

Optical coherence tomography angiography for glaucoma diagnosis and observation

Optical coherence tomography angiography for glaucoma

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Abstract

Glaucoma is a neurodegenerative optic neuropathy characterized by loss of retinal ganglion cells (RGCs) and RGCs axons, resulting in atrophy of the optic nerve. Optical coherence tomography angiography (OCTA) is the most recent modality in ophthalmic imaging field for diagnosis of different ophthalmic disorders, providing a high-resolution view of the vascular structures in the retina and optic nerve head. OCTA provides three-dimensional (3D) vascular information with the detection of motion contrast from the blood flow and an advanced approach to visualize retinal vasculature without the need of any dye injections that are non-invasive, fast and reproducible. In contrast to fluorescein angiography (FA) and indocyanine green angiography (ICGA), OCTA is a fast, safe, non-invasive and cost-effective diagnostic method. Another substantial superiority of the OCTA over FA and ICGA methods is that it provides high-resolution, depth-resolved blood flow data and segments the vascular layers in slabs of varying thickness in a few seconds. In addition, OCTA is a reliable and objective imaging technique with high reproducibility compared to the visual field (VF) testing. OCTA is also faster than VF testing and is less dependent on patient collaboration. Given the current population growth trends and hence the increase in glaucoma prevalence, the analysis of FA and ICGA images or VA testing is more likely to be time-consuming, costly, and prone to adverse effects. Therefore, these challenges can only be solved with the help of potentially promising diagnostic analyzes.

Keywords

Glaucoma; Ocular Circulation; Ophthalmic Imaging; Optic Disc; Retina

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Introduction

Optical coherence tomography (OCT) is relatively old and a non-invasive imaging technology based on low coherence interferometry. It produces high-resolution, cross-sectional images that allow clinicians to evaluate structural changes in different retinal diseases. However, structural OCT is an inadequate application to observe vascular changes due to low contrast between capillaries and retinal tissues. Given that many ocular diseases occur along with vascular problems, the ability to visualize, conceptualize and measure the blood flow in the eye is of great importance for the universal ophthalmic society. Conventionally, fluorescein angiography (FA) and indocyanine green angiography (ICGA) are used for qualitative clinical assessment of retinal and choroidal circulations. It is a necessary intravenous injection of contrast agents for them, which is time-consuming and more likely to have potentially serious side effects. Moreover, FA and ICGA provide two-dimensional (2D) images of ocular circulations in ophthalmic setting and thus limiting depth perception and detailed investigation of the retinal and choroidal vasculatures. However, their clinical use has been limited progressively due to their complexity, poor repeatability and reproducibility, and current population growth, changes in population demographics [1-3]. Optical coherence tomography angiography (OCTA) is a novel, non-invasive imaging modality, providing evaluation of the retinal and choroidal vasculature. OCTA is a more recent development, producing high-resolution, three-dimensional (3D) angiograms of the retinal and choroidal vascular networks and detecting the motion of blood using intrinsic signals to capture the location of blood vessels. Nevertheless, its insensitivity to leak and the comparatively small field of view, the advent and development of OCTA has the potential to improve ophthalmologists' knowledge of the physiology and pathophysiology of the ocular conditions [3,4]. In this review article, we discuss the potential technical principles of OCTA as well as its clinical applications for glaucoma and elucidate its future perspectives.

Material and Methods

With the use of the following keywords: "glaucoma", "optical coherence tomography angiography", "optic nerve head", "retinal ganglion cells", and "retinal nerve fiber layer", we searched various literatures, potential eligible research articles and reviews studies regarding ophthalmology published on the PubMed, Cochrane Library, Embase, Science Direct, Web of Science, and Google Scholar databases. This review emphasises the potential technical principles of OCTA, advantages and disadvantages of OCTA as well as its clinical applications and elucidates its future perspectives for glaucoma. OCTA was applied to patients with both glaucomatous eyes and normal eyes to obtain optic nerve head images (vertical cup/disc and linear cup/disc ratio) and macular field images. Moreover, OCTA imaging technology has been employed to visualize and quantify ocular circulations, including en face images of the radial peripapillary capillaries of the optic nerve head and the peripapillary retina. The search was focused on glaucoma and limited to specific years particularly recent years and the English language was applied.

