



Optical coherence tomography angiography findings in retinal vein occlusion

Nardeen Nabil Fouad Khalil, Laila Mohamed Hammouda, Mahmoud Mohamed

Mohamed Genaidy, Hosam A. Ibrahim Elzembely, Asmaa Anwar Mohamed Mohamed

Ophthalmology Department, Faculty of Medicine, Minia University

Abstract

Optical coherence tomography angiography (OCTA) is a new, non-invasive, dye-free imaging technique that provides high resolution, depth-resolved imaging of the retinal vasculature and also allows detection more details about micro vascular changes in different diseases which are not visible by other tradition imaging methods .OCTA as dye free technique, it can be used frequently in follow up of different pathologies through treatment for better prognosis avoiding side effects of dye injection. OCTA technology is depending on detecting signal differences between repeated transverse section optical coherence tomography (OCT) images taken from the same site of the retina in quick succession. This process detects areas of blood flow, enabling visualization of the microvasculature down to the capillary level, with high resolution near to histological precision. As OCTA is based on OCT technology, which provides structural cross-sectional images of the retina, this allows segmentation and analysis of blood vessels in different layers of the retina. various tissue layers or “slabs” can be segmented to produce two dimensional enface images of different vascular plexuses in a particular layer of the retina is in contrast to traditional fluorescein angiogram (FA) images. Retinal vein occlusion (RVO) represents the second leading cause of retinal vascular disorders, with a uniform sex distribution worldwide. RVO has been traditionally subdivided into two main types: (1) central (CRVO) with a prevalence of 0.1% to 0.4% and (2) branch (BRVO) affecting 0.6% to 1.2% of individuals. Management of RVO and its complications including conservative, medical, and surgical approaches. OCTA as a new imaging technique with recent therapeutic options enable better chances to diagnose and treat these conditions.

Keywords: Optical coherence tomography angiography (OCTA), Retinal vein occlusion (RVO), Quantitative changes, Qualitative changes

Full length article *Corresponding Author, e-mail: dm.nabil@yahoo.com

1. Introduction

Optical coherence tomography angiography (OCTA) is a new, non-invasive, dye-free imaging technique that provides high resolution, depth-resolved imaging of the retinal vasculature (Figure 1) [1-3]. OCTA technology is depending on detecting signal differences between repeated transverse section optical coherence tomography (OCT) images taken from the same site of the retina in quick succession [4-5]. This process detect areas of blood flow, enabling visualization of the microvasculature down to the capillary level, with high resolution near to histological precision [6-7]. As OCTA is based on OCT technology, which provides structural cross-sectional images of the retina, this allows segmentation & analysis of blood vessels in different layers of the retina. various tissue layers or “slabs” can be segmented to produce 2D en face images of different vascular plexuses in a particular layer of the retina

(Figure 2 A to C) is in contrast to traditional fluorescein angiogram (FA) images (Figure 2D) [8].

2. Significance

OCTA allows visualization and evaluation of micro vascular details of retinal tissue, which are not available by traditional examination tools as fundus fluorescein angiography (FFA) or indocyanine green angiography (ICGA). It also allows evaluation of pathological changes occurring in retinal vascular disorders & follow up of those changes several times through treatment avoiding side effects of dye-based methods.

3. OCTA

There are many commercially available OCT-A devices in market include Topcon Nidek, Carl Zeiss, Canon, Optopol, Optovue, and Heidelberg Engineering [11-12].

- **ZEISS Angioplex™** OCT angiographic imaging on the CIRRUS™ HD-OCT platform, with a scanning rate up to 68,000 A-scans per second and an improved tracking software known as FastTrac™. A three-dimensional image is obtained depicting erythrocyte flow as well as the microvasculature of the superficial, deep, and avascular layers of the retina [11].
- **Optovue AngioVue®** (Optovue, Inc., Fremont, CA), which uses split-spectrum amplitude-decorrelation angiography algorithm, which minimizes motion noise. This system also allows quantitative analysis, since it provides numerical data about flow area and flow density maps [11].
- **Topcon®** uses a different algorithm, OCTA RatioAnalysis, which benefits from being paired with SD-OCT, and improves detection sensitivity of low blood flow and reduced motion artifacts without compromising axial resolution [11].
- **Heidelberg engineering®** uses the active eye-tracking system (TruTrack™) that assesses simultaneously fundus and OCT images acquisition in order to achieve a better signal-to-noise ratio [11].
- **Optopol REVO NX 130** (Optopol Technology Zawiercie, Poland) SD ultrafast OCT device with integrated OCTA module. Light source is superluminescent diode with wavelength bands of 830 nm with 130.000 scans per second [13].
- **Nidek AngioScan** uses modified OMAG algorithm. It provides a 12 x 9 (12 x 3 mm x 3 mm) scans [14].
- **Canon Angio eXpert** is an OCTA system has auto fundus tracking by scanning laser ophthalmoscope [14].

4. OCTA versus dye-based Angiography

Dye-based angiographic methods, FA and indocyanine green angiography (ICGA), have been considered as the “gold standard” clinical imaging methods for visualizing vascular changes in the retina and choroid, respectively [16]. However, these methods are facing several important limitations such as:

- First, FA and ICGA require intravenous dye injection, which is invasive, time-consuming, has a limited “transit window”, and a potential side effects [17-18].
- Second, these methods have limited resolution even under ideal circumstances [19]. FA does not provide detailed resolution down to the level of the retinal capillaries.
- Third, dye-based methods offer limited depth information due to the 2D, en face nature of image acquisition. Imaging acquired on FA shows mainly the superficial vascular plexus, while the deeper retinal capillary plexuses cannot be evaluated well [20]. ICGA has longer wavelength of fluorescence enables visualization of the choroidal vessels below the retinal pigment epithelium (RPE), but still there are difficulties in discerning the different layers of choroidal vessels.

- Finally, FA exhibits prominent dye leakage. Leakage of fluorescein dye provides an assessment of vascular permeability and the integrity of the inner blood-retinal barrier, which is not possible with current OCTA technology. But on the same time, excessive dye leakage blurs vessel boundaries and obscures vascular details, particularly in the late phases of the angiogram [20].

5. Limitations and Artifacts in OCTA Imaging

Despite good advantages over traditional dye-based angiography, OCTA has some limitations as well such as:

- First, with no dye leakage with OCTA, it does not provide information on vascular integrity, leakage, or permeability, which is mainly and frequently assessed on FA.
- Second, OCTA has lower sensitivity than dye-based modalities in capturing low-flow states as it works by detecting differences in signal as a result of erythrocyte movement. So, vascular lesions with low, turbulent flow, such as sclerosed or partially thrombosed microaneurysms or polypoidal choroidal vasculopathy (PCV) lesions, may go undetected as they fall below OCTA flow detection thresholds [6, 21].
- Dye-based angiography allows wide field of view (Current ultra-widefield (UWF) imaging systems allow for a 110° to 220°) compared to OCTA (OCTA fields of view are much smaller, ranging from 3×3 mm scans focusing on the perifoveal area, up to about 12×12 mm scans (Figure 3A), or 15×9 mm scans) which gives valuable information about vascular abnormalities and perfusion in the far periphery, which can affect assessment and management decisions in retinal vascular disease including DR, RVOs, retinal vasculitis, and sickle-cell retinopathies (Figure 3B) [21]. Newer, faster, swept source (SS) OCTA scanning systems enable the acquisition of progressively larger fields of view, especially when coupled with extended field imaging (EFI) or montage techniques [22-26].
- Fourth, because of depth resolution and segmentation, the interpretation and analysis of OCTA images is more complex than traditional angiography. Errors in segmentation need to be taken into account, and these are particularly common in pathological eyes with disruption of normal anatomic landmarks, such as diabetic macular edema (DME) or age-related macular degeneration (AMD), where there is often. Manual adjustment of segmentation boundaries is often required
- Finally, OCTA scans are subject to more artifacts and image quality issues than FA and ICGA [27-28]. Sources of OCTA imaging artifacts include eye motion, image acquisition, image processing, and display strategies [29]. The need for repeated successive B-scans in the same exact location makes OCTA particularly susceptible to motion artifacts, in the form of both bulk motion and saccadic eye movement [30].

- When near-infrared light beams passing through superficial blood vessels encounter deeper tissues below, projection artifacts occur. Artifacts occur when these light beams are reflected off deeper structures, they may be detected by the OCTA instrument as motion signals as the overlying blood vessels. As a result, the presence of spurious flow (a false or ghost blood flow signal) may be inaccurately identified within deeper layers [31-32].

