

# Clinical application and development of OCT and OCTA in fundus diseases

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**Abstract.** Optical coherence tomography (OCT), which uses light wave as the imaging method, is a new medical imaging technology based on optical coherence. Optical coherence tomography angiography (OCTA) is a non-invasive imaging method gradually emerging in recent years. This technique can detect flowing blood and evaluate tissue morphology by detecting normal flow of red blood cells in blood vessels. Because of the advantages of high resolution, easy operation and three-dimensional imaging, it is widely used in the diagnosis and evaluation of fundus diseases (such as diabetic retinopathy, choroidal neovascularization, retinal vein occlusion, etc.). This article reviews the application status and progress of OCT and OCTA in clinical diagnosis and treatment of fundus diseases.

**Keywords:** OCT; OCTA; fundus diseases; clinical diagnosis and treatment.

## 1. Introduction of OCT

### 1.1. Principle of OCT imaging

Optical coherence tomography (OCT) is a non-invasive, high-resolution cross-sectional imaging examination method. By using low coherence light to perform cross-sectional scanning of biological tissues, OCT can provide one-dimensional depth, two-dimensional cross-sectional tomography, and three-dimensional real-time scanning images with micrometer resolution based on the characteristics of different tissue structures with different reflection intensities [1]. The principle of OCT is similar to ultrasound imaging, but the difference is that ultrasound is replaced by light waves. OCT can achieve real-time non-destructive non-contact imaging with axial resolution of micrometers within a depth range of millimeters, effectively filling the gap between ultrasound and confocal microscopy.

### 1.2. Classification of OCT

OCT can be divided into time-domain OCT and frequency-domain OCT based on technical principles. Frequency domain OCT can be divided into spectral domain OCT (SD OCT) and swept source OCT (SS OCT) according to the different light sources and detection schemes used. This section provides a brief introduction to the principles of time-domain OCT and frequency-domain OCT.

#### 1.2.1. Time Domain OCT (TD OCT)

In 1991, Fujimoto team of MIT in USA first proposed OCT technology and successfully applied it to live two-dimensional imaging of human retina [2]. TD-OCT is the first generation OCT imaging system that uses low coherence light sources for coherent imaging. At that time, one of the important technical issues that needed to be addressed was how to improve the scanning speed of the reference mirror at the required imaging depth. A faster imaging system is required for a reference mirror with higher scanning speed. The imaging time of a cross-sectional image is approximately 190 seconds. TD-OCT imaging involves overlapping and interfering signal light reflected from tissue with reference light reflected from reflector at the same time. Therefore, the change in signal light depends on optical path of the reflector, which resulting in long scanning time and seriously limits clinical application of TD-OCT [3].

### **1.2.2. Frequency domain OCT (FD OCT)**

The imaging speed of TD-OCT is relatively slow and cannot achieve real-time imaging, which cannot better meet the needs of further examination. The characteristic of FD-OCT is that the position of the reference light and reflector is fixed, and the interference of signal light is achieved by changing the frequency of the light wave emitted by the light source. The signal spectrum received by the detector is converted by fast Fourier transform to obtain tissue information at different depths [3]. The emergence of new technology FD-OCT has greatly improved imaging speed and sensitivity.

### **1.3. Limitations of OCT**

OCT, one of the fastest developing technologies in ophthalmic imaging, is a non-invasive ophthalmic examination and has innovative significance in ophthalmic imaging examinations. However, it still has certain problems despite continuous improvement, such as limited scanning quantity resulting in poor scanning resolution; poor point-to-point correlation between the scanning range and the patient's fundus; sampling density difference, etc. Under the gradual improvement and update of technology, optical coherence tomography angiography (OCTA) has emerged.

## **2. Introduction of OCTA**

### **2.1. Imaging principle of OCTA**

As a new non-invasive ultrasound imaging technology, OCTA can generate high-resolution vascular images containing volume and blood flow information in just a few seconds, with ultrasound to detect the echoes at each acoustic interface of tissue, and motion contrast imaging technology to select low coherence light for cross-sectional scanning of biological tissue [4]. The imaging principle is to continuously scan the same position and observe the received feedback optical signal. OCTA detects the movement of blood cells in the vascular cavity through continuous cross-sectional scans, and then integrates the information of each cross-sectional scan to reconstruct a three-dimensional vascular image of the retina and choroid [5]. OCTA is an emerging technology that does not require the use of contrast agents and has minimal impact on patients. It has broad application prospects in the diagnosis and treatment of ophthalmic diseases.