Results

Glaucoma is a neurodegenerative optic neuropathy that causes optic nerve atrophy and thus blindness. OCTA is a more recent diagnostic modality in the diagnosis of glaucoma, providing the appearance of vascular structures in the retina and optic nerve head and choroidal vasculature. OCTA has many advantages over FA, ICGA, visual field (VF), OCT and other ophthalmic imaging methods. In contrast to other ophthalmic imagines, OCTA provides 3D vascular information. It is also a reliable and an objective imaging technique without the need for any dye injections, less dependent on patient collaboration, non-invasive, safe, fast, reproducible and cost-effective. In addition, OCTA provides high-resolution, depth-resolved blood flow data and segments the vascular layers in slabs of varying thickness. Nevertheless, there are some disadvantages of OCTA, due to its insensitivity to leak and the comparatively small field of view. Besides, OCTA has other limitations, including artefacts of motion, blinks, vessel ghosting or other shadows, image interpretation flow projection, and signal strength variation. Visualization and reliable measurement of optic nerve head (ONH) vasculature were successfully performed with OCTA in many studies. In fact, the sensitivity and specificity of OCTA in glaucoma patients have been very high in many studies. According to the scientific sources and our clinical observations, there has been a close correlation between OCTA images in the optic nerve head vasculature, peripapillary area and the severity of glaucoma.

Discussion

OCTA has numerous practices in a variety of retinal diseases, such as glaucoma [5,6], diabetic retinopathy [7,8], choroidal neovascularization [9]: a) Neovascular age-related macular degeneration [9,10], b) polypoidal choroidal vasculopathy [11,12], c) central serous chorioretinopathy [9,13], and non-neovascular age-related macular degeneration [3,14,15], retinal vascular disorders including branch and central retinal arterial and venous occlusion [16,17], retinopathy of prematurity [18], inherited retinal dystrophies [3,19], macular telangiectasia [20], ocular tumors [21], inflammatory diseases [22], radiation maculopathy [23], and multiple sclerosis [24].

Glaucoma is a neurodegenerative optic neuropathy characterized by loss of retinal ganglion cells (RGCs) and their axons, which may result in atrophy of the optic nerve, leading to progressive VF defects and blindness [25]. Early diagnosis and treatment of glaucoma are crucial to protect and sustain VF [25]. The loss of RGCs is irreversible and can be detected with special devices before VF defects [26]. The relationship between glaucoma progression and the structural changes of the optic nerve head (ONH), RGC layer, and retinal nerve fiber layer (RNFL) in glaucoma is well-known [26]. The detection and monitoring of glaucoma involve multifactorial processes, including intraocular pressure measurements, subjective evaluation of the ONH, OCT, and VF testing. The advent of OCTA offers a sophisticated opportunity for visualization of non-invasive and dye-free retinal vasculature, which can help identify vascular abnormalities in glaucoma. Representative en face images (3x3 mm²) of the radial peripapillary capillaries of the optic nerve head and a normal eye, showing the normal RNFL thickness, the

