healthy individuals. Different oxygen levels result in varying blood flow densities, suggesting that oxygen content or ion concentration could be potential factors influencing retinal perfusion regulation [6].

3. OCTA in ocular diseases

In various ocular diseases, changes in blood flow measured by OCTA accurately reflect differences in perfusion and underlying pathophysiological variations within patient populations.

Glaucoma is a leading cause of irreversible blindness, and its severity is closely linked to the perfusion density in the peripheral and macular regions. Intraocular pressure (IOP) is a critical factor in glaucoma, significantly affecting intraocular perfusion. When IOP rises, blood flow to the optic nerve head and choroid decreases, potentially increasing susceptibility to glaucomatous damage, especially in older patients. For elderly patients, elevated IOP can lead to reduced optic nerve perfusion, resulting in optic nerve atrophy. OCTA assessments have shown that changes in the avascular area of the macula or optic nerve perfusion may help identify microenvironmental variations associated with the progression of glaucoma and other ocular diseases [7]. These features can serve as early imaging biomarkers for glaucoma and IOP-related optic neuropathies, potentially providing support for precise treatment before visual field damage occurs. OCTA may thus play an active role in assessing the risk of glaucoma development in patients.

A sudden increase in IOP can cause rapid, temporary, or permanent changes in retinal blood perfusion, leading to ischemic or non-ischemic alterations. Even a slight elevation of IOP above normal levels can significantly reduce blood flow in the macula and optic nerve [8]. Conversely, lowering IOP can quickly and significantly improve capillary density and perfusion within the nerve fiber layer, highlighting the importance of IOP control for restoring retinal perfusion. These findings suggest the existence of individual differences and varied regulatory mechanisms for retinal blood flow.

In patients with a history of optic neuropathies, OCTA detects reduced retinal perfusion in the optic nerve and macular regions, demonstrating its capability to visualize and quantify optic nerve blood perfusion with excellent reproducibility. This provides greater insights into changes in perfusion during the clinical progression of optic nerve development. OCTA has also identified significant alterations in peripapillary blood flow in patients with non-inflammatory anterior ischemic optic neuropathy, thyroid-related eye diseases, and chiasmal compression. The density of peripapillary vessels may offer valuable insights into the underlying causes of optic nerve ischemia.

Wide-field OCTA has provided images showing abnormal microvascular patterns in the peripheral regions of patients with uveitis. When assessing retinal and choroidal vascular changes in patients with uveitis, with or without retinal vasculitis, reductions in microcirculation around the macula have been identified, which may contribute to cystoid macular edema [9]. Clinically, wide-field OCTA is utilized to monitor capillary non-perfusion and neovascularization in diabetic retinopathy [10]. Studies have shown a significant reduction in foveal thickness in pre-diabetic stages, suggesting that neuronal damage might precede microvascular damage, potentially signaling optic nerve atrophy or functional decline [11]. OCTA's detection of deep retinal microvascular neovascularization and subtle changes in acute inflammatory microvasculature may serve as imaging biomarkers for peripheral nerve-related diseases. Therefore, OCTA's quantitative blood flow data can be used to develop sensitive and specific imaging markers to guide treatment and prognosis.

Myopia is the most common refractive error, with an increasing prevalence across Asia. High myopia is associated with numerous complications, some of which may lead to permanent vision loss. Moderate to high myopia results in the loss of deep microvessels in the macular region. Superficial macular vessel density remains unaffected in children and adolescents with non-pathological myopia. Therefore, deep vascular density or blood perfusion density could serve as biological markers to evaluate the progression or severity of myopia.

Diabetic retinopathy involves disruptions in the blood-retinal barrier, loss of vascular wall cells, and capillary occlusion. Early changes in diabetic retinopathy include reduced perfusion and potential neovascularization. Increased vascular permeability is one of the earliest observations in non-proliferative diabetic retinopathy. OCTA provides an objective, continuous, and reliable method to accurately quantify vascular density, perfusion density, and other parameters across retinal layers [12]. These metrics correlate with the progression stages of diabetic retinopathy, potentially offering new insights for computational algorithms to quantify dynamic microvascular leakage in diabetic retinopathy.

