Review

Eur Arch Med Res 2018; 34 (Suppl. 1): S37-S41

Optical Coherence Tomography Angiography: A New Vision Into The Future of Retinal Imaging

Burak Erden

Department of Ophthalmology, University of Health Sciences, Okmeydanı Education and Research Hospital, İstanbul, Turkey

Abstract

Optical coherence tomography angiography (OCTA) is a brand new imaging tool developed and clinically introduced recently into the ophthalmological diagnostic tool armamentarium. OCTA enables a segmented and detailed examination of retinal vasculature and structure in a non-invasive fashion within a few seconds based on the present and widespread OCT technology. Retinal and glaucoma specialists can evaluate vascular circulation in every possible separate layer for the first time in ocular imagining history and acquire a new understanding in the pathological process of ophthalmological diseases using OCTA. The developing process of this innovative technology is still in progress by companies based on the clinical feedback of the leading clinicians, in software and hardware, overcoming the technical limitations of OCTA and leading to re-evaluation of well-known diseases.

Keywords: Optical coherence tomography angiography, retina, glaucoma

INTRODUCTION

There are several milestones in ophthalmological imaging that contributed to the clinical understanding and treatment approaches of retinal diseases. First, in the 1960s, fundus fluorescein (FFA) (1) and indocyanine green angiography (2) were introduced based on the optical fluorescence characteristics of intravenous dyes, widening our knowledge about choroidal and retinal circulation and vascular pathologies. In the 2000s, optical coherence tomography (OCT) appeared into our daily practice, enlightening the microstructure of both retina and choroid in microns, enabling clinicians and researchers to understand the pathogenesis of daily encountered diseases, and leading to a much superior clinical approach. Recently, another milestone in imaging, optical coherence tomography angiography (OCTA), is developed based on the principles of conventional OCT. Now, for the first time in ophthalmological history, we can demonstrate the retinal microcirculation in segmented fashion. The non-invasive OCTA enabled the separate evaluation of the superficial and deep capillary plexi of the retina, choroid, and peripapillary circulation. Even mysterious vascular lesions hidden under the retina pigment epithelium (RPE) can be detected and evaluated. Although this brand new tool may have been underestimated by some retinal specialists, especially due to the technical limitations, at the beginning, its fast progress, with the feedback between the leading clinicians and companies, led to perfection. The many publications in the literature in several subspecialties of ophthalmology, such as glaucoma, cornea, or retina alone, indicated that OCTA has already become a must of our imaging armamentarium.

Technical Features

Optical coherence tomography angiography (OCTA) is technically derived from the conventional OCT technology. It compares the decorrelation signal (differences in the backscattered OCT signal intensity or amplitude) between sequential OCT B-scans obtained precisely at the same cross-section of the retina to construct a three-dimensional map of blood flow. This technique

ORCID ID of the author:
B.E. 0000-0003-0650-4552.

Cite this article as:
Erden B. Optical Coherence Tomography Angiography: A New Vision Into The Future of Retinal Imaging. Eur Arch Med Res 2018; 34 (Suppl. 1): S37-S41.

Corresponding Author:
Burak Erden

E-mail:
drburakerden@gmail.com

Received: : 01.10.2018

Accepted: 24.10.2018

DOI: 10.5152/eamr.2018.40427

may be comparable with subtraction of two consecutive images to represent motional differences (Figure 1). The sites of signal differences between sequential OCT high-resolution B-scans represent automatically and only erythrocyte movements in the retinal vessels, leading to an angiographical image in a non-invasive fashion (Figure 2). The OCTA required naturally higher scanning speeds (70 kHz vs. 25 kHz) and faster eye trackers than conventional OCT systems in order to obtain signal differences at precisely the same retinal loci without increasing the scanning time. Several medical imaging companies released different models into the market (Figure 3) and are still developing software and hardware systems in cooperation with the clinicians on the retinal field to solve the real-life conflicts of their systems. Recently, although AngioPlex (Carl Zeiss Meditec, Dublin, CA, USA) is also widely evaluated in many publications, the AngioVue OCTA (Optovue, Inc., Fremont, CA, USA) has a minor superiority in aspects of clinical usefulness over the other companies.