rim area, and normal cupping are presented in Figure 1. It demonstrates a glaucomatous eye with the reducing of the total RNFL thickness and the rim area. However, there is an increase in the vertical cup/disc ratio, linear cup/disc ratio and cup volume. Besides, the red and turquoise dye increase in the peripapillary area is remarkable (Figure 2). It has shown that retinal and optic nerve head vessel densities and blood flow indices were decreased in numerous studies in patients with glaucoma measured by OCTA [27]. OCT is a routine tool to aid in the detection of glaucoma and its progression [25]. OCT is unhelpful in advanced glaucoma and myopic tilt. However, OCTA may potentially support current glaucoma diagnostic tools to assist in the early detection of glaucoma. In fact, OCTA measures the microcirculation rather than the nerve tissue itself, improving diagnostic usefulness in glaucoma [6]. Representative en face images (3x3 mm²) of the radial peripapillary capillaries of the optic nerve head are seen. A normal eye with the compact capillary network around the optic nerve head is presented in Figure 3. A glaucomatous eye with global damage in the optic nerve head and the peripapillary retina are shown in Figure 4. Capillary dropout is obvious on OCTA and showing advanced cupping in the optic nerve head (Figure 4). OCTA studies in patients with glaucoma have demonstrated reduced microcirculation in the superficial optic nerve, peripapillary field, and macula [5,6]. VF testing is necessary for clinical evaluation and progression of glaucoma. However, VF is sensitive only to late stages of glaucoma and its reproducibility is also quite poor [3]. When compared to VF, OCT is more sensitive and reliable for detection and progression of glaucoma. However, VF and OCT are still not sensitive enough to detect early glaucoma and measure RNFL and ganglion cell complex [28]. Vascular changes make a substantial contribution to the pathophysiology of primary open-angle glaucoma (POAG) [29]. OCTA can conceptualize and visualize and reliably quantify optic nerve head (ONH) vasculature and perfusion parameters [3]. It has been confirmed that OCTA ONH is able to detect glaucoma in the structural and functional glaucomatous damage [30,31]. The loss of retinal ganglion cells and their axons in NFL in glaucomatous eye is related to a decrease in perfusion [32]. OCTA demonstrates vascular changes in the peripapillary retina. A substantial reducing was reported in peripapillary vessel density in glaucomatous eye [5]. OCTA can discriminate glaucoma suspect and glaucomatous retina from healthy retinas [33]. The sectoral analysis of the retinal peripapillary region with OCTA is characterized by a significant association of microvascular disruption with VF defects [34]. There is a close association between lamina cribrosa and pathophysiology of glaucoma [35]. The retinal vessel density decreases in the peripapillary region with lamina cribrosa defect [36]. These findings emphasize the close relation between lamina cribrosa damage and retinal microvasculature abnormalities [3]. It is clear that optic nerve perfusion is impaired by elevated IOP. Moreover, ONH and peripapillary vessel density are reduced in PACG and poorly controlled IOP eyes [3]. By using OCTA in primary angle-closure glaucoma (PACG), retinal perfusion has been studied and reported [3]. There is significantly lower perfusion in the inferotemporal region in the POAG eyes, which corresponds to the frequent superonasal VF damage in POAG [3].

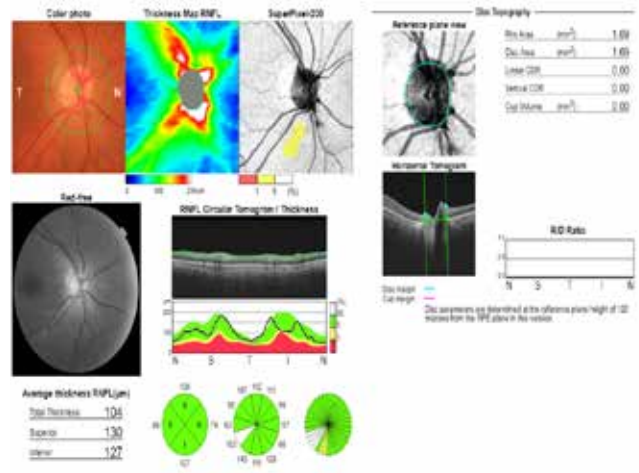


Figure 1. En face images (3x3 mm²) of the radial peripapillary capillaries of the optic nerve head. A normal eye of a 70-year-old woman showing the normal RNFL thickness, the rim area, and normal cupping.

