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Flash Look

OCT angiography: redefining standards

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BACKGROUND

The advent of optical coherence tomography (OCT) revolutionized retinal imaging by providing a fast, simple, and noninvasive method to assess retinal structure at a microscopic level[1,2]. Since its debut more than two decades ago, the technology behind OCT has evolved drastically, with profound improvements in speed, resolution and imaging depth. The explosive growth of OCT in clinical practice was noted after the commercial introduction of the Stratus OCT by Carl Zeiss Meditec (Jena, Germany). With the emergence of spectral-domain (SD) OCT systems, higher scanning speeds and eye tracking have led to higher-resolution cross-sectional images of the retina that cannot be obtained by any other noninvasive diagnostic technique[3]. SD--OCT has improved the quality of clinical decision making[4], hence becoming an invaluable tool for any retinal specialist.

With enhance depth imaging (EDI) and swept-source (SS) OCT systems, better penetration and improved signal strength in the choroid have facilitated a qualitative and quantitative assessment of this structure[5]. However, even the most advanced structural OCTs do not provide an adequate visualization of the choriocapillaries, rendering it necessary to call upon angiography systems - fluorescein angiography (FA) and indocyanine green angiography (ICGA).

Both FA and ICGA are invasive imaging techniques that require intravenous injection of a dye – fluorescein or indocyanine green, respectively. Although generally safe, side effects like nausea, vomiting or even severe allergic reactions may develop in a minority of patients, thus limiting its repeated use[6,7]. Furthermore, given its dynamic nature, ICGA and FA are time-dependent, with an initial, intermediate and late phase[8]. FA has been adopted as the gold standard for *in vivo* evaluation of the retinal circulation because the architecture of the blood vessels, the blood flow and leakage from damaged/diseased retinal capillaries can be evaluated easily[9]. However, not all the capillary networks can be appraised with FA[9,10]. Fluorescein spreads through the fenestrations of the choriocapillaries, rendering it difficult to accurately assess this vascular layer[8]. To overcome this issue, ICGA is usually performed whenever a good visualization of the choroidal anatomy is needed (e.g. exudative age-related macular degeneration, namely in polypoidal choroidal vasculopathy or occult choroidal neovascularization)[11]. Nevertheless, ICGA is neither available nor routinely performed in many institutions throughout the world.

OPTICAL COHERENCE TOMOGRAPHY ANGIOGRAPHY

OCT angiography (OCTA) is a revolutionary imaging technique that allows noninvasive, three-dimensional visualization of the retinal and choroidal vasculature via motion contrast imaging[12,13]. Angio-OCT is capable of detecting endoluminal flow by mapping erythrocyte movement over time and comparing sequential OCT B-scans at a given crosssection[12]. The split-spectrum amplitude-decorrelation angiography (SSADA) algorithm and the motion correction tool are two patented primary technologies developed to improve the signal-to-noise ratio of flow detection and to remove unavoidable saccadic artifacts, respectively[14,15]. These technologies have significantly improved the quality of the vascular images, thus enabling the *in vivo* acquisition of high-speed, dyeless, microvascular angiograms, representing a true extension of capabilities from SD-OCT[4,13]. The inherent advantages of OCTA appear to be the ability to optically dissect and visualize flow in various layers of the retina, the high obtainable resolution and the freedom and safety of frequent examinations because of not having to use an injected dye[9].

By using the en face OCT technology, layer segmentation is automatically generated to identify areas of interest, such as the superficial and deep retinal vascular plexuses or the choriocapillaries (Fig 1). The superficial vascular plexus, located in the ganglion cell layer (GCL) and nerve fiber layer (NFL) is exposed at a thickness of 60 µm from the internal limiting membrane (ILM). Although anatomically distinct,

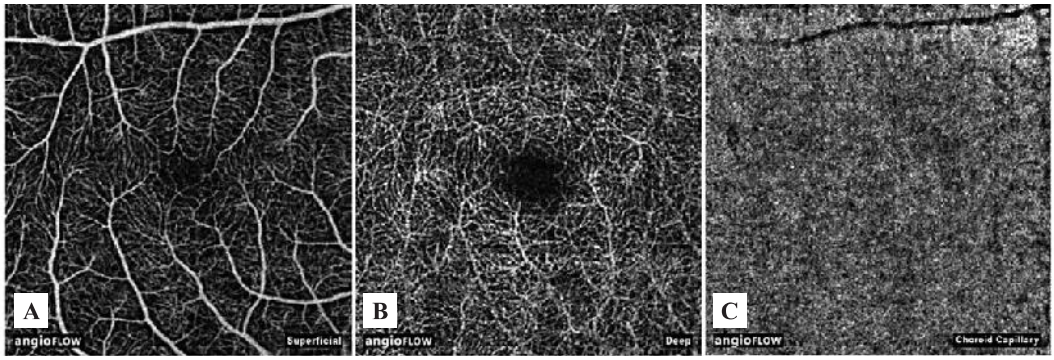

Fig. 1 | Optical coherence tomography angiography (OCTA) of a healthy subject showing the superficial vasculae plexus (**A**), deep vascular plexus (**B**) and choriocapillaris (**C**). The clear individualization of the superficial and deep vascular plexuses is a remarkable novelty in retinal imaging brought by OCTA.

the two deep plexuses, located in the inner nuclear layer (INL) and outer plexiform layer (OPL), cannot be individualized and are thus seen as one single vascular plexus (Fig 1B).