Comparison of OCTA with Conventional FFA

In contrast to OCTA, conventional FFA examination is basically an invasive test requiring intravenous administration of fluorescein dye and a time-consuming practice, depending on the clinical situation, up to 10 min. With FFA, clinicians can evaluate the functional status and integrity of the microvascular structure of the retina, choroid, and even RPE based on the specific patterns of fluorescein, such as leakage, pooling, or staining. However, this two-dimensional FFA angiogram lacks the capacity of differentiation of over- or underlying tissues, making the exact imaging of, for example, type 2 choroidal neovascular membranes (CNVs) under RPE impossible, which were ill-defined by FFA and had been called as "occult membranes." These blurred borders of type 2 CNVs complicated the photodynamic therapy, which was the only treatment option in wet age-related macular degeneration (AMD) one decade ago. Nowadays, through OCTA, we can analyze the "occult membranes" in details and evaluate even the maturity of these CNVs. In contrast to conventional FFA, OCTA is non-invasive, captured in seconds, and three-dimensional. These three-dimensional images enable retinal specialists to evaluate each vascular layer separately. The only inferiority of OCTA is its lack of information about vascular integrity and function (Table 1).

Figure 1. The basic principle of OCTA. Imaging of motion differences of two consecutive photo images digitally reproduces the image of water flow from a tap

Clinical Applications of OCTA

Diabetic retinopathy (DRP) can be defined as a microvascular disease, developed secondary to chronic hyperglycemia, based mainly on capillary and microcirculation changes of the retina. Ischemia and non-perfusion areas are crucial to determine the degree and status of the disease (3). With conventional FFA, non-perfusion and leakage areas can be detected, unless images are obscured by superposing of the capillary plexi (4). In many cases, chronic capillary leakage in the late phases of the conventional angiograms superposes the critical foveal avascular zone (FAZ) or peripheral non-perfusion areas so that the clinicians cannot determine the status of the macula or periphery reliably. Through OCTA, superficial and deep capillary plexi can be evaluated by automated segmentation separately so that FAZ enlargement secondary to macular ischemia can be detected in deep or superficial plexus (5), pointing out to worse prognosis at even the early non-proliferative DRP stages. Lately, the major disadvantage of lacking wide-field imaging in OCTA has been overcome by various montage techniques in recent software versions so that real peripheral capillary dropout areas can be determined without the FFA superposing leakage effect (6); clinicians can determine for proper treatment mo-