### **2.2. Advantages of OCTA**

OCTA is a technical method gradually developed and applied in clinical practice on the basis of OCT. It displays the density of fundus blood flow and the structure of fundus tissue by scanning red blood cells flowing in blood vessels, thereby achieving visualization of blood flow. It has advantages such as high resolution, easy operation, fast scanning, and three-dimensional imaging [6]. In addition, OCTA can quantitatively analyze vascular density and blood flow index, which greatly enhances the detection ability of microvascular lesions [7].

OCTA is now widely used for vascular imaging of the retina, choroid, and optic nerve. Before the advent of OCTA, fluorescein fundus angiography (FFA) and indocyanine green angiography (IGA) were the gold standards for diagnosing retinal and choroidal vascular system diseases. The above methods can obtain two-dimensional images of retinal and choroidal blood vessels through intravenous injection of contrast agents. The entire examination process is time-consuming and invasive, with potential systemic adverse reactions, which to some extent limit the application of the above tests. The emergence of OCTA has greatly solved the existing problems.

## **3. Application of OCT and OCTA in diabetes retinopathy**

Diabetes retinopathy (DR) is the most common retinal vascular disease and one of the serious complications of diabetes. Hyperglycemia is the direct cause of DR, which can damage the retinal

capillaries, causing capillary leakage and occlusion, ultimately leading to the formation of late retinal neovascularization (RNV) and fundus changes [8].

### **3.1. Application in the diagnosis and treatment of microaneurysms**

The early pathological changes of DR are the loss of pericytes and the proliferation of endothelial cells, leading to the weakening of vascular walls and the formation of microaneurysms (MAs) [9]. The leakage of MAs causes macular edema, and cystic and spindle shaped vascular dilation can be observed on OCTA [10], which is one of the reasons for DR related visual loss. In the past, the main examination methods for macular edema were angiography and OCT, both of which had certain shortcomings. Borrelli et al. [11] collected data from 20 DR patients and found that the results of detecting MAs using OCTA were similar to those of histopathological studies, indicating that the 3D visualization of OCTA can provide valuable information about the characteristics of MAs. In 2017, Parravano et al. [12] found that high reflectivity MAs were more easily detected on deep capillary plexus, while OCTA had an advantage in observing deep capillary plexus. This indicates that OCTA has the advantages of non-invasive and good repeatability compared to FFA, and is of great significance in the detection and clinical application of high reflectivity MAs.

### **3.2. Application in the diagnosis and treatment of retinal ischemia**

#### **3.2.1. Foveal avascular zone (FAZ)**

Johannesen et al. [13] conducted a systematic review of 8 studies on the changes of FAZ in DR patients, and found that the FAZ area, vertical radius and horizontal radius of diabetes patients were larger than those of healthy people, and with the progression of DR, the FAZ area was further expanded. La Mantia et al. [14] used FFA and OCTA to simultaneously measure the FAZ area of 41 eyes in 21 DR patients, and they found that FFA and OCTA had high consistency in detecting the area of FAZ with correlation analysis. In summary, OCTA can quantitatively measure the FAZ area of the retina at different stages of DR occurrence and development, providing a relatively objective evaluation of the progression of DR. Compared to FFA, OCTA has a significant advantage in non-invasive treatment.

#### **3.2.2. Diabetic macular ischemia (DMI)**

The characteristics of macular ischemia in diabetes are occlusion and loss of macular capillary network or capillary shedding. Cennamo et al. [15] evaluated the images of retinal capillary plexus according to the research criteria for early treatment of diabetes retinopathy, and found that compared with the gold standard FFA for diagnosis of DMI, OCTA has good consistency in evaluating the grading results of DMI, and can provide images with higher relevant details [16]. Yasin Alibhai et al. [17] found that quantitative measurement of OCTA in blood vessels can further assist in screening and monitoring DMI in DR patients without clinical evidence. With the further development of technology, OCTA is expected to replace FFA as a non-invasive detection method for DMI.