The parameters for the deep plexuses are defined with reference to the inner plexiform layer (IPL) in a 30 µm thick scan[8]. To evaluate the choriocapillaries, segmentation is performed at the level of Bruch's membrane.

CLINICAL APPLICATIONS

Recently, the 70 kHz Avanti RTVue XR equipped with the AngioVue software (Optovue, Fremont, CA, USA) has become commercially available, facilitating a wider-spread clinical access to OCTA. While still in a germinal stage, descriptive studies on the clinical applications of OCTA are beginning to materialize[12,13,16-21]. Exudative age-related macular degeneration and other causes of choroidal neovascularization (CNV); diabetic retinopathy (DR); retinal vein occlusions (RVO) and glaucoma are some of the finest examples.

An unrivaled visualization of the CNV net is now possible with OCTA. The morphology (tree-like, glomerular, fragmented), the presence of a fibrovascular capsule, afferent feeder trunk and peripheral anastomosis can be clearly assessed. Furthermore, the non-invasive nature of the technique allows for a convenient lesion monitoring through sequential examinations during and after treatment (Fig 2).

In RVO, OCTA may show capillary dropout and focal non-perfusion as dark areas (similar to FA), foveal ring disruption, increased foveal avascular zone (FAZ) and collaterals, both in the superficial and in the deep vascular plexuses (Fig 3).

In patients with DR, OCTA shows a foveal avascular zone (FAZ) larger than in healthy subjects (normal FAZ ~500 µm) and according to Lumbroso et al[8] this is an early

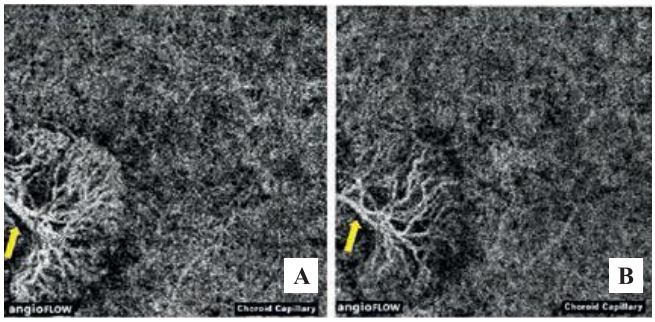

Fig. 2 | A tree-like choroidal neovascularization net of a patient with exudative age-related macular degeneration before (**A**) and 1 week after (**B**) an intravitreal injection of aflibercept. Note the afferent feeder trunk (yellow arrow), the peripheral anastomosis and the loss of peripheral capillaries, vessel fragmentation and decreased vessel density after treatment (right).

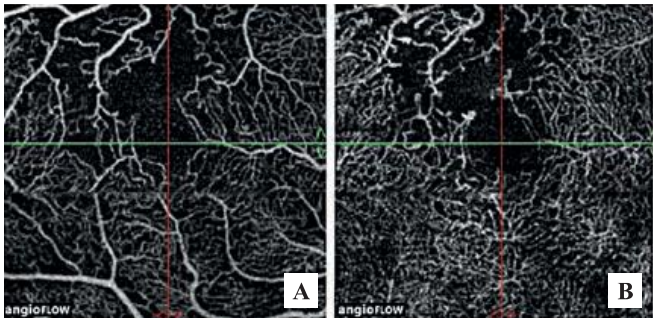

Fig. 3 | Superficial (**A**) and deep (**B**) retinal vascular plexuses in a patient with superior temporal branch retinal vein occlusion (BRVO). Note the areas of capillary dropout and nonperfusion (dark areas), the disruption of the foveal ring, increased foveal avascular zone (FAZ) and collaterals. All the changes are evident in both vascular networks.