In contrast to projection artifacts, retinal pathology such as drusen, hyper-reflective foci, hard exudates, or extra-retinal features such as floaters or vitreous hemorrhage produce shadowing artifacts removing true flow signals and stem from OCT signal attenuation [32]. These shadowing artifacts may mimic the appearance of non-perfusion areas and capillary dropout [33]. Lastly, an important source of artifacts stems from segmentation error [28]. The parameters used by automated algorithms to segment retinal layers for en face imaging are based on normal retinal architecture and may be especially disrupted in pathological states, including intraretinal fluid, large pigment epithelial defects, or choroidal neovascularization [5].

6. Clinical Applications

6.1. Retina

As a fast, safe and noninvasive procedure to assess the chorioretinal microvasculature, OCT-A has been increasingly used in retinal diseases. The number of studies reporting new findings and utilities is exponentially growing. OCT-A has been reported to be useful in the diagnosis and understanding of many retinal conditions, namely:

- **Diabetic retinopathy** - identifying neovascular complexes, and quantifying foveal avascular zone and nonperfused areas, showing good agreement with FA findings [34-36].
- **Dry age-related macular degeneration** - a general decrease in choriocapillaris flow has been reported, typically extending beyond the borders of areas of atrophy. Devices using SS-OCT are associated with better definition of choroidal vasculature changes [22,37].
- **Wet age-related macular degeneration** - qualitative and quantitative analysis of choroidal neovascular membranes (CNVM), being able to classify them, and to follow-up structural changes after intravitreal injections. It has also been raised the potential for detection of these neovascular complexes in non-exudative cases, which would be difficult to detect using SD-OCT or FA, and thus contribute to a more effective and closer follow-up [30,38].
- **Central serous corioretinopathy** - overlap between findings in FA of a pigmented epithelium detachment (PED) and CNVM may lead to situation of misdiagnosis. Especially in suspicious cases of flat and irregular PEDs, OCT-A may be helpful in diagnosis and management of CNVM[39]. Although some reports mention a decreased choriocapillaris blood flow [40-41].
- **Vascular occlusions** - evaluation of nonperfused areas and the integrity of superficial and deep plexus. The preservation of the deep vasculature has been associated with better visual outcomes [42-43].
- **Macular telangiectasia** - identification of the dilated, irregular telangiectatic vessels and, occasionally, the choroidal communication. Since OCT-A does not detect leakage, its combination with the OCT B-scan may help stage and manage MacTel without using FA [44-45].
- **Choroidal neovascular membranes** of miscellaneous causes (e.g. associated with high myopia), with good sensitivity and specificity for detection [46].

6.2. Glaucoma

OCT-A is also gaining increasing popularity for optic nerve disorders assessment, such as glaucoma. It has been reported as a useful tool for evaluating optic disc perfusion in glaucomatous eyes, since attenuated peripapillary and macular vessel density was detectable in pre-perimetric glaucoma patients. Therefore, there is enthusiasm about the role of OCT-A in early detection of glaucomatous damage. Moreover, the quantitative data from these retinal vessels may prove useful in analyzing metabolic activity from the inner layers of the retina and thus provide further advances in monitoring function and progression in this disease [30, 47].

6.3. Uveitis

Francesco Pichi and collaborators recently reviewed the uses and importance of OCT-A in uveitis [11]. For the sake of this article, only a brief summary will be reported. The authors divided the findings among the standard layers obtained with OCT-A:

- **Superficial retinal capillary plexus** - involved in inflammatory vasculitis, in which OCT-A is able to detect capillary dropout of superficial retinal vessels, capillary remodeling and a lower vessel density in uveitic eyes. The vascular reserve can be interpreted, which may be useful in management decisions. Also, in birdshot corioretinopathy, it has been suggested by recent OCT-A findings that the main ischemic insult responsible for secondary macular thinning may be in these inner retinal vessels [48-49].
- **Deep retinal capillary plexus** - although smaller changes were detected when compared to superficial plexus in inflammatory conditions, OCT-A is able to detect patterns associated with cystoid macular edema. However, one should always bear in mind the potential for artifacts in deep plexus visualisation (see below) [48,50].
- **Choriocapillaris** - in inflammatory conditions associated with choroidal flow reduction or ischemia, OCT-A was able to detect flow void areas, that correlated with indocyanine-green angiography findings [11].

7. Changes in OCTA of Eyes with RVO

The changes visible in OCTA can be classified into qualitative and quantitative.

7.1. Qualitative changes

7.1.1. Non-perfusion areas (NPAs)

These are also called grayish areas and areas with decreased vascular perfusion [52-54]. These areas are regions without visible perfused capillaries. In RVOs, they are more extensive in the DCP than in the SCP [51-52, 54-56]. These areas are more readily visible with OCTA than with FA [57]. There may be a decrease in the vascular perfusion in both the SCP and DCP of the fellow eye of RVO patients relative to normal controls, which may be a sign of previous silent RVOs in these eyes Figures 5 to 8 [54].

7.1.2. Vascular tortuosity

This is similar to what is visible in larger vessels in OCTA, and may also include kinking, angulation, and/or spiral twisting of vessels. Tortuosity is seen in both central RVOs (CRVOs) and branch RVOs (BRVOs) and in some fellow eyes (Figure 5 to 7) [59].

7.1.3. Collateral vessel formation

It manifests as a long vessel traversing the area with blocked perfusion, or as a group of tortuous vessels beside the area with blocked perfusion. These vessels can be seen in both CRVO and BRVO eyes (Figure 8) [54].

7.1.4. Disruption of the perifoveal capillary plexus

The perifoveal capillary net is distorted in ischemic maculopathies including RVOs. Disruption of the FAZ is more common in the DCP than in the SCP [31]. Coscas et al found that there is relation between the degree of disruption of the perifoveal capillary network and the presence of peripheral ischemia in FA. They did not find any peripheral ischemia in FA in cases with an intact perifoveal capillary network and suggested that OCTA may be a screening tool to decide whether need to perform FA (Figures 5-8) [51-53].

7.1.5. Dilation of the capillary plexus and venous dilation

This sign is more commonly seen in the DCP and better detected by OCTA than FA.[51,55,57,59-60]. It is mostly caused by two mechanisms: 1) an increase in the intravascular resistance, and 2) the effect of the different cytokines and growth factors produced during the disease process (Figures 5-7) [61].

7.1.6. Microaneurysms

These are detected by OCTA in BRVO, and they are more common in the DCP than in the SCP [53]. They usually form at the border of NPAs, and in collateral vessels (Figure 8) [26].

7.1.7. Cystoid spaces

Cystoid spaces in the SCP are more commonly seen in CRVO, and those in the DCP are more common in BRVO than in CRVO. It is easier to find macular cystoid spaces in OCTA than in OCT and FA [51]. Cystoid spaces have no signal and coincide with areas of perfusion abnormalities (Figures 5-8) [55]. Absence of OCTA signals in the area of

cystoid spaces usually due to one of two reasons [62]. The first is the displacement of capillaries by cysts, which is favored by the observation of an increase in vascular perfusion indices after treatment in some studies [52]. The second is the development of cysts in non-perfused areas [55]. The previously described “hyper-reflective” cystoid spaces appear as “diffuse and splotchy” OCTA signals [63]. Kashani et al named these pockets as “edema with hard exudates” and proposed that these areas contain intraretinal fluid with high concentrations of lipids (a stage before complete absorption of the intraretinal fluid and formation of hard exudates [55].

7.1.8. Intraretinal hemorrhages

The shadowing effect of intraretinal hemorrhages may obscure images of one or both intraretinal vascular plexuses, and the level of the hemorrhage can be determined from the degree to which the images are obscured: if images of both plexuses are obscured, then the hemorrhage is above both; if neither image is obscured, it is beneath both; and if only the image of the DCP is obscured, then it lies between the two vascular plexuses [55].

7.1.9. Non-perfused ghost vessels

These can be diagnosed when a vessel is visible on the en face OCT image, but is not detectable in OCTA. These vessels also cannot be seen in FA [64].

7.1.10. Optic disc venous collaterals (OVCs) and neovascularization of disc (NVD)

OCTA shows optic disc collaterals at the level of the superficial peripapillary plexus whereas neovascular vessels are visible above the retina at the level of the vitreous. OVCs are loopy vessels whereas new vessels are a mesh of fine vessels. OCTA delineates OVCs better than both fundus photographs and FA [56,65]

7.1.11. Neovascularization elsewhere (NVE)

This phenomenon can be detected using OCTA, and the visibility of new vessels with OCTA is greater than that with FA because of the absence of leakage in OCTA[66]. This modality may enable physicians to perform quantitative follow-up of new vessels and evaluate the response to treatment.