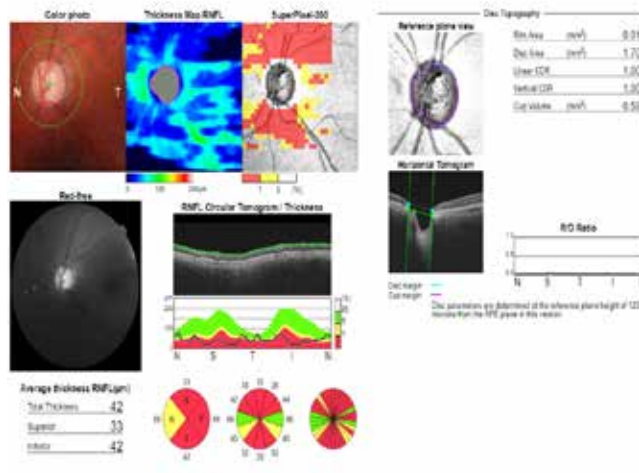


Figure 2. En face images (3x3 mm²) of the radial peripapillary capillaries of the optic nerve head. A glaucomatous eye of a 70-year-old woman showing the total RNFL thickness and the rim area reducing but increasing both the vertical cup/disc and linear cup/disc ratio and cup volume; the red and turquoise dye increase in the peripapillary area is remarkable.

Advantages of OCTA

VF testing can only detect damage after 25–35% retinal ganglion cell loss. When compared to the VF testing, OCTA has the advantage of being a reliable, objective technique with high reproducibility. OCTA is also faster than VF testing and less dependent on patient collaboration. OCTA parameters were more strongly correlated with visual function than OCT parameters. However, it is ambiguous whether OCTA provides additional knowledge for the detection and monitoring of glaucoma compared with OCT measurements [37]. OCTA has evident superiorities upon FA and ICGA in the appraisal of optic nerve and retinal diseases and the ability of OCT is obtaining volumetric scans segmented to certain depths. OCTA is a recent imaging technique and provides non-invasive simultaneous 3D structural and blood flow data, allowing for detailed evaluation of

glaucoma progression. Other advantages of OCTA demonstrate structural and blood flow data and utilize motion contrast instead of intravenous dye and provides exact size and localization information, and thus visualizes both the retinal and choroidal vasculature in seconds. Another substantial advantage of this technology is that it can provide depth information and certainly discern diverse sorts of choroidal neovascularisation [9]. Its ability to quantify angiographic information readily and quickly allows for objective monitoring of a variety of patients without any time consuming. Although it does not show leakage and has a relatively small field of view, the development of OCTA has the potential to improve our knowledge of eye physiology and pathophysiology over time [3]. However, it is certain that more clinical experience and further research are required to elucidate the application of OCTA findings for clinical decision-making of glaucoma management [3,38].

Current disadvantages of OCTA and potential promising possible solutions

OCTA has a variety of superiorities over the conventional angiography techniques. OCTA has a 3D structure, allowing for more extensive visualization and quantification of ocular microvasculature. However, it has certain technical limitations for the field of view of imaging to the posterior pole of retina. The limited field of view and inability to view leakage are disadvantages of OCTA. However, the field of view limitation and inability to view leakage may facilitate the development of sophisticated speedy OCT systems and wide-field OCTA scans. In addition, OCTA has other limitations, including artefacts of motion, blinks, vessel ghosting or other shadows, image interpretation flow projection, and signal strength variation. In order to reduce these artefacts and improve the reliability of blood vessel density, the accuracy of automated segmentation blood vessel area, flow measurements, and as well as detection and quantification of pathologies, it is necessary to improve the processing of automated image algorithms of OCTA in clinical ophthalmic settings. Along with the expected technological developments in the near future, we believe that OCTA is likely to be a major tool in glaucoma management and standard ophthalmic care [3,38].