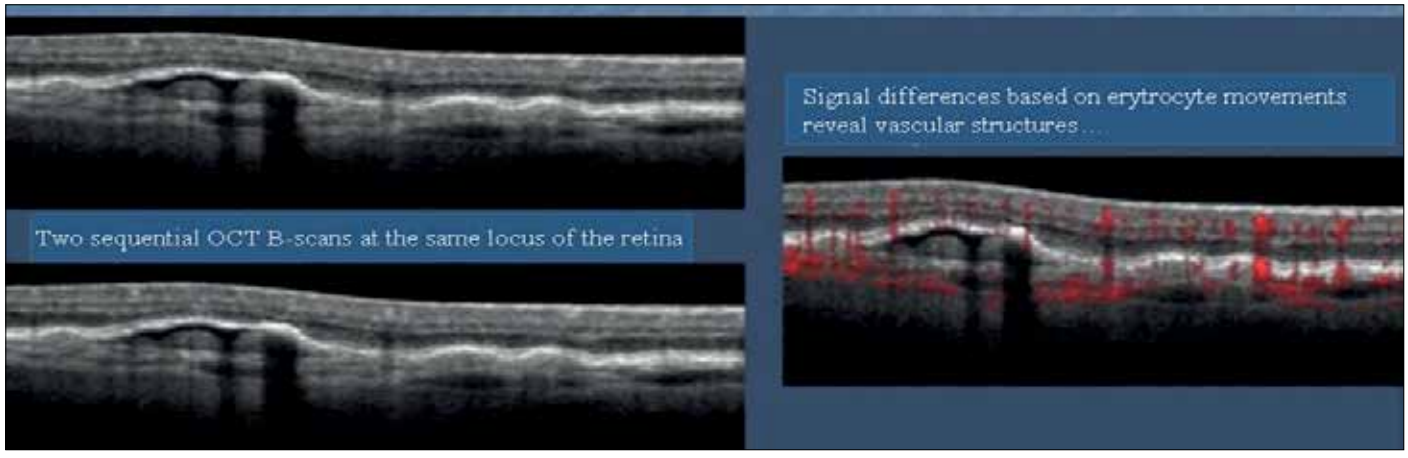
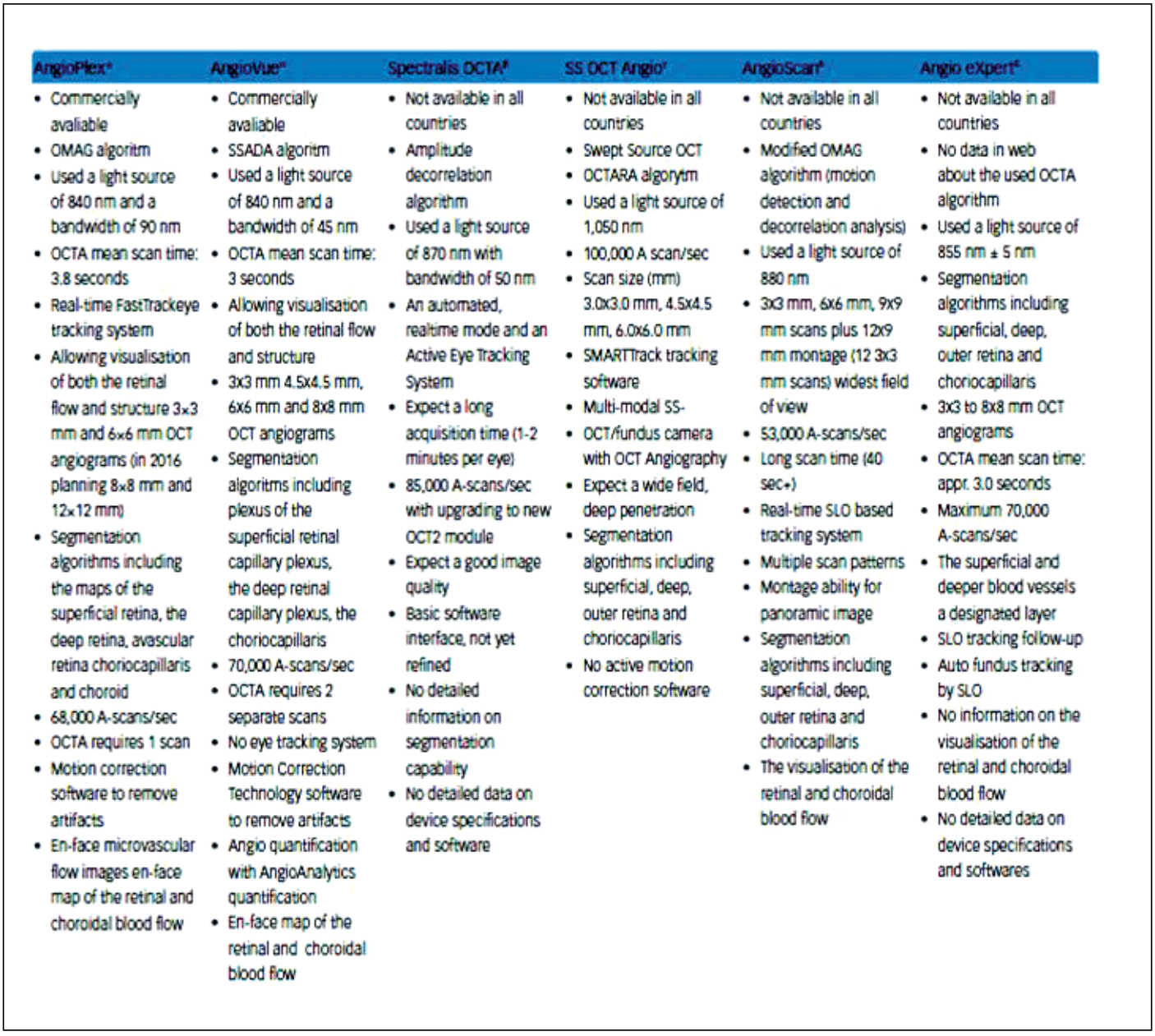


Figure 2. The signal differences between two sequential structural B-scans reveal vascular structure based on intravascular erythrocyte movements



AngioPlex®	AngioVue®	Spectralis OCTA®	SS OCT Angio®	AngioScan®	Angio eXpert®
• Commercially avaliable • OMAG algoritm • Used a light source of 840 nm and a bandwidth of 90 nm • OCTA mean scan time: 3.8 seconds • Real-time FastTrackeye tracking system • Allowing visualisation of both the retinal flow and structure 3×3 mm and 6×6 mm OCT angiograms (in 2016 planning 8×8 mm and 12×12 mm) • Segmentation algorithms including the maps of the superficial retina, the deep retina, avascular retina choriocapillaris and choroid • 68,000 A-scans/sec • OCTA requires 1 scan • Motion correction software to remove artifacts • En-face microvascular flow images en-face map of the retinal and choroidal blood flow	• Commercially avaliable • SSADA algoritm • Used a light source of 840 nm and a bandwidth of 45 nm • OCTA mean scan time: 3 seconds • Allowing visualisation of both the retinal flow and structure • 3x3 mm 4.5x4.5 mm, 6x6 mm and 8x8 mm OCT angiograms • Segmentation algoritms including plexus of the superficial retinal capillary plexus, the deep retinal capillary plexus, the choriocapillaris • 70,000 A-scans/sec • OCTA requires 2 separate scans • No eye tracking system • Motion Correction Technology software to remove artifacts • Angio quantification with AngioAnalytics quantification • En-face map of the retinal and choroidal blood flow	• Not available in all countries • Amplitude decorrelation algorithm • Used a light source of 870 nm with bandwidth of 50 nm • An automated, realtime mode and an Active Eye Tracking System • Expect a long acquisition time (1-2 minutes per eye) • 85,000 A-scans/sec with upgrading to new OCT2 module • Expect a good image quality • Basic software interface, not yet refined • No detailed information on segmentation capability • No detailed data on device specifications and software	• Not available in all countries • Swept Source OCT • OCTARA algorytm • Used a light source of 1,050 nm • 100,000 A scan/sec • Scan size (mm) 3.0x3.0 mm, 4.5x4.5 mm, 6.0x6.0 mm • SMARTTrack tracking software • Multi-modal SS- • OCT/fundus camera with OCT Angiography • Expect a wide field, deep penetration • Segmentation algorithms including superficial, deep, outer retina and choriocapillaris • No active motion correction software	• Not available in all countries • Modified OMAG algorithm (motion detection and decorrelation analysis) • Used a light source of 880 nm • 3x3 mm, 6x6 mm, 9x9 mm scans plus 12x9 mm montage (12 3x3 mm scans) widest field of view • 53,000 A-scans/sec • Long scan time (40 sec+) • Real-time SLO based tracking system • Multiple scan patterns • Montage ability for panoramic image • Segmentation algorithms including superficial, deep, outer retina and choriocapillaris • The visualisation of the retinal and choroidal blood flow	• Not available in all countries • No data in web about the used OCTA algorithm • Used a light source of 855 nm ± 5 nm • Segmentation algorithms including superficial, deep, outer retina and choriocapillaris • 3x3 to 8x8 mm OCT angiograms • OCTA mean scan time: appr. 3.0 seconds • Maximum 70,000 A-scans/sec • The superficial and deeper blood vessels a designated layer • SLO tracking follow-up • Auto fundus tracking by SLO • No information on the visualisation of the retinal and choroidal blood flow • No detailed data on device specifications and softwares