7.2. Quantitative Changes

7.2.1. Foveal and perifoveal vascular density

Vascular density both in the foveal and parafoveal areas and all over the scanned area have been reported to be lower in RVO eyes relative to those in control eyes. However, there are different results regarding the layers that are affected in each type of RVO [53,59,67]. Vascular perfusion density is another significant factor associated with photoreceptor integrity and visual acuity [42,68]. Changes in vascular density in the presence of macular edema have also been reported. Mastropasqua et al reported significant positive correlations between macular thickness and the vascular density in superficial, deep, and choriocapillary plexuses, and this correlation has been related to the high levels of VEGF, which increases both the macular thickness and the vascular diameter, thereby increasing the percentage of detected flow pixels by the instrument [53].

Meanwhile, Koullis et al described decreased SCP vascular density in the presence of macular edema due to RVO compared to that in eyes without edema, while DCP and non-segmented vascular densities were not affected [67]. This discrepancy may be due to the different inclusion criteria for macular edema or different OCTA platforms used. Seknazi et al, in a retrospective study, consider that a vascular density of less than 46% in the DCP in eyes with CRVO is the limit below which peripheral retinal non-perfusion becomes more probable and suggested the use this limit as an indication for doing FA in CRVO patients [68].

7.2.2. Measurement of FAZ

The FAZ is enlarged in the DCP of RVO eyes relative to those in normal controls and fellow eyes, and relative to the FAZ of the SCP [26,59,69] despite the variability of FAZ size in normal individuals [69-70]. FAZ findings of the SCP maybe variable. As while Rispoli et al and Casselholmde Salles et al repored an enlargement of the SCP ischemic area, Suzuki et al found no significant alterations[26]. Casselholmde Salles et al also reported an association between EZ disruption and the superficial FAZ area [69]. Suzuki et al reported that the FAZ was larger in

eyes with CRVO than in eyes with BRVO. The authors proposed that FAZ size may be related to the intraocular VEGF levels, as they found larger FAZs in both plexuses in eyes receiving fewer intraocular injections [26].

7.2.3. Measurement of choriocapillary VD

Retinal vein occlusions alter the hemodynamic properties of the choroid leading to structural changes. These changes may be secondary to a compensatory mechanism to supply oxygen to hypoxic retina .Eyes with RVO had a lower choriocapillaris flow density compared to both fellow and control eyes [71].

7.2.4. Measurement of NPA

In a study involving manual measurement of NPA in the parafoveal area, this parameter was found to be the most significant factor associated with VA and macular sensitivity in microperimetry in eyes with RVO, and was even more significant than the ellipsoid zone (EZ) continuity [43]. Qualitative grading of non-perfusion in both plexuses was also reported to be significantly correlated with peripheral non-perfusion [68].

Table 1: Characters of most popular OCTA instruments.

	Spectralis (Heidelberg)	AngioPlex (Zeiss)	DRI (Topcon)	RTVue XR Avanti (Optovue)
Type	Spectral domain	Spectral domain	Swept-source	Spectral domain
Wavelength	870 nm	840 nm	1050 nm	840 nm
OCTA algorithm	FS-ADA	OMAG	OCTARA	SSADA
A-scan rate	85 KHz	68 KHz	100 KHz	70 KHz
Repeat B-scan	4–7	4	4	2
Eye track	TruTrack	FastTrac	SMARTtrack	VTRAC
Segmentation boundary for the SCP	ILM and outer boundary of the IPL	ILM and approximation of the IPL (0.7*thickness between the ILM and the OPL from the ILM)	2.6 μm beneath the ILM and 15.6 μm beneath the interface of the IPL/INL	3 μm below the ILM and 15 μm below the inner boundary of the IPL
Segmentation boundary for the DCP	Outer boundary of the IPL and outer boundary of the OPL	Approximation of IPL (0.7*thickness between the ILM and the OPL from the ILM) and approximation of the OPL (110 μm from the RPE boundary)	15.6 μm beneath the interface of the IPL/INL and 70.2 μm beneath the IPL/INL	15 μm below the inner border of the IPL and 70 μm below the inner border of the IPL (≈outer border of OPL)

DCP = deep capillary plexus; FS-ADA = full-spectrum amplitude decorrelation algorithm; ILM = inner limiting membrane; IPL = inner plexiform layer; INL = inner nuclear layer; OCTA = optical coherence tomography angiography; OCTARA = OCTA ratio analyses; OMAG = OCT-microangiography complex algorithm; OPL = outer plexiform layer; SCP = superficial capillary plexus; SSADA = split spectrum amplitude decorrelation algorithm [15-16].

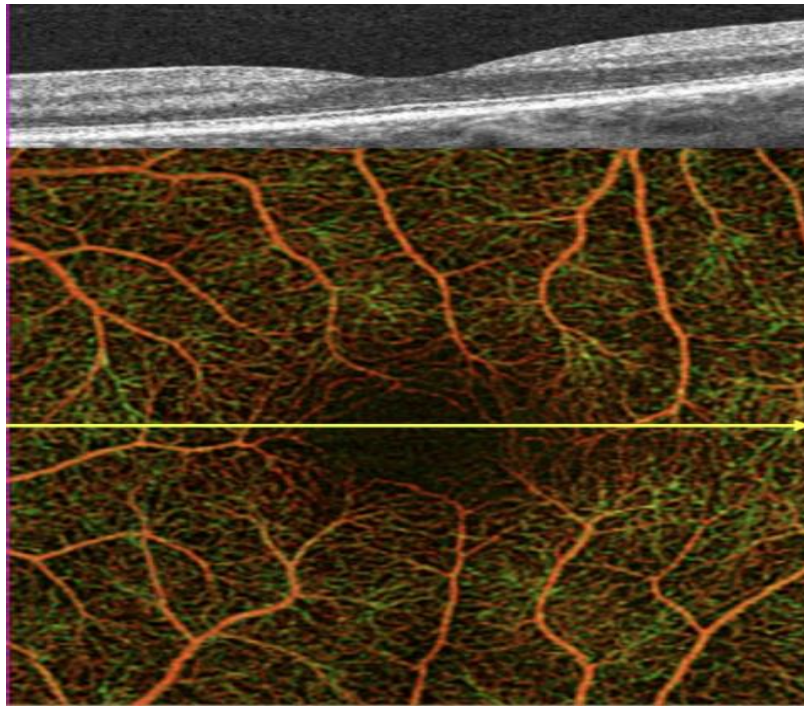


Figure 1: Full thickness color depth-encoded OCT angiogram of a normal eye. Red-orange appearing vessels comprise the superficial vascular plexus while green appearing vessels comprise the deep capillary plexus. Above is a single structural OCT b-scan through the center of the angiogram (yellow) [9].

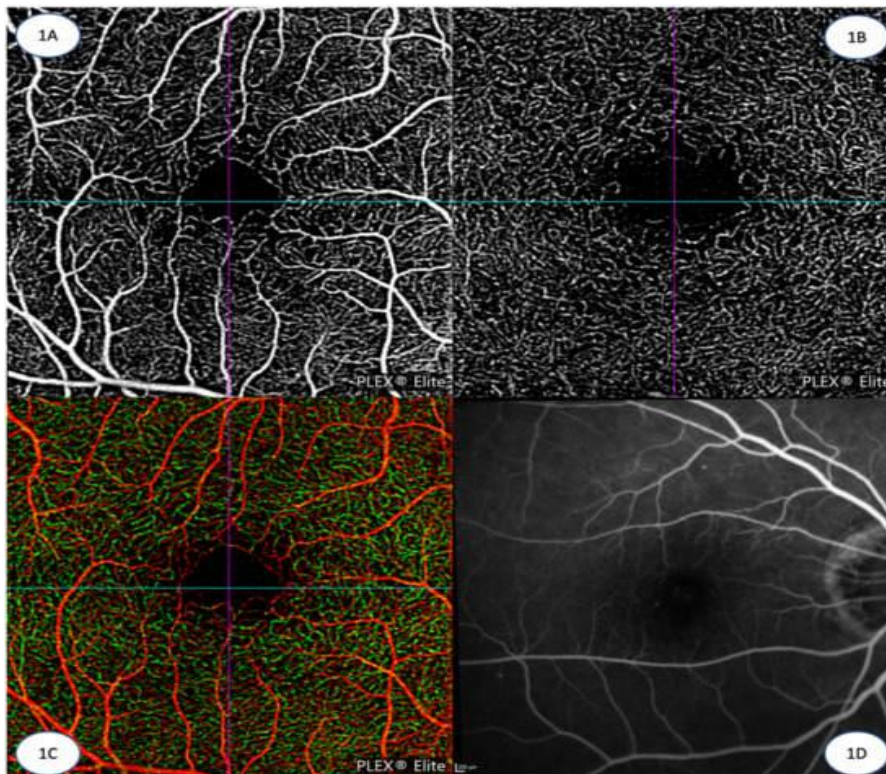


Figure 2 OCTA image of healthy (Zeiss PLEX Elite 9000, Carl Zeiss Meditec, Jena, Germany) (A): 3 mm × 3 mm OCTA image of the superficial capillary plexus (B): 3 mm × 3 mm OCTA image of the deep capillary plexus (C): 3 mm × 3 mm OCTA image with color coding combining both the deep (in green) and superficial capillary plexuses (in red) (D): 30 degree fundus fluorescein angiography image of the posterior pole (Spectralis HRA + OCT, Heidelberg Engineering, Heidelberg, Germany) [10].