#### **3.2.3. Retinal non perfusion areas (RNPA)s**

Non perfusion of retinal capillaries is a preliminary characteristic of DR proliferation. Kaizu et al. [18] used OCTA and FFA to detect the non-perfusion zone in 41 eyes of 29 DR patients and found that measuring retinal flow density using OCTA can quantify related diseases and is superior to the qualitative evaluation of FFA. Couturier et al. [19] used OCTA and FFA to detect the non-perfusion areas in the shallow and deep layers of 20 eyes of 14 DR patients, and found that undetected RNPA)s on FFA could be observed in the superficial capillary plexus by OCTA. Dodo et al. [20] used OCTA and OCT to analyze 101 eyes of 69 DR patients and found that the transverse length of the non-perfusion zone of the deep capillary plexus was related to the length of the capsule cavity in the inner core layer or Henle fiber layer, which further demonstrates the feasibility of using OCTA to evaluate the shallow and deep capillary plexus in the diagnosis of RNPA)s.

### **3.2.4. Changes in microcirculation of the optic papilla**

Liu et al. [21] analyzed 72 eyes of 72 diabetes patients, and found that there was a significant correlation between the severity of DR and the vascular density in the area around capillaries, and found that the vascular density in the area around capillaries with increased DR severity had a statistically significant decline. Cao et al. [22] studied 60 cases of diabetes patients without DR with OCTA and found that the blood flow density of the optic papilla and its surroundings were lower than that of normal people. In addition, Li et al. [23] used OCTA to analyze 44 eyes of diabetes patients, and found that the capillary density in the optic disc of diabetes patients without DR was significantly lower than that of normal people. These results have certain guiding significance for us to detect blood flow density through OCTA and identify DR as soon as possible in the future.

### **3.3. Application in the diagnosis and treatment of retinal neovascularization (RNV)**

The clinical manifestation of proliferative diabetes retinopathy (PDR) is long-term retinal ischemia and hypoxia and abnormal activation of vascular endothelial growth factor (VEGF), which ultimately leads to the occurrence of abnormal neovascular network [8]. Lupidi et al. [24] demonstrated that OCTA can quantitatively evaluate the retinal neovascularization of PDR before and after photocoagulation laser therapy. OCTA can effectively identify the origin and morphology of neovascularization during PDR. The classification of RNV morphology helps us better understand the pathophysiological mechanisms of DR and develop corresponding treatment measures [25].

## **4. The Application of OCT and OCTA in Choroidal Neovascularization**

Choroidal neovascularization (CNV) refers to the abnormal growth of neovascular tissue in the choroidal capillaries, which breaks through or is located below the retinal pigment epithelium layer, leading to decreased vision and visual deformation. Many diseases can lead to the formation of CNV, among which age-related macular degeneration (AMD) is the most common disease causing CNV [26].

Although traditional OCT can reflect the manifestation and progression of AMD through structural changes, it cannot observe and evaluate changes in the choroidal capillary layer [27]. As an emerging imaging technology, OCTA can provide clear imaging of various structures by detecting the flow of red blood cells in capillaries and ultimately retinal blood flow [28].

### **4.1. Application of OCTA in dry AMD**

The development of dry AMD is slower than that of wet AMD, with the number of patients accounting for approximately 85% to 90% of the total number of AMD cases [29]. Vitreous warts are one of the typical features of early AMD and also a sign of depletion of choroidal capillary function [30]. Cicinelli et al. [31] used OCTA to observe hyaline warts and choroidal capillaries, and concluded that OCTA can detect insufficient choroidal vascular perfusion to identify hyaline warts and diagnose choroidal capillary dysfunction. Geographic atrophy (GA) is a typical characteristic change in late stage dry AMD [32]. OCTA shows a significant decrease in capillary signal within the GA lesion, while the signal in the surrounding area is normal. Choi et al. [33] also demonstrated through research that OCTA can be used to distinguish varying degrees of choroidal capillary changes and flow damage within and around GA.