Figure 3. Comparison of technical features of leading ophthalmological imaging companies' OCTA systems. From left to right: Zeiss, Optovue, Heidelberg, Topcon, Nidek, and Canon

dalities according to these new findings. In patient follow-up, the progression or regression of foveal or peripheral ischemia, capillary dropout in deep or superficial plexi, can be also easily visualized.

In neovascular wet AMD, three different subtypes of CNV were defined; type 1 is underlying beneath the RPE, type 2 CNVs are of classic nature, originating from the choroid branching into the retina, and type 3 CNVs are called as retinal angiomatous proliferations, whereas these lesions are mainly developing in the retinal layers. OCTA can detect all these three subgroups of choroidal neovascular membranes, mapping them in different colors to differentiate these lesions from normal retinal capillary plexi. This ability of visualization enables us to isolate, define, understand, and follow the treatment response of CNVs (Figure 4). Recently, the degree of maturity of CNVs was described in various publications, changing our anti-vascular endothelial growth factor (VEGF) treatment indications in a proactive fashion (7). In contrast to structural OCT scans, where the retinal specialists search for disease activation in the form of intra- or subretinal fluid, the immaturity of CNVs might be a new indication for anti-VEGF treatment, preventing the patients' visual impairment in a proactive fashion. OCTA can detect even polypoidal choroidal vasculopathy lesions (8), underneath the highly reflective RPE, and their treatment response in a reliable degree (9). Another often conventional OCT scans mysterious lesions are pigment epithelial detachments (PEDs) of different types. Owing to the high reflectivity of RPE, PEDs are different to classify, and recently combined with en face OCT scans OCT angiograms, clinicians