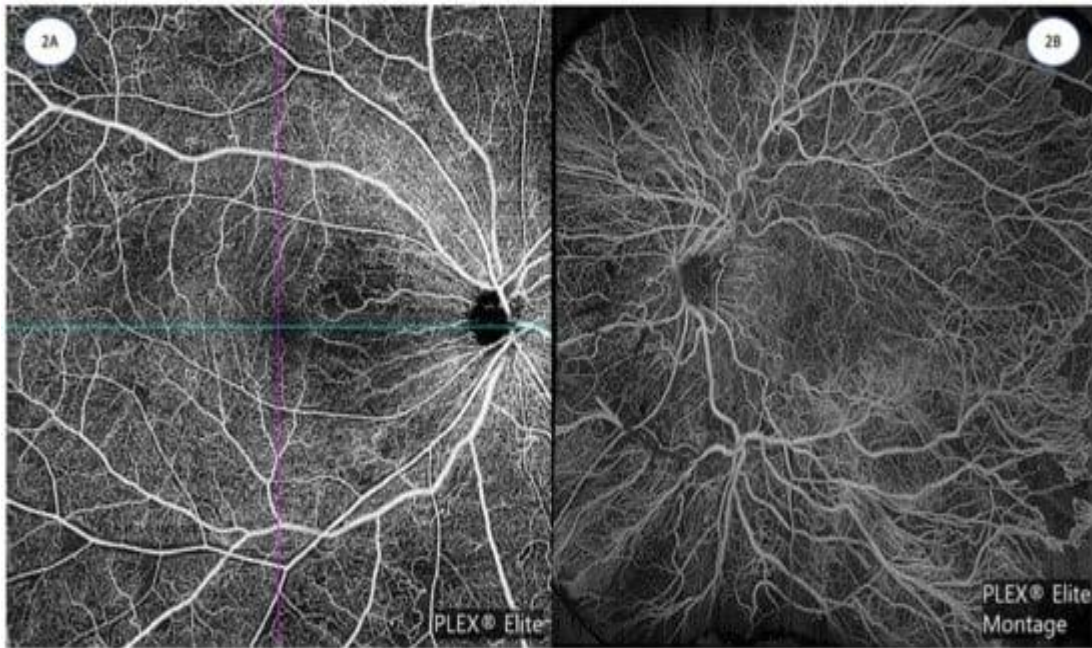


Figure 3: (A): 12 mm × 12 mm OCTA image of non-proliferative diabetic retinopathy, demonstrating patchy areas of capillary non-perfusion, microaneurysms, dilated vessels, intraretinal microvascular abnormalities, and mild FAZ enlargement and irregularity. (Zeiss PLEX Elite 9000, Carl Zeiss Meditec), (B): 15 mm × 9 mm montage OCTA image of proliferative diabetic retinopathy, demonstrating very large fronds of neovascularization, adjacent to areas of retinal non-perfusion. (Zeiss PLEX Elite 9000, Carl Zeiss Meditec). Images courtesy of K Sandhanam [10].

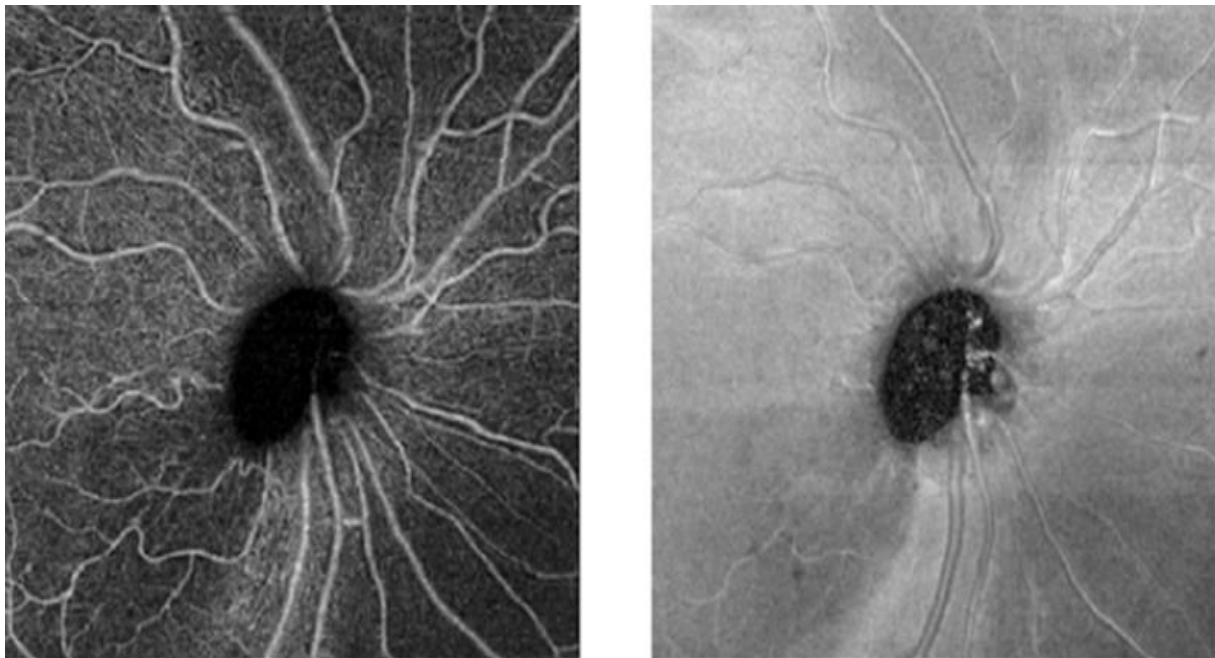


Figure 4: OCT-A (left) and *en face* structural imaging (right) of a glaucoma patient, revealing inferior temporal loss of retinal fiber layer and the anatomical correspondence with decreased vessel density in the OCT-A image [10].