4. OCTA and ophthalmic surgery

An observational study using OCTA found that patients who underwent epiretinal membrane peeling surgery exhibited a significant increase in retinal and choroidal vascular density and perfusion density [13]. Lens opacity and intraocular inflammation can significantly affect retinal blood flow measurements and reperfusion in OCTA. However, among different parameters, the foveal avascular zone (FAZ) measurement remains one of the most reliable indicators for assessing media opacity [14]. FAZ might be the most sensitive parameter for detecting changes in intraocular pressure (IOP) post-surgery, potentially serving as a useful tool for evaluating vascular reperfusion after glaucoma surgery [15]. Even when surface IOP appears to have normalized, localized blood flow deficits may persist, potentially leading to chronic retinal damage over the long term [16].

Cataract surgery itself may exacerbate or hinder the aqueous humor barrier in diabetic patients, aggravating diabetic retinopathy or causing cystoid macular edema [17]. Regardless of the severity of cataracts, OCTA monitoring has shown that after routine cataract surgery, both superficial capillary plexus (SCP) vessel density and superficial macular perfusion density increase [18]. OCTA could help enhance the understanding of potential postoperative changes in blood flow perfusion and their prognostic implications.

OCTA measurements before and after anti-VEGF therapy in patients with diabetic macular edema (DME) have shown that good retinal perfusion is directly related to visual acuity and resolution [19]. OCTA has distinct advantages in quantifying macular perfusion and blood flow, providing detailed insights into retinal vascular areas, such as the SCP, deep capillary plexus (DCP), and FAZ.

5. OCTA and systemic disease applications

Retinal vessels are unique as the only blood vessels that can be directly visualized on the body's surface, making the retina an essential window for studying vascular diseases. Any interruption or significant reduction in retinal blood flow can threaten normal vision. As a direct window to microvascular changes, retinal vessel density and macular perfusion density findings could represent potential biomarkers for vascular abnormalities in other organs, such as those seen in COVID-19 infections. This indicates that the retina can directly reflect changes in cerebral and systemic vasculature. Hypertension and diabetes are two common chronic systemic conditions that contribute significantly to healthcare burdens worldwide.

Previous studies have found that severe hypertension can lead to impaired retinal and choroidal capillary perfusion, with high blood pressure reducing retinal perfusion [1]. Research has shown that retinal blood flow regulation involves local microvascular changes, metabolic shifts, and physical factors like light exposure. Additionally, retinal blood flow is modulated by the metabolic activity of glial cells and neurons surrounding retinal vessels [20]. Studies have linked glycated hemoglobin levels to microvascular changes detectable by OCTA in patients with type 1 diabetes [21]. Quantitative measures of superficial retinal vessel density, perfusion density, and FAZ parameters can predict the progression stages of diabetic retinopathy. In type 2 diabetes, superficial retinal vessel density indicators also correlate with age. These findings suggest that retinal microvascular imaging may reflect systemic complications associated with diabetes.

In the early stages of diabetes, retinal blood flow decreases by about one-third [22]. Before the onset of diabetic retinopathy, OCTA has already detected structural changes in the retina of diabetic patients, particularly alterations in FAZ area, which may serve as easily accessible indicators for monitoring and screening the severity of diabetes [23]. The applications of OCTA in central nervous system disorders are expanding, including direct or indirect uses in conditions such as optic chiasm compression due to pituitary adenomas, rare genetic diseases, multiple sclerosis, and Alzheimer's disease. OCTA has detected characteristic blood flow signals indicating vessel loss around the retina and macular regions in these conditions, suggesting that microvascular changes in the retina could serve as biomarkers for diagnosing and screening neurological disorders [24].