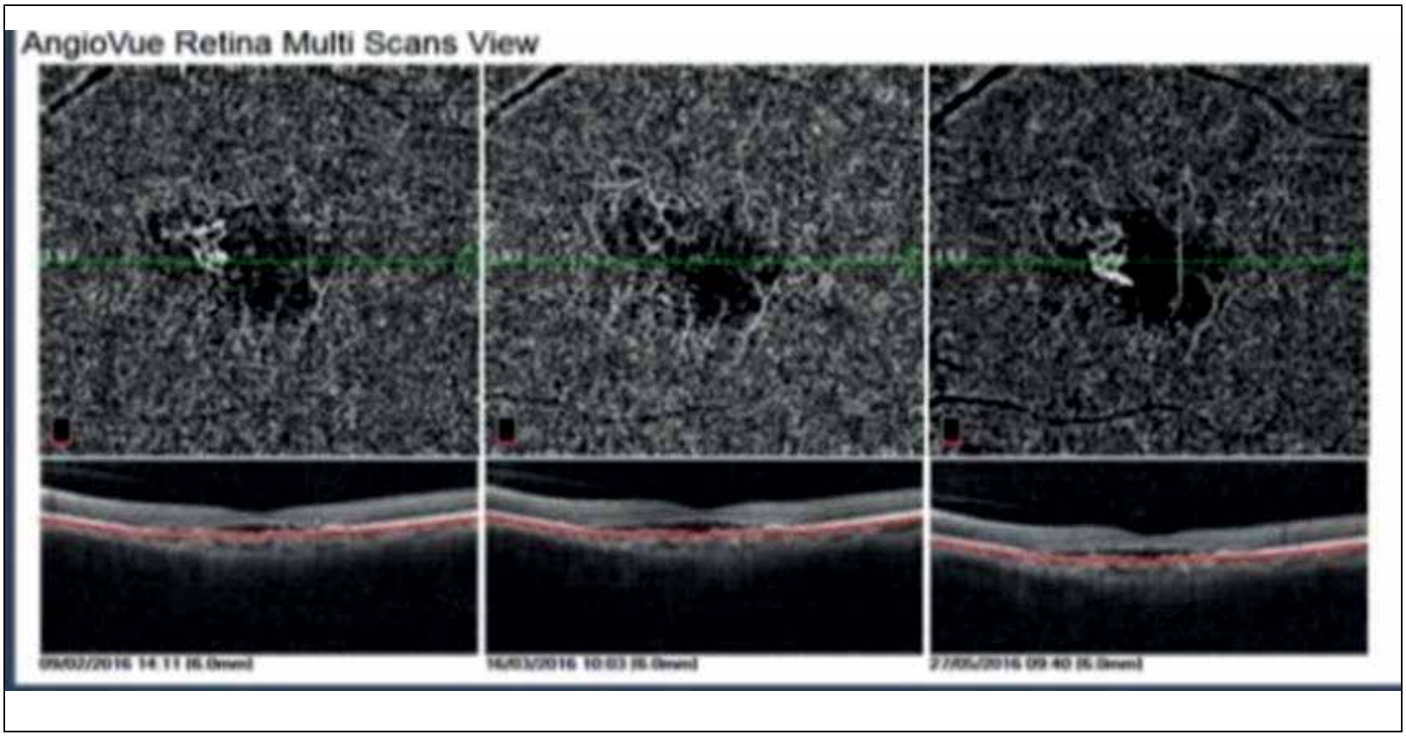


Figure 4. A type 2 CNV detected at the outer retina beneath the RPE (left) regresses after anti-VEGF treatment (middle) and reactivates in follow-up (right) as demonstrated by AngioVue follow-up modus

Table 1. The faster acquisition time, its' non-invasive nature and ability of segmentation are dominant advantages of OCTA, whereas FFA is still crucial to obtain information about the integrity and function of retinal vasculature

	FFA	OCTA
Segmentation	-	+
Duration	10-15 min	3sec
Need of Dye	+	-
Artefacts	-	+
Information	Functional	Structural
Wide-field	+	-/+

can evaluate the critical component of PEDs, namely vascularization (10). In chronic central serous chorioretinopathy cases, there was an ongoing debate about the treatment options. The most commonly suspected etiology for chronicity of this disease was a possible CNV, which was shown also by OCTA angiograms (11), thus indicating the anti-VEGF treatment for such chronic recurrent cases.

In the area of glaucoma, a progressive disease, where glaucoma specialists relied on visual field examinations and retinal nerve fiber analyses with structural OCT for detection of progression, OCTA enlighten the subtle peripapillary vascular changes prior to any clinical or imaging findings (12). Kumar et al. found that the glaucoma severity score in OCTA identifies preperimetric glaucoma and early glaucoma better than visual fields (13). Averaging the decorrelation signal in OCT angiograms allows us to calculate the flow index of the optic disc area, which is lower in glaucomatous eyes (14) than in the normal population (15).

CONCLUSION

The introduction of OCTA into our daily practice has changed our understanding and clinical approach in certain diseases dramatically. This new technologies' ability of further progress is welcomed by the ophthalmological society, even in each subspecialty. The cooperation and co-work of companies with clinicians is producing new astonishing results ready to change and widen our vision into ophthalmic diseases greatly in the coming years. OCTA itself has already become a must in our daily diagnostic technological armamentarium.

Peer-review: Externally peer-reviewed.

Conflict of Interest: The author has no conflicts of interest to declare.

Financial Disclosure: The author declared that this study has received no financial support.