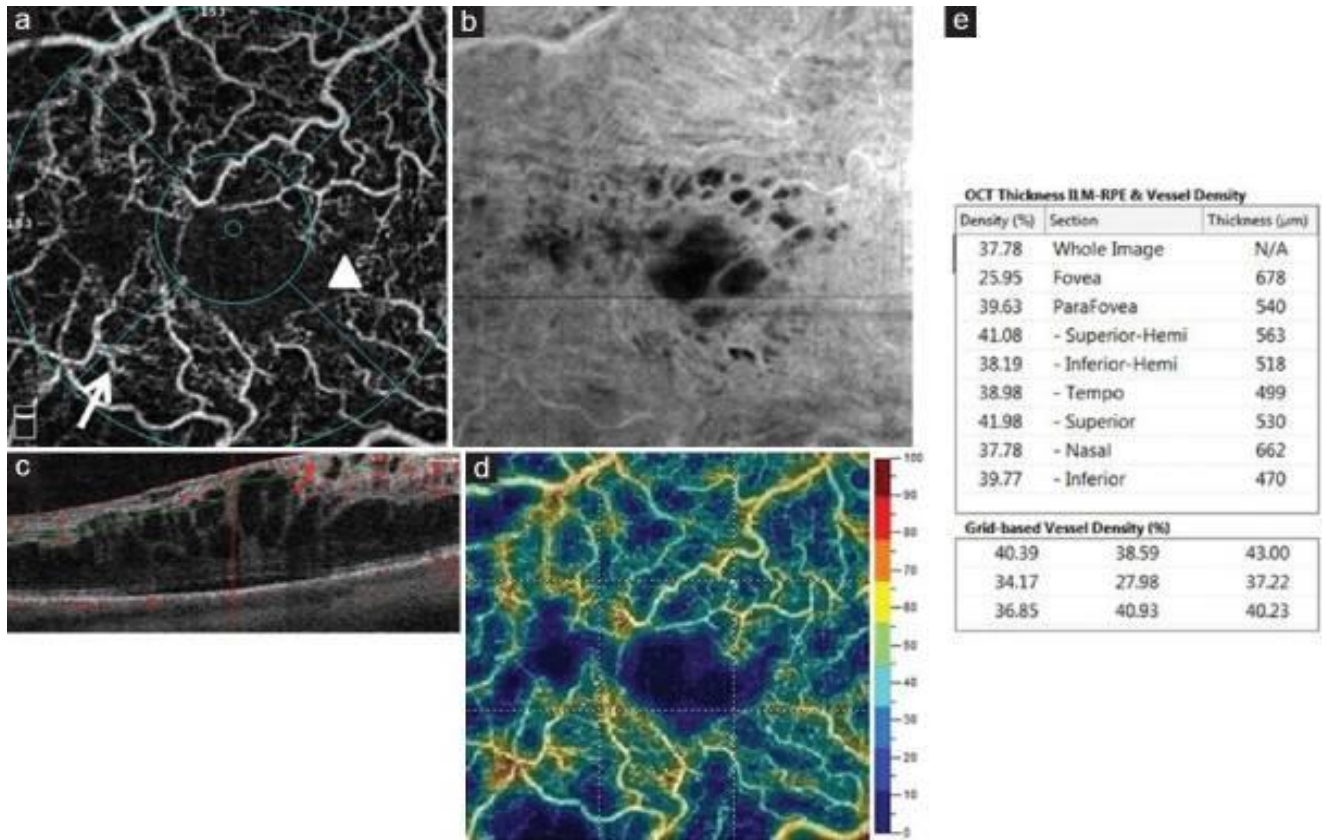


Figure 5: OCTA (3 × 3 mm) in a case of CRVO, (a) OCTA at the level of the superficial capillary plexus (SCP) showing vascular tortuosity, dilation and telangiectasia (arrow) along with decreased vascular density and non-perfusion areas. Also note the irregular and enlarged foveal avascular zone, (b) En face OCT at the level of the SCP shows the presence of cystoid edema, which corresponds to dark circular areas without vessel signals in OCTA (arrowhead in A), (c) B-scan OCT with perfusion overlay and segmentation lines, (d) Color-coded vascular density map, (e) Numerical report of the vascular density [58].

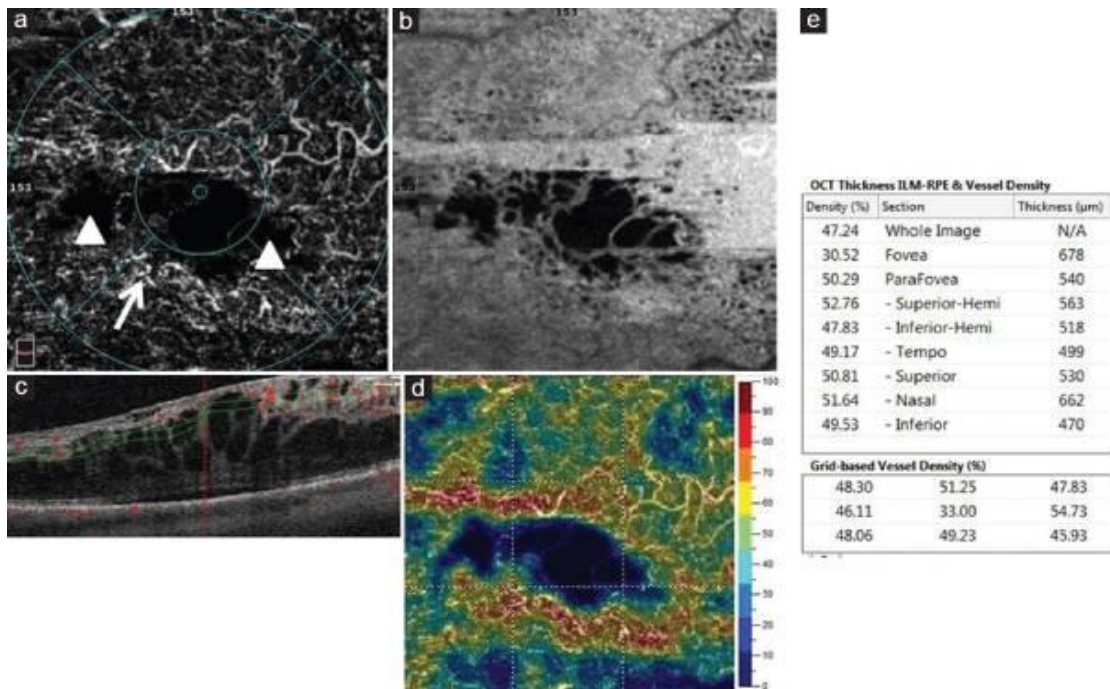


Figure 6: OCTA (3 × 3 mm) in a case of CRVO, (a) OCTA at the level of the deep capillary plexus (DCP) showing vascular tortuosity, dilation, and telangiectasia (arrow) along with decreased vascular density and non-perfusion areas. Also note the irregular and enlarged foveal avascular zone, (b) En face OCT at the level of the DCP. Note the presence of cystoid edema corresponding to dark circular areas without vessel signals in OCTA (arrowheads in a), (c) B-scan OCT with perfusion overlay and segmentation lines, (d) Color-coded vascular density map, (e) Numerical report of the vascular density [58].

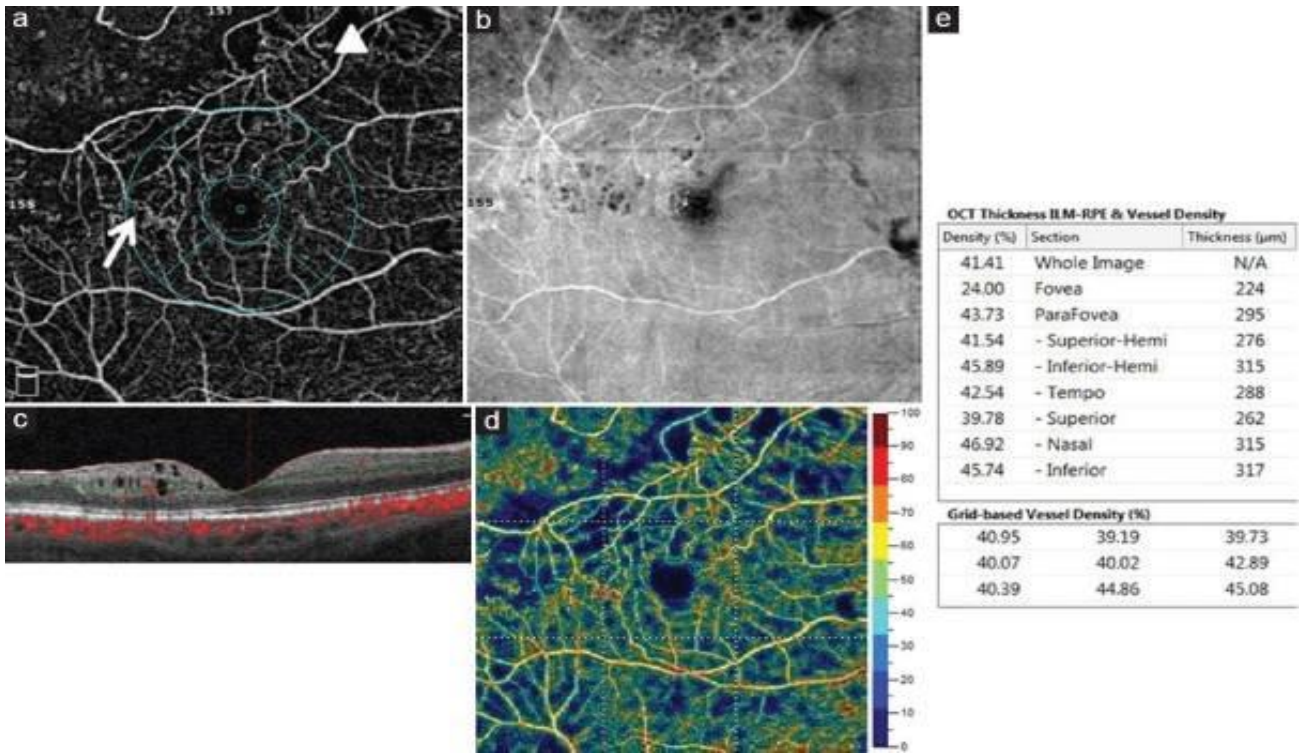


Figure 7: OCTA (6 × 6 mm) of a case of BRVO. (a) OCTA at the level of the superficial capillary plexus (SCP) showing vascular tortuosity, dilation and telangiectasia (arrow) along with decreased vascular density and non-perfusion areas in the superotemporal region (a), (b) En face OCT at the level of the SCP. Note the presence of cystoid edema corresponding to dark circular areas without vessel signals in OCTA (arrowhead in a), (c) B-scan OCT with perfusion overlay and segmentation lines showing the level of OCTA in (a), (d) Color-coded vascular density map, (e) Numerical report of the vascular density [58].

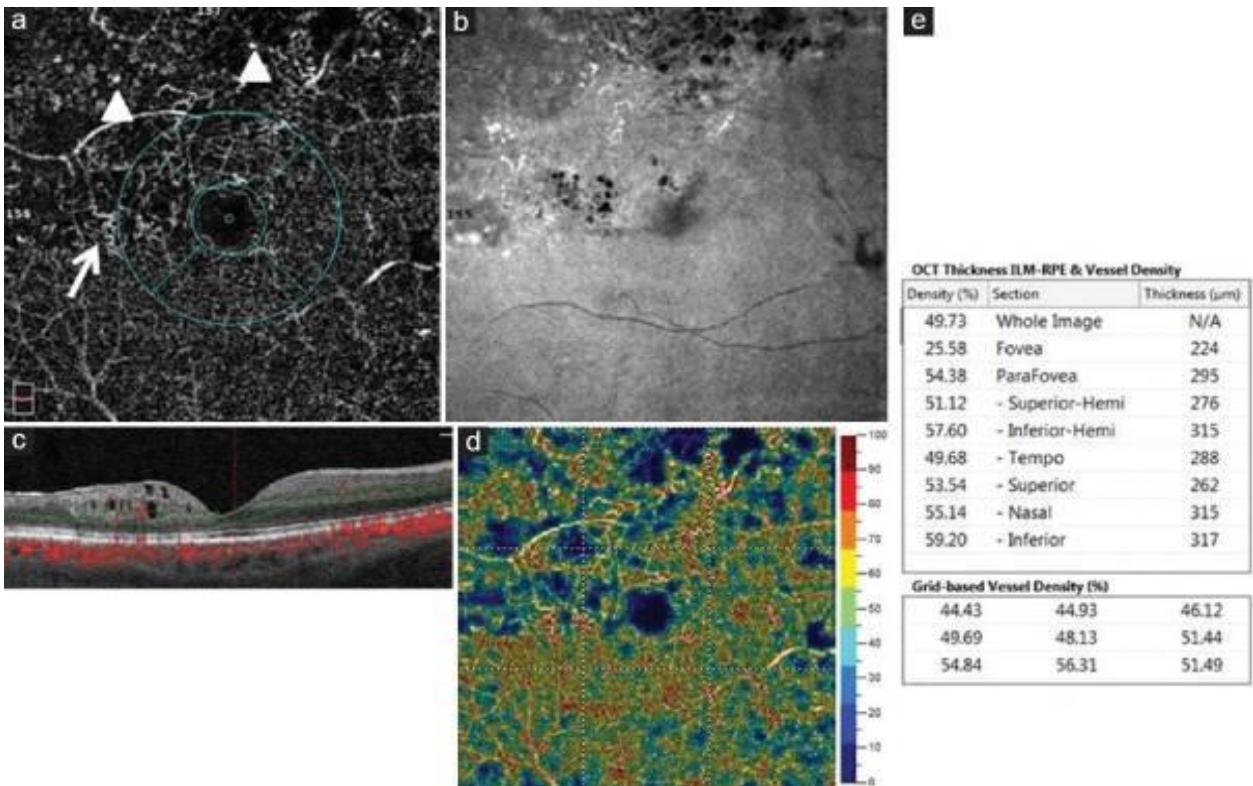


Figure 8: OCTA (6 × 6 mm) of a case of BRVO. (a) OCTA at the level of the deep capillary plexus (DCP). Shunt vessels (arrow) and microaneurysms (arrowheads) are visible in the superotemporal area along with decreased vascular density and non-perfusion areas (a), (b) En face OCT at the level of the DCP, (c) B-scan OCT with perfusion overlay and segmentation lines showing the level of OCTA in (a), (d) Color-coded vascular density map, (e) Numerical report of the vascular density [58].

8. Conclusions

Optical Coherence Tomography Angiography (OCTA) is rapid non-invasive imaging technology allowing high resolution three-dimensional images of retinal & choroidal vasculature. It allows visualization of different vascular structures which were not available by traditional examination method as FFA, therefore it allows more advances in diagnosis and management of different retinal pathologies. As it's dye-free technique, it allows easy & frequent follow up of different pathologies for better prognosis.

References

- [1] S. S. Gao, Y. Jia, M. Zhang, J. P. Su, G. Liu, T. S. Hwang, S. T. Bailey, D. Huang. (2016). Optical coherence tomography angiography. *Investigative ophthalmology & visual science*. 57 (9): e27-e36.
- [2] A. H. Kashani, C. L. Chen, J. K. Gahm, F. Zheng, G. M. Richter, P. J. Rosenfeld, Y. Shi, R. K. Wang. (2017). Optical coherence tomography angiography: a comprehensive review of current methods and clinical applications. *Progress in retinal and eye research*. 60 (1): e66-e100.
- [3] R. F. Spaide, J. G. Fujimoto, N. K. Waheed, S. R. Sadda, G. Staurengi. (2018). Optical coherence tomography angiography. *Progress in retinal and eye research*. 64 (1): e1-e55.
- [4] M. Ang, A. C. Tan, C. M. G. Cheung, P. A. Keane, R. Dolz-Marco, C. C. Sng, L. Schmetterer. (2018). Optical coherence tomography angiography: a review of current and future clinical applications. *Graefes Archive for Clinical and Experimental Ophthalmology*. 256 (1): e237-e245.
- [5] A. C. Tan, G. S. Tan, A. K. Denniston, P. A. Keane, M. Ang, D. Milea, U. Chakarvarthy, C. M. G. Cheung. (2018). An overview of the clinical applications of optical coherence tomography angiography. *Eye*. 32 (2): e262-e286.
- [6] D. R. Matsunaga, J. J. Yi, L. O. De Koo, H. Ameri, C. A. Puliafito, A. H. Kashani. (2015). Optical coherence tomography angiography of diabetic retinopathy in human subjects. *Ophthalmic Surgery, Lasers and Imaging Retina*. 46 (8): e796-e805.
- [7] R. F. Spaide, J. M. Klancnik, M. J. Cooney. (2015). Retinal vascular layers imaged by fluorescein angiography and optical coherence tomography angiography. *JAMA ophthalmology*. 133 (1): e45-e50.
- [8] M. E. van Velthoven, F. D. Verbraak, L. A. Yannuzzi, R. B. Rosen, A. G. Podoleanu, M. D. De Smet. (2006). Imaging the retina by en face optical coherence tomography. *Retina*. 26 (2): e129-e136.
- [9] D. C. Sousa, J. Breda, L. A. Pinto. (2018). Optical coherence tomography angiography. *American Academy of Ophthalmology*.
- [10] C. J. T. Ong, M. Y. Z. Wong, K. X. Cheong, J. Zhao, K. Y. C. Teo, T. E. Tan. (2023). Optical Coherence Tomography Angiography in Retinal Vascular Disorders. *Diagnostics*. 13 (9): e1620.
- [11] F. Pichi, D. Sarraf, S. Arepalli, C. Y. Lowder, E. T. Cunningham Jr, P. Neri, T. A. Albin, V. Gupta, K. Baynes, S. K. Srivastava. (2017). The application of optical coherence tomography angiography in uveitis and inflammatory eye diseases. *Progress in retinal and eye research*. 59 (1): e178-e201.
- [12] I. Lains, J. C. Wang, Y. Cui, R. Katz, F. Vingopoulos, G. Staurengi, D. G. Vavvas, J. W. Miller, J. B. Miller. (2021). Retinal applications of swept source optical coherence tomography (OCT) and optical coherence tomography angiography (OCTA). *Progress in retinal and eye research*. 84 (1): e100951.
- [13] M. Chlebiej, I. Gorczyńska, A. Rutkowski, J. Kluczewski, T. Grzona, E. Pijewska, B. L. Sikorski, A. Szkulmowska, M. Szkulmowski. (2019). Quality improvement of OCT angiograms with elliptical directional filtering. *Biomedical optics express*. 10 (2): e1013-e1031.
- [14] B. Turgut. (2016). Optical coherence tomography angiography—a general view. *Journal-Optical Coherence Tomography Angiography—A General View*.
- [15] K. E. Choi, C. Yun, J. Cha, S. W. Kim. (2019). OCT angiography features associated with macular edema recurrence after intravitreal bevacizumab treatment in branch retinal vein occlusion. *Scientific reports*. 9 (1): e14153.
- [16] P. A. Keane, S. R. Sadda. (2014). Retinal imaging in the twenty-first century: state of the art and future directions. *Ophthalmology*. 121 (12): e2489-e2500.
- [17] M. Hope-Ross, L. A. Yannuzzi, E. S. D. R. Gragoudas, J. S. Guyer, J. S. Slakter, J. A. Sorenson, S. Krupsky, D. A. Orlock, C. A. Puliafito. (1994). Adverse reactions due to indocyanine green. *Ophthalmology*. 101 (3): e529-e533.
- [18] M. López-Sáez, E. Ordoqui, P. Tornero, A. Baeza, T. Sainza, E. J. Zubeldia, M. L. Baeza, M. L. Baeza. (1998). Fluorescein-induced allergic reaction. *Annals of Allergy, Asthma & Immunology*. 81 (5): e428-e430.
- [19] K. R. Mendis, C. Balaratnasingam, P. Yu, C. J. Barry, I. L. McAllister, S. J. Cringle, D. Y. Yu. (2010). Correlation of histologic and clinical images to determine the diagnostic value of fluorescein angiography for studying retinal capillary detail. *Investigative ophthalmology & visual science*. 51 (11): e5864-e5869.
- [20] R. F. Spaide, C. A. Curcio. (2017). Evaluation of segmentation of the superficial and deep vascular layers of the retina by optical coherence tomography angiography instruments in normal eyes. *JAMA ophthalmology*. 135 (3): e259-e262.
- [21] D. A. Sim, P. A. Keane, R. Rajendram, M. Karampelas, S. Selvam, M. B. Powner, M. Fruittiger, A. Tufail, C. A. Egan. (2014). Patterns of peripheral retinal and central macula ischemia in diabetic retinopathy as evaluated by ultra-widefield fluorescein angiography. *American journal of ophthalmology*. 158 (1): e144-e153.

- [22] W. Choi, E. M. Moul, N. K. Waheed, M. Adhi, B. Lee, C. D. Lu, T. E. de Carlo, V. Jayaraman, P. J. Rosenfeld, J. S. Duker, J. G. Fujimoto. (2015). Ultrahigh-speed, swept-source optical coherence tomography angiography in nonexudative age-related macular degeneration with geographic atrophy. *Ophthalmology*. 122 (12): e2532-e2544.
- [23] X. N. Wang, X. Cai, S. W. Li, T. Li, D. Long, Q. Wu. (2022). Wide-field swept-source OCTA in the assessment of retinal microvasculature in early-stage diabetic retinopathy. *BMC ophthalmology*. 22 (1): e1-e11.
- [24] A. Couturier, P. A. Rey, A. Erginay, C. Lavia, S. Bonnin, B. Dupas, A. Gaudric, R. Tadayoni. (2019). Widefield OCT-angiography and fluorescein angiography assessments of nonperfusion in diabetic retinopathy and edema treated with anti-vascular endothelial growth factor. *Ophthalmology*. 126 (12): e1685-e1694.
- [25] J. Yang, B. Zhang, E. Wang, S. Xia, Y. Chen. (2021). Ultra-wide field swept-source optical coherence tomography angiography in patients with diabetes without clinically detectable retinopathy. *BMC ophthalmology*. 21 (1): e1-e8.
- [26] N. Suzuki, Y. Hirano, T. Tomiyasu, Y. Esaki, A. Uemura, T. Yasukawa, M. Yoshida, Y. Ogura. (2016). Retinal hemodynamics seen on optical coherence tomography angiography before and after treatment of retinal vein occlusion. *Investigative ophthalmology & visual science*. 57(13): 5681-5687.
- [27] K. G. Falavarjani, M. Al-Sheikh, H. Akil, S. R. Sadda. (2016). Image artefacts in swept-source optical coherence tomography angiography. *British Journal of Ophthalmology*.
- [28] R. F. Spaide, J. G. Fujimoto, N. K. Waheed. (2015). Image artifacts in optical coherence angiography. *Retina (Philadelphia, Pa.)*. 35 (11): e2163.
- [29] A. Zhang, Q. Zhang, C. L. Chen, R. K. Wang. (2015). Methods and algorithms for optical coherence tomography-based angiography: a review and comparison. *Journal of biomedical optics*. 20 (10): e100901.
- [30] T. E. De Carlo, A. Romano, N. K. Waheed, J. S. Duker. (2015). A review of optical coherence tomography angiography (OCTA). *International journal of retina and vitreous*. 1 (1): e1-e15.
- [31] Y. Huang, Q. Zhang, R. K. Wang. (2015). Efficient method to suppress artifacts caused by tissue hyper-reflections in optical microangiography of retina in vivo. *Biomedical optics express*. 6 (4): e1195-e1208.
- [32] K. K. Dansingani, A. C. Tan, F. Gilani, N. Phasukkijwatana, E. Novais, L. Querques, N. K. Waheed, J. S. Duker, G. Querques, L. A. Yannuzzi, D. Sarraf, K. B. Freund. (2016). Subretinal hyperreflective material imaged with optical coherence tomography angiography. *American journal of ophthalmology*. 169 (2): e235-e248.
- [33] T. T. Hormel, T. S. Hwang, S. T. Bailey, D. J. Wilson, D. Huang, Y. Jia. (2021). Artificial intelligence in OCT angiography. *Progress in Retinal and Eye Research*. 85 (1): e100965.
- [34] W. A. Samara, A. Shahlaee, M. K. Adam, M. A. Khan, A. Chiang, J. I. Maguire, J. Hsu, A. C. Ho. (2017). Quantification of diabetic macular ischemia using optical coherence tomography angiography and its relationship with visual acuity. *Ophthalmology*. 124 (2): e235-e244.
- [35] R. F. Spaide. (2015). Volume-rendered optical coherence tomography of diabetic retinopathy pilot study. *American journal of ophthalmology*. 160 (6): e1200-e1210.
- [36] P. R. C. De Oliveira, A. R. Berger, D. R. Chow. (2017). Optical coherence tomography angiography in chorioretinal disorders. *Canadian Journal of Ophthalmology*. 52 (1): e125-e136.
- [37] N. K. Waheed, E. M. Moul, J. G. Fujimoto, P. J. Rosenfeld. (2016). Optical coherence tomography angiography of dry age-related macular degeneration. *OCT Angiography in Retinal and Macular Diseases*. 56 (1): e91-e100.
- [38] D. Huang, Y. Jia, M. Rispoli, O. Tan, B. Lumbroso. (2015). OCT angiography of time course of choroidal neovascularization in response to anti-angiogenic treatment. *Retina (Philadelphia, Pa.)*. 35 (11): e2260.
- [39] T. E. de Carlo, A. Rosenblatt, M. Goldstein, C. R. Baumal, A. Loewenstein, J. S. Duker. (2016). Vascularization of irregular retinal pigment epithelial detachments in chronic central serous chorioretinopathy evaluated with OCT angiography. *Ophthalmic Surgery, Lasers and Imaging Retina*. 47 (2): e128-e133.
- [40] M. M. Teussink, M. B. Breukink, M. J. van Grinsven, C. B. Hoyng, B. J. Klevering, C. J. F. Boon, E. K. de Jong, T. Theelen. (2015). OCT angiography compared to fluorescein and indocyanine green angiography in chronic central serous chorioretinopathy. *Investigative ophthalmology & visual science*. 56 (9): e5229-e5237.
- [41] S. M. McClintic, Y. Jia, D. Huang, S. T. Bailey. (2015). Optical coherence tomographic angiography of choroidal neovascularization associated with central serous chorioretinopathy. *JAMA ophthalmology*. 133 (10): e1212-e1214.
- [42] T. Wakabayashi, T. Sato, C. Hara-Ueno, Y. Fukushima, K. Sayanagi, N. Shiraki, M. Sawa, Y. Ikuno, H. Sakaguchi, K. Nishida. (2017). Retinal microvasculature and visual acuity in eyes with branch retinal vein occlusion: imaging analysis by optical coherence tomography angiography. *Investigative ophthalmology & visual science*. 58 (4): e2087-e2094.
- [43] S. Kadomoto, Y. Muraoka, S. Ooto, Y. Miwa, Y. Iida, K. Suzuma, T. Murakami, R. Ghashut, A. Tsujikawa, N. Yoshimura. (2018). Evaluation of macular ischemia in eyes with branch retinal vein