Conclusion

OCTA is the most recent modality in ophthalmic imaging field for diagnosis of different ophthalmic disorders, providing a high-resolution view of the 3D vascular structures and depth-resolved blood flow data in the retina and optic nerve head. In addition, OCTA provides an improved sophisticated approach to visualize the retinal vasculature in noninvasively, rapid, and reproducible without the requirement of any dye injection. It is more likely that analysing of FA and ICGA images is time consuming, costly, and tend to adverse effects. In addition, when compared to the VF testing, OCTA has the advantage of being a reliable, objective technique with high reproducibility [37]. However, OCTA is fast, safe, non-invasive, cost-effective and less dependent on patient collaboration. Consequently, given the changes in population demographics and lifestyle, the current population growth trends, the extension of average lifespan and thus increase in glaucoma prevalence which creates a rising demand for such imaging. Therefore, these challenges may be only resolved by the application of novel analysis methods

such as OCTA. OCTA is a novel technology, still developing, and promising characteristics. However, OCTA is extremely vulnerable to multiple artefacts, including motion, projection, shadow, superficial vessels, vitreous opacities, pigment epithelial detachment, and blinking artefacts. In contrast to FFA and ICGA, interestingly OCTA cannot detect vascular leak [39]. Therefore, it is certain that new OCTA modalities need to be developed to eliminate existing deficiencies and artefacts in the near future. Potentially well-enhanced OCTA is expected to be broadly an imaging modality in the field of ophthalmology. It is expected that OCTA will also lead to a new concept in glaucoma diagnosis in the forthcoming years. However, further longitudinal studies are needed to elucidate the sensitivity, specificity, and clinically validity of OCTA in the progression of glaucoma. Considering these promising results, we believe that OCTA may be a part of daily glaucoma management, alongside OCT images and VF testing.

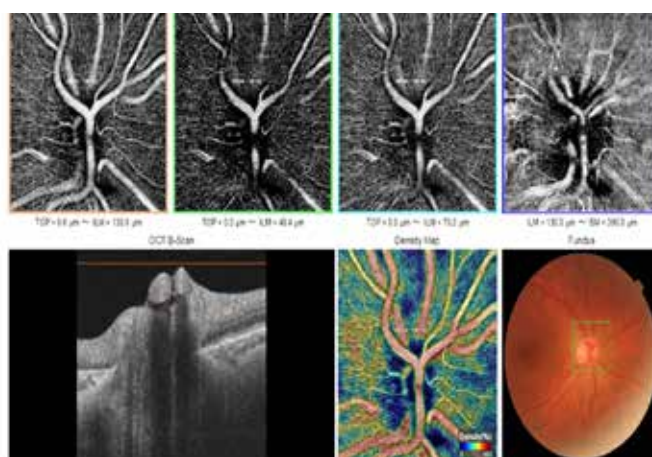


Figure 3. En face images (3x3 mm²) of the radial peripapillary capillaries of the optic nerve head. Normal eye: note the compact capillary network around the optic nerve head.

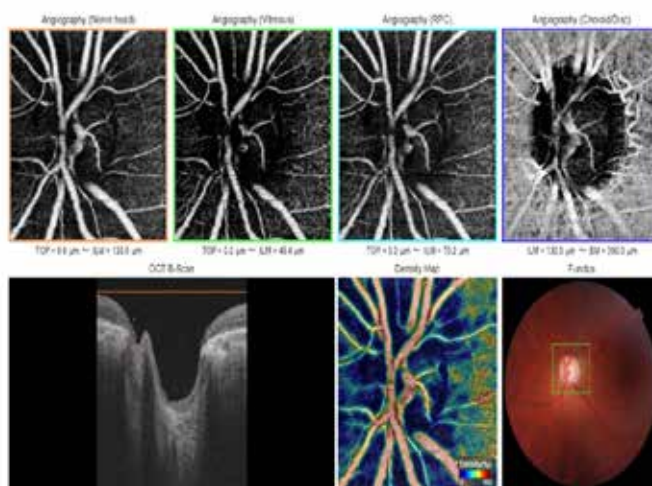


Figure 4. En face images (3x3 mm²) of the radial peripapillary capillaries of the optic nerve head. A glaucomatous eye of a 70-year-old woman with global damage in the optic nerve head and the peripapillary retina. Capillary dropout is obvious on OCTA and showing advanced cupping in optic nerve head.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest

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