REFERENCES

1. Novotny HR, Alvis DL. A method of photographing fluorescence in circulating blood in the human retina. Circulation 1961; 24: 82-6. [CrossRef]
2. Yannuzzi LA, Slakter JS, Sorenson JA, Guyer DR, Orlock DA. Digital indocyanine green videoangiography and choroidal neovascularization. Retina 1992; 12: 191-223. [CrossRef]
3. Arend O, Wolf S, Jung F, Bertram B, Pöstgens H, Toonen H, et al. Retinal microcirculation in patients with diabetes mellitus: dynamic and morphological analysis of perifoveal capillary network. Br J Ophthalmol 1991; 75: 514-8. [CrossRef]
4. Mendis KR, Balaratnasingam C, Yu P, Barry CJ, McAllister IL, Cringle SJ, et al. Correlation of histologic and clinical images to determine

the diagnostic value of fluorescein angiography for studying retinal capillary detail. Invest Ophthalmol Vis Sci 2010; 51: 5864-9. [CrossRef]
5. Couturier A, Mané V, Bonnin S, Erginay A, Massin P, Gaudric A, et al. Capillary Plexus Anomalies in Diabetic Retinopathy on Optic Coherence Tomogaphy Angiography. Retina 2015; 35: 2384-91. [CrossRef]
6. Or C, Sabrosa AS, Sorour O, Arya M, Waheed N. Use of OCTA, FA, and Ultra-Widefield Imaging in Quantifying Retinal Ischemia: A Review. Asia Pac J Ophthalmol (Phila)2018; 7: 46-51. [CrossRef]
7. Miere A, Butori P, Cohen SY, Semoun O, Capuano V, Jung C, et al. Vascular Remodeling of Choroidal Neovascularization After anti-Vascular Endothelial Growth Factor Therapy Visualized on Optical Coherence Tomography. Retina 2017; DOI: 10.1097/IAE.0000000000001964. [CrossRef]
8. de Carlo TE, Kokame GT, Kaneko KN, Lian R, Lai JC, Wee R. Sensitivity and Specificity of Detecting Polypoidal choroidal Vasculopathy With En Face Optical Coherence Tomography and Optical Coherence Tomography Angiography. Retina 2018; DOI: 10.1097/IAE.0000000000002139. [CrossRef]
9. Eriş E, Perente İ, Vural E, Yaşa D, Ozkaya A. Assessment of focal laser photocoagulations' early effect on polypoidal choroidal vasculopathy with optical coherence tomography angiography. Lasers Med Sci 2018; DOI: 10.1007/s10103-018-2463-3. [CrossRef]
10. Tan ACS, Freund KB, Balaratnasingam C, Simhaee D, Yannuzzi LA. Imaging of Pigment Epithelial Detachments with Optical cohernece Tomography Angiography. Retina 2018; 38: 1759-69. [CrossRef]
11. Moussa M, Leila M, Khalid H, Lolah M. Detection of Silent Type I Choroidal Neovascular Membrane in Chronic Central Serous Chorioretinopathy Using En Face Swept-Source Optical Coherence Tomography Angiography. J Ophthalmol 2017; DOI: 10.1155/2017/6913980. [CrossRef]
12. Lee EJ, Lee KM, Lee SH, Kim TW. OCT Angiography of the Peripapillary Retina in Primary Open-Angle Glaucoma. Invest Ophthalmol Vis Sci 2016; 57: 6265-70. [CrossRef]
13. Kumar RS, Anegondi N, Chandapura RS, Sudhakaran S, Kadambi SV, Rao HL, et al. Discriminant Function of Optical Coherence Tomography Angiography to Determine Disease Severity in Glaucoma. Invest Ophthalmol Vis Sci 2016; 57: 6079-88. [CrossRef]
14. Jia Y, Wei E, Wang X, Zhang X, Morrison JC, Parikh M, Lombardi LH, et al. Optical coherence tomography angiography of optic disc perfusion in glaucoma. Ophthalmology 2014; 121: 1322-32. [CrossRef]
15. Jia Y, Morrison JC, Tokayer J, Tan O, Lombardi L, Baumann B, et al. Quantitative OCT angiography of optic nerve head blood flow. Biomed Opt Express 2012; 3: 3127-37. [CrossRef]