### **4.2. Application in wet AMD**

Although wet AMD accounts for less than 20% of the total reported cases of AMD, it causes 90% of AMD related severe visual loss [29]. Compared with traditional imaging techniques, OCTA can perform layered imaging of retinal and choroidal capillaries without the need for injection of contrast agents. OCTA can classify wet AMD into three types based on the location of abnormal neovascularization, with type 1 and type 2 blood vessels originating from the choroidal circulation. Kim et al. [34] used OCTA to analyze the lesion size and vascular density of type 1 and type 2 CNVs

before and after 12 months of treatment. The results showed that according to the location of neovascularization in AMD, the anti VEGF treatment effect of type 2 CNVs was more significant than that of type 1 CNVs. In CNV patients, OCTA images show abnormal blood flow signals in the outer retinal layer, and the morphology of new blood vessels can be clearly observed. This allows for a more accurate assessment of the condition based on the size and morphological changes of new blood vessels, and the qualitative and quantitative analysis of CNV [4].

## **5. Application of OCT and OCTA in retinal vein occlusion**

Retinal vein occlusion (RVO) is a common retinal vascular disease whose incidence rate is second only to DR due to various reasons. Its typical manifestations include slow retinal vein flow velocity, tortuous retinal vein expansion, capillary non perfusion area, retinal hemorrhage, macular edema, which can cause painless visual loss [35]. FFA is the gold standard for detecting retinal vascular diseases, but it requires injection of dye. For invasive examination, it may lead to varying degrees of adverse reactions in some patients, and sometimes the leakage of fluorescent contrast agent can also affect observation. Moreover, FFA can only develop shallow retinal blood vessels and cannot observe retinal blood vessels in layers, which limits FFA's ability to detect and diagnose RVO. OCTA can detect more tortuous dilation of capillaries, non-perfusion areas, and collateral vessels, and performs better in evaluating retinal ischemia.

In recent years, multiple studies have shown that OCTA is superior to FFA in observing retinal capillaries. OCTA is not only non-invasive, fast, and clear, but also can display small structural changes in various layers of the retina and choroidal capillaries. OCTA can clearly display changes in the shape of the macular arch, non-perfusion areas of the retina, disorder of vascular morphology, abnormal neovascularization, and other lesions. The results are consistent with FFA results, and even clearer than FFA display. Coscas et al. [36] used OCTA and FFA to examine patients with retinal branch vein occlusion, and found that OCTA was superior to FFA in detecting macular cystoid edema and central foveal capillary arch rupture. At the same time, it was observed that when RVO occurred, ischemia and hypoxia caused by deep capillaries were more severe, and vascular perfusion was reduced. Samara et al. [37] measured the vascular density in the macular area of 17 eyes of 17 patients with retinal branch vein occlusion using OCTA, and found that the vascular density in the deep and shallow macular areas of the patients decreased compared to healthy eyes. At the same time, the vascular density in the macular area of the occluded area was lower than that in the non occluded area. The study by Sellam et al. [38] showed that before and after receiving anti VEGF treatment, RVO patients showed a significant reduction in macular cystoid edema and a significant recovery in central foveal capillary arch rupture through OCTA examination. In addition, the evaluation of vascular related parameters and their correlation with visual acuity is also an important issue in the diagnosis and follow-up of RVO. Marta et al. [39] developed a new method for evaluating visual acuity based on OCTA related information of RVO patients. They evaluated different vascular parameters through OCTA, and based on the extracted vascular parameters, used equipment data and manual measurement of FAZ results to evaluate visual acuity, which is helpful for the diagnosis and treatment of RVO, with advantages such as less time consumption, objectivity and more accurate vision estimation. These above studies indicate that OCTA has important guiding significance for the diagnosis, prognosis, and dynamic follow-up of RVO patients.

## **6. Summary and prospect**

As a new imaging technology, OCTA is widely used in clinic because of its advantages such as non-invasive, safe, efficient, clear, layered and quantifiable analysis. At present, OCTA has been widely used in common fundus diseases such as diabetic retinopathy, choroidal neovascularization and retinal vein occlusion, and has gradually replaced many previous gold standard examination methods in clinical diagnosis and treatment. In the future, OCTA still has great potential in the development of ophthalmic diseases, and more in-depth research can be carried out to achieve its new progress in

the field of ophthalmology by further improving the scanning speed, expanding the single scanning area, providing clearer images and so on. At the same time, with the development of artificial intelligence, people pay more attention to how to combine the use of OCTA with artificial intelligence to solve more clinical problems, so that it has higher diagnostic efficiency and predictive value. To sum up, with the deepening of the understanding of fundus diseases, more clinical studies are needed to provide theoretical and data support in the future, so as to promote the further development of OCTA in the clinical application of ophthalmology diseases.

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