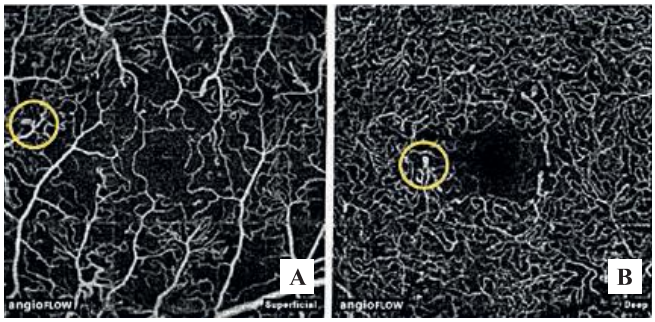

Fig. 4 | Superficial (**A**) and deep (**B**) retinal vascular plexuses in a patient with long.standing type 2 diabetes mellitus and mild nonproliferative diabetic retinopathy. Note the microaneurysms both in the superficial and deep plexuses (yellow circles), areas of capillary dropout and nonperfusion (dark areas) and a large and irregular foveal avascular zone (FAZ) with loss of the usual centripetal arrangement of the bordering vascular network.

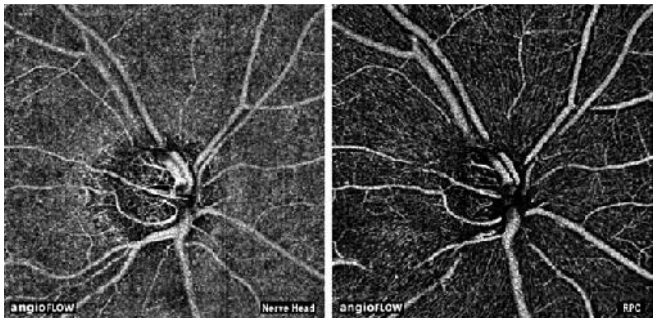

Fig. 5 | Optical coherence tomography angiography (OCTA) of a healthy subject showing a dense vascular network inside and around the optic disc.

sign of DR that appears before the inception of microaneurysms. As clearly depicted in Figure 4, a loose network with large and sparse meshes can be easily appreciated, even in patients with mild nonproliferative DR. Microaneurysms appear as focally dilated saccular or fusiform capillaries on OCT angiograms of the superficial and/or deep capillary plexus (Fig 4). Retinal non-perfused areas are seen as lesions with no or sparse capillaries on OCT angiograms (Fig 4). Ishibazawa et al[17] have concluded from a pilot study with OCTA in diabetic retinopathy that this new imaging technique may be clinically useful to evaluate the microvascular status and therapeutic effect of treatments for DR. Neovascularization at the optic disc or posterior pole can also be imaged and clearly discernible with OCTA[8,17].

OCTA of the optic nerve head of healthy subjects shows a very dense vascular network around the disc that cannot be detected in FA (Fig 5). Jia et al[18] have found that this network is greatly attenuated in glaucomatous discs. Further studies are needed to determine its correlation with the rate of progression and whether disc perfusion can be used as a prognostic indicator.

CONCLUSION

This path-breaking imaging modality is redefining our understanding of several vascular disorders by conveying detailed, depth-resolved information on the retinal and choroidal vascular networks, both at a structural and functional level. Although far from perfect, the technology behind OCTA may very well be the future gold standard of retinal and choroidal imaging.

REFERENCES

1. Huang D, Swanson EA, Lin CP, et al. Optical coherence tomography. Science 1991;254:1178-81.
2. Swanson EA, Izatt JA, Hee MR, et al. In vivo retinal imaging by optical coherence tomography. Optics Letters 1993;18:1864-6.
3. Drexler W, Fujimoto JG. State-of-the-art retinal optical coherence tomography. Progress in Retinal and Eye Research 2008;27:45-88.
4. Puliafito CA. OCT angiography: the next era of OCT technology emerges. Ophthalmic Surgery, Lasers & Imaging retina 2014;45:360.
5. Alasil T, Ferrara D, Adhi M, et al. En face imaging of the choroid in polypoidal choroidal vasculopathy using swept-source optical coherence tomography. American Journal of Ophthalmology 2015;159:634-43 e2.
6. Su Z, Ye P, Teng Y, Zhang L, Shu X. Adverse reaction in patients with drug allergy history after simultaneous intravenous fundus fluorescein angiography and indocyanine green angiography. Journal of ocular pharmacology and therapeutics : the official journal of the Association for Ocular Pharmacology and Therapeutics 2012;28:410-3.
7. Lipson BK, Yannuzzi LA. Complications of intravenous fluorescein injections. International Ophthalmology Clinics 1989;29:200-5.
8. Lumbroso BH, D.; Jia, Y; Fujimoto, J.G.; Rispoli, M. Clinical Guide to Angio-OCT: Non Invasive, Dyeless OCT Angiography. First ed: Jaypee Brothers Medical Publishers; 2015.
9. Spaide RF, Klancnik JM, Jr., Cooney MJ. Retinal vascular layers imaged by fluorescein angiography and optical coherence tomography angiography. JAMA Ophthalmology 2015;133:45-50.
10. Matsunaga D, Yi J, Puliafito CA, Kashani AH. OCT

angiography in healthy human subjects. Ophthalmic Surgery, Lasers & Imaging Retina 2014;45:510-5.
11. Stanga PE, Lim JