International Journal of Medical Ophthalmology

**E-ISSN:** 2663-8274
**P-ISSN:** 2663-8266
www.ophthalmoljournal.com
IJMO 2023; 5(1): 59-62
Received: 11-02-2023
Accepted: 25-03-2023

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# A study on optical coherence tomography in diabetic retinopathy

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**DOI:** https://doi.org/10.33545/26638266.2023.v5.i1a.186

**Abstract**
This article provides an overview of a comprehensive study on Optical Coherence Tomography (OCT) and its advanced variant, OCT Angiography (OCT-A), in the context of diabetic retinopathy. OCT is a non-invasive imaging technique that utilizes low-coherence interferometry for depth-resolved imaging of ocular structures. Since its introduction in 1991, OCT has been a pivotal tool in ophthalmology, allowing detailed visualization of anatomic structures within the eye. OCT-A, a newer iteration, enhances this by using the motion of red blood cells to image blood flow in the retina and choroid without the need for dye injections. This advancement provides significant improvements over traditional methods like fluorescein angiography, offering 3D representations of vasculature and better differentiation of retinal layers. The study emphasizes the clinical relevance of OCT and OCT-A in diagnosing, monitoring, and managing retinal diseases, particularly diabetic retinopathy, showcasing their ability to detect subtle vascular changes and their potential in guiding therapeutic decisions.

**Keywords:** Optical Coherence Tomography (OCT), diabetic retinopathy, retinal disease management

## Introduction
Optical coherence tomography (OCT) is a noninvasive imaging technique that uses low-coherence interferometry to produce depth-resolved imaging. A beam of light is used to scan an area of the eye, say the retina or anterior eye, and interferometrical measurements are obtained by interfering with the backscatter or reflectance from ocular structures with the known reference path of traveling light. This modification of classic Michelson interferometry allows for the generation of structural images of anatomy when using OCT. OCT has become widely adopted in the field of ophthalmology since its introduction in 1991 and has since continually been improved. Until optical coherence tomography angiography (OCT-A), conventional structural OCT images predominantly provided visualization of anatomic changes with low contrast between small blood vessels and tissue within retinal layers. Thus, other imaging modalities such as fluorescein or indocyanine green angiography was generally used to evaluate retinal vasculature and choroidal vasculature, respectively.
OCT-A uses the principle of diffractive particle movement of moving red blood cells to determine vessel location through various segments of the eye without the need of any intravascular dyes. OCT-A technology allows for the ability to image flow in the retinal, and choroidal vasculature can be displayed through en face, depth-encoded slabs. These slabs are presented alongside structural OCT B scans. Together, they provide detailed flow imaging of the deep retinal vascular plexus and choriocapillaris, which were not well visualized with previous imaging modalities.
It is important to distinguish the differences between Doppler OCT and OCT-A. Although they both use phase information, Doppler OCT quantifies blood flow in larger vessels and measures total retinal blood flow using phase-shift while OCTA analyzes scatter from a static background tissue to create angiograms.

## History of the development of Ocular Coherence Tomography
Optical coherence tomography is the optical equivalent of ultrasound to generate images using time delay and light echo magnitudes. The use of echoes of light to examine biological tissue was originally proposed by Michel Duguay at the AT&T Bell Laboratories, published by him as "Light photographed in flight" in the American Scientist in 1971. He was the first to show that using high-speed shutters; it was possible to "see inside biological tissues." The field of Femtosecond optics was further developed by Erich Ippen of the Massachusetts Institute of Technology in the mid-1970s.

His group collaborated with Dr. Carmen Puliafito of the Massachusetts Eye and Ear Infirmary, and they studied femtosecond laser effects on the retina and the cornea. Together with S DeSilvestri of Milan, Italy, and R. Margolis and A. Oseroff from the Department of Dermatology at the Massachusetts General Hospital, they further developed Duguay's initial work to "see inside tissues." They initially used lasers at a 625-nm wavelength and later progressed to using longer 1300-nm wavelengths, which allowed the reduction of scattering. The first application of low-coherence interferometry, which was used to measure the axial length of the eye, was reported by Fercher *et al*. of the Medical University of Vienna, Austria, in 1988.

An Electrical Engineering undergraduate, John Apostolopoulos, used low-coherence laser diodes in 1989 to describe the potential ophthalmic applications of this technology, although the sensitivity was limited. The breakthrough came after ongoing research into low-coherence interferometry by David Huang, an MD/Ph.D. student, in 1991. He showed the practical applicability of coherence interferometry using an 800-nm low-coherence laser diode. Higher sensitivities were achieved, which yielded information on eye structures such as the lens and the iris. The first OCT images were demonstrated by David Huang in Science in 1991. Unpublished concepts of a similar system were also demonstrated by Tanno *et al*. in Japan.

Swanson *et al*. developed the first *in vivo* retinal images in 1993, and a similar retinal system was demonstrated by Fercher *et al*. of Vienna. Practical advances were then rapidly made by the MIT group working with Carmen Puliafito and Joel Schuman of the New England Eye Center of the Tufts University School of Medicine in Boston. OCT examination protocols for circumpapillary scanning for the assessment of glaucoma and to assess macular edema were developed by Michael Hee, an expert programmer who used the early Apple Macintosh computers.

Michael Hee was largely responsible for the major development in the 1990s, publishing more than 30 papers during his doctorate. His 1997 doctorate thesis, "Optical coherence tomography of the eye," remains a seminal reference work on OCT in ophthalmology. The first OCT atlas was organized by Carmen Puliafito in 1996 (Optical Coherence Tomography of Ocular Diseases, Slack, 1995). The Advanced Ophthalmic Diagnostics (AOD) Company set up by C Puliafito, E Swanson, and J Fujimoto in 1992, was acquired by Humphrey Zeiss two years later and went on to develop machines that were introduced into clinical use, the first machine being introduced in 1996. As with many new techniques, clinical adoption by the ophthalmic community was slow in the latter 1990s, with only 180 units in use until 2000. By 2004, the company had developed further machines that were faster and had better resolution images, and by 2004, more than 10 million OCT imaging procedures had been obtained worldwide. OCT has since become a standard of care in the ophthalmic community. OCT imaging is now used in ophthalmology, cardiovascular medicine, dermatology, neurology, gastroenterology, dentistry, otolaryngology, urology, pulmonology, gynecology, and other subspecialties with new applications being found every year.

**Specimen Collection**

Conventional OCT devices obtain an axial scan or A-scan by analyzing the reflectance or scatter of light of various structures of tissue at various depths. A B-scan, cross-sectional image, is then generated by combining multiple A-scans obtained as the light beam scans the tissue in the transverse direction. Acquiring multiple B-scans that are displaced perpendicular to the B-scan image can provide volumetric information that composes a raster scan. The elements expanded upon through OCT-A is provided by the motion of blood within the tissue being predominantly the only movement when scanning the stationary retina. Thus, the comparison of repeated OCT B-scans allows for imaging of blood flow by comparing the pixel-by-pixel differences between scans.

OCT-A allows for noninvasive detection of blood flow and 3D representation of vasculature. OCT-A identifies vasculature by analyzing differences within a repeatedly scanned transverse cross-sectional area of tissue. Two of the current methods for motion detection used are amplitude-decorrelation and phase variance. Amplitude decorrelations work by detecting the difference in amplitude between OCT B-scans while phase variance compares the variations of the emitted light wave properties when it intercepts moving objects. Both methods utilize the concept that non-mobile tissue will remain identical on consecutive OCT scans while moving erythrocytes will cause changes in successive OCT scans. Furthermore, OCT-A uses the same idea between spectral-domain OCT, wavelengths near 800nm, and swept-source OCT, wavelengths near 1050nm, where longer wavelengths have high penetrance to analyze vasculature at various levels of tissue.

Due to the high sensitivity to movement during OCT-A imaging, devices commonly implement eye-tracking methods to improve visualization and reduce background interference. The most notable methods in use are the split spectrum amplitude decorrelation technique and volume averaging technique.

**Indications**

The clinical indications for using OCT-A have not been determined by the field as a whole, but its capabilities open a vast array of possibilities for research into the pathogenesis of diseases, disease quantification, and treatment evaluation. Below is a not all-inclusive list based on research investigating the utility of OCT-A:

- Isolate locations of vascular pathology.
- Analyze each retinal vascular plexus separately.
- Evaluate the foveal avascular zone.
- Examine the perifoveal endocapillary area.
- Examine retinal microcirculation.
- Evaluate response to anti-VEGF therapy.

**Comparing OCT-A to Fluorescein Angiography and Indocyanine Green Angiography**

Fluorescein angiography (FA) and indocyanine green angiography (ICGA) require administration of intravenous dye. FA has been used in clinical practice for over 50 years and is the gold standard for the detection of retinal neovascularization, neovascularization of the disc, and choroidal neovascularization. Both FA and ICGA supply a 2D image with visualization of dynamic blood flow, such as patterns of dye leakage, pooling of dye, staining of structures. Although OCT-A cannot show the dynamic properties of dye within the vasculature, it does not require injectable dye, allows for quantitative and qualitative analysis of multiple layers, and provides 3D imaging in addition to 2D imaging.

**Normal and Critical Findings**

There are ongoing studies to determine the normal and abnormal findings observable by OCT-A. Below is a listing of findings from studies referenced by De Carlo *et al*.

**Diabetes**

- Choriocapillaris abnormalities
- Retinal microvasculature abnormalities
- Vascular remodeling of adjacent foveal avascular zone
- Enlarged foveal avascular zone
- Capillary tortuosity and dilation
- Areas of retinal non-perfusion
- Reduced capillary density

**Dry age-related Macular Degeneration**

- Areas of impaired choriocapillaris flow extending beyond areas of geographic atrophy
- A decrease in choriocapillaris density

**Neovascular age-related Macular Degeneration**

- Choriocapilalris alterations surrounding choroidal neovascularization
- Retinal angiomatous proliferation

**Vascular Occlusion**

- Areas of capillary non-perfusion with clear delineation of the ischemic boundary Microaneurysms
- Telangiectasis
- Anastomosis

**Glaucoma**

- Attenuation of peripapillary microvasculature

**Interfering Factors**

OCT-A is not without its limitations. OCT-A is highly sensitive to motion, and although eye- tracking methods are commonly deployed within devices, patient collaboration is required. Motion artifact can show up as white or black lines or misalignment of the retinal vasculature. Segmentation errors can also occur when imaging abnormal retina, although it can often be manually edited.

OCT-A technology is also dependent on the light source and, as such, is limited by media opacities, leading to signal attenuation and shadowing artifact. This aspect can also be seen when superficial blood vessels obscure deeper vessels. Additionally, a projection artifact can occur when superficial vasculature erroneously appears in segmented views of deeper layers. Lastly, the current automated area of visualizations in OCT-A spans from 2 mm to 12 mm, which can also add the limitation of being unable to image the peripheral retina.

**Complications**

OCT-A is a non-invasive imaging procedure and does not have significant complications.

**Patient Safety and Education**

Optical Coherence Tomography (OCT) is a noninvasive imaging technology used to obtain high-resolution cross-sectional images of the retina. The layers within the retina can be differentiated, and retinal thickness can be measured for early detection and diagnosis of retinal diseases. Patients may be given an OCT scan for monitoring the progression of the disease, verification, or rule out of suspected swelling in the retina, or used to evaluate medication side effects. OCT testing is a standard of care for the diagnosis, management, and treatment of most retinal conditions. The OCT uses light rays to measure retinal thickness and does no exhibit radiation or X-rays. There is no contact of the eye during the OCT scan. It does not hurt and is considered to generally be uncomfortable when patients are able to easily be positioned. OCT is commonly compared to ultrasound, with the exception that it uses light rather than sound.

Patients may be administered dilating eye drops to widen the pupil for imaging. Generally, the patient will sit in front of the OCT machine, and the patient's head will rest on the support. It is important that the patient remained still and follow the instructions of the imager when directed to look a certain direction. Scanning of the eye can take anywhere from 5-10 minutes, where the patient will see some lights.

**Clinical Significance**

The method in which OCT-A images are obtained allows for the tandem viewing of correlating en face and cross-sectional B-scans, allowing for the evaluation of anatomical features with microvascular features visualized on OCTA.

The clinical significance of OCT-A continues to mature as the usage of the technology grows. Three areas that have shown evidence for the utility of OCT-A is with glaucoma, uveitis, and various retinal pathologies. Diabetic retinopathy is associated with extensive effects on the retinal vasculature. The identification of retinal changes such as microaneurysms or neovascular complexes and the quantification of nonperfused areas of the eye such as the foveal avascular zone using OCT-A can aide in the management of diabetic retinopathy.

Evaluation of changes in choriocapillaris flow, analysis of choroidal neovascular membranes, and detection of retinal changes in age-related macular degeneration can also be aided by OCT-A. Furthermore, management of other retinal diseases such as central serous chorioretinopathy, macular telangiectasia, vascular occlusion, and choroidal neovascular membranes have been shown to have potential benefits with the usage of OCT-A.

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**How to Cite This Article**
Yadav AK and Dr. Dev K. A study on optical coherence tomography in diabetic retinopathy. International Journal of Medical Ophthalmology. 2023; 5(1): 59-62.