- occlusion: an optical coherence tomography angiography study. *Retina*. 38 (2): e272-e282.
- [44] Q. Zhang, R. K. Wang, C. L. Chen, A. D. Legarreta, M. K. Durbin, L. An, U. Sharma, P. F. Stetson, J. E. Legarreta, L. Roisman, G. Gregori, P. J. Rosenfeld. (2015). Swept source OCT angiography of neovascular macular telangiectasia type 2. *Retina (Philadelphia, Pa.)*. 35 (11): e2285.
- [45] R. F. Spaide. (2015). Volume-rendered angiographic and structural optical coherence tomography. *Retina*. 35 (11): e2181-e2187.
- [46] L. Querques, C. Giuffrè, F. Corvi, I. Zucchiatti, A. Carnevali, L. A. De Vitis, F. Bandello. (2016). Optical coherence tomography angiography of myopic choroidal neovascularisation. *British Journal of Ophthalmology*.
- [47] A. Yarmohammadi, L. M. Zangwill, A. Diniz-Filho, L. J. Saunders, M. H. Suh, Z. Wu, P. I. C. Manalastas, T. Akagi, F. A. Medeiros, R. N. Weinreb. (2017). Peripapillary and macular vessel density in patients with glaucoma and single-hemifield visual field defect. *Ophthalmology*. 124 (5): e709-e719.
- [48] A. Y. Kim, D. C. Rodger, A. Shahidzadeh, Z. Chu, N. Koullisis, B. Burkemper, X. Jiang, K. L. Pepple, R. K. Wang, C. A. Puliafito, N. A. Rao, A. H. Kashani. (2016). Quantifying retinal microvascular changes in uveitis using spectral-domain optical coherence tomography angiography. *American journal of ophthalmology*. 171 (1): e101-e112.
- [49] J. J. Park, B. T. Soetikno, A. A. Fawzi. (2016). Characterization of the middle capillary plexus using optical coherence tomography angiography in healthy and diabetic eyes. *Retina (Philadelphia, Pa.)*. 36 (11): e2039.
- [50] N. Phasukkijwatana, N. Iafe, D. Sarraf. (2017). Optical coherence tomography angiography of A29 birdshot chorioretinopathy complicated by retinal neovascularization. *Retinal Cases and Brief Reports*. 11 (1): e68-e72.
- [51] F. Coscas, A. Glacet-Bernard, A. Miere, V. Caillaux, J. Uzzan, M. Lupidi, G. Coscas, E. H. Souied. (2016). Optical coherence tomography angiography in retinal vein occlusion: evaluation of superficial and deep capillary plexa. *American journal of ophthalmology*. 161 (1): e160-e171.
- [52] A. Glacet-Bernard, A. Sellam, F. Coscas, G. Coscas, E. H. Souied. (2016). Optical coherence tomography angiography in retinal vein occlusion treated with dexamethasone implant: a new test for follow-up evaluation. *European Journal of Ophthalmology*. 26 (5): e460-e468.
- [53] R. Mastropasqua, L. Toto, L. Di Antonio, E. Borrelli, A. Senatore, M. Di Nicola, P. Carpineto. (2017). Optical coherence tomography angiography microvascular findings in macular edema due to central and branch retinal vein occlusions. *Scientific reports*. 7 (1): e40763.
- [54] M. Adhi, M. A. Bonini Filho, R. N. Louzada, L. Kuehlewein, T. E. de Carlo, C. R. Baumanal,... & N. K. Waheed. (2016). Retinal capillary network and foveal avascular zone in eyes with vein occlusion and fellow eyes analyzed with optical coherence tomography angiography. *Investigative ophthalmology & visual science*. 57 (9): e486-e494.
- [55] A. H. Kashani, S. Y. Lee, A. Moshfeghi, M. K. Durbin, C. A. Puliafito. (2015). Optical coherence tomography angiography of retinal venous occlusion. *Retina*. 35 (11): e2323-e2331.
- [56] E. A. Novais, N. K. Waheed. (2016). Optical coherence tomography angiography of retinal vein occlusion. *OCT angiography in retinal and macular diseases*. 56 (1): e132-e138.
- [57] N. Suzuki, Y. Hirano, M. Yoshida, T. Tomiyasu, A. Uemura, T. Yasukawa, Y. Ogura. (2016). Microvascular abnormalities on optical coherence tomography angiography in macular edema associated with branch retinal vein occlusion. *American journal of ophthalmology*. 161 (1): e126-e132.
- [58] G. Tsai, T. Banaee, F. F. Conti, R. P. Singh. (2018). Optical coherence tomography angiography in eyes with retinal vein occlusion. *Journal of ophthalmic & vision research*. 13 (3): e315.
- [59] M. Rispoli, M. C. Savastano, B. Lumbroso. (2015). Capillary network anomalies in branch retinal vein occlusion on optical coherence tomography angiography. *Retina (Philadelphia, Pa.)*. 35 (11): e2332.
- [60] S. Ricco, M. Chen, H. Ishikawa, G. Wollstein, J. Schuman. (2009). Correcting motion artifacts in retinal spectral domain optical coherence tomography via image registration. In *Medical Image Computing and Computer-Assisted Intervention—MICCAI 2009: 12th International Conference, London, UK, September 20-24, 2009, Proceedings, Part I*. 12 (1): e100-e107.
- [61] R. F. Spaide. (2016). Retinal vascular cystoid macular edema: review and new theory. *Retina*. 36 (10): e1823-e1842.
- [62] A. Couturier, V. Mané, S. Bonnin, A. Erginay, P. Massin, A. Gaudric, R. Tadayoni. (2015). Capillary plexus anomalies in diabetic retinopathy on optical coherence tomography angiography. *Retina*. 35 (11): e2384-e2391.
- [63] M. C. Liang, R. A. Vora, J. S. Duker, E. Reichel. (2013). Solid-appearing retinal cysts in diabetic macular edema: a novel optical coherence tomography finding. *Retinal Cases & Brief Reports*. 7 (3): e255-e258.
- [64] M. B. Powner, D. A. Sim, M. Zhu, J. Nobre-Cardoso, R. Jones, A. Syed, M. Fruttiger. (2016). Evaluation of nonperfused retinal vessels in ischemic retinopathy. *Investigative ophthalmology & visual science*. 57 (11): e5031-e5037.
- [65] A. Singh, A. Agarwal, S. Mahajan, S. Karkhur, R. Singh, R. Bansal, V. Gupta. (2017). Morphological differences between optic disc collaterals and neovascularization on optical coherence tomography angiography. *Graefes Archive for Clinical and Experimental Ophthalmology*. 255 (1): e753-e759.
- [66] K. Sogawa, T. Nagaoka, A. Ishibazawa, A. Takahashi, T. Tani, A. Yoshida. (2015). En-face optical coherence tomography angiography of

- neovascularization elsewhere in hemicentral retinal vein occlusion. *International Medical Case Reports Journal*. e263-e266.
- [67] N. Koulisis, A. Y. Kim, Z. Chu, A. Shahidzadeh, B. Burkemper, L. C. Olmos de Koo, A. H. Kashani. (2017). Quantitative microvascular analysis of retinal venous occlusions by spectral domain optical coherence tomography angiography. *PloS one*. 12 (4): e0176404.
- [68] D. Seknazi, F. Coscas, A. Sellam, F. Rouimi, G. Coscas, E. H. Souied, A. Glacet-Bernard. (2018). Optical coherence tomography angiography in retinal vein occlusion: correlations between macular vascular density, visual acuity, and peripheral nonperfusion area on fluorescein angiography. *Retina (Philadelphia, Pa.)*. 38 (8): e1562.
- [69] M. C. Salles, A. Kvanta, U. Amrén, D. Epstein. (2016). Optical coherence tomography angiography in central retinal vein occlusion: correlation between the foveal avascular zone and visual acuity. *Investigative ophthalmology & visual science*. 57 (9): e242-e246.
- [70] W. A. Samara, E. A. Say, C. T. Khoo, T. P. Higgins, G. Magrath, S. Ferenczy, C. L. Shields. (2015). Correlation of foveal avascular zone size with foveal morphology in normal eyes using optical coherence tomography angiography. *Retina*. 35 (11): e2188-e2195.
- [71] Y. K. Aribas, A. M. Hondur, T. H. Tezel. (2020). Choroidal vascularity index and choriocapillary changes in retinal vein occlusions. *Graefe's Archive for Clinical and Experimental Ophthalmology*. 258 (1): e2389-e2397.