OCTA findings (e.g., superficial retinal vessel density) may also aid in imaging diagnostics during perinatal periods, in systemic lupus erythematosus, and in certain sex chromosome-linked metabolic disorders, potentially serving as markers of inflammatory activity [25]. During the early stages of the COVID-19 pandemic, researchers used OCTA to assess ocular blood perfusion in infected individuals, collecting retinal images indicating microvascular damage. Most of these abnormalities were reversible, and short-term retinal vascular anomalies observed in COVID-19 patients were likely linked to a prothrombotic state associated with the virus [26].

Some studies have evaluated diurnal variations in macular and optic disc capillary perfusion in subjects with or without obstructive sleep apnea-hypopnea syndrome using OCTA, but no significant changes were found. Conversely, an increased trend in macular vessel density and blood flow perfusion has been observed in individuals with autism [27]. Studies suggest that melanin has a minimal impact on OCTA penetration, enabling its use in assessing vascular abnormalities in pigment-related tumors and the sensitive detection of reduced ocular perfusion caused by carotid artery stenosis [28]. This opens possibilities for the clinical application and expansion of OCTA in non-invasive detection of cerebral microcirculation disorders.

During hemodialysis, OCTA measurements indicated that retinal blood perfusion and vessel density remained unaffected [29]. Compared to healthy controls, OCTA showed an overall increase in superficial macular blood flow in patients with thyroid-related eye diseases, which then decreased as the condition worsened [30]. This change may be associated with post-orbital tissue remodeling and increased mechanical tension in advanced hyperthyroidism.

6. OCTA in acute trauma or emergencies

Studies have used OCTA to detect reduced macular perfusion in cases of traumatic brain injury (TBI) where visual function declined, showing a correlation with the loss of the local ganglion cell layer [31]. In cases of blunt ocular trauma, OCTA has proven to be a valuable, non-invasive tool for assessing dynamic changes in peripheral retinal ischemia over time [32]. Non-invasive OCTA measurements of blood flow density from the retina may serve as useful imaging markers for diagnosing eye injuries, acute brain injuries, or strokes.

7. Effects of medications on retinal blood flow perfusion density

The topical application of decongestants, such as deoxyepinephrine, has been shown to reduce retinal vessel density in peripheral regions, but not in the macular area. Therefore, studies using OCTA, especially those focused on peripheral regions, should consider the impact of deoxyepinephrine on vessel density [33].

8. Conclusion

OCTA is a novel technology that offers several advantages, including being non-invasive and capable of rapidly acquiring optical scans of the retina and choroid at specific depths. It provides precise size and localization information, visualizing the vascular systems of the retina and choroid while simultaneously displaying both structural and blood flow information. This capability makes it an invaluable tool for diagnostic support. However, OCTA has limitations, including a restricted field of view, an inability to detect leakage, and a susceptibility to artifacts (e.g., from blinking, motion, or vascular ghosting). Additionally, it cannot detect blood flow signals below a certain threshold, though advancements in technology are expected to overcome these challenges.

OCTA has been proven effective for evaluating common ocular conditions, such as age-related macular degeneration (AMD), diabetic retinopathy, arterial and venous occlusions, glaucoma, and refractive errors, as well as for assessing a healthy vascular system. Many studies suggest that some OCTA imaging parameters may serve as biomarkers for systemic diseases, which explains the expanding application of OCTA. The retinal microvascular system provides a unique window for assessing systemic microcirculation. Progress will continue in utilizing the eye's vascular system to obtain relevant information or features of systemic diseases. In the future, rapid OCTA scanning will be crucial for obtaining wider fields of view and higher resolution. With advancements, OCTA will continue to capture more precise information on vascular-related diseases, aiding in the prediction of disease progression or outcomes. Its clinical utility is expected to grow significantly.

Disclosure statement

The authors declare no conflict of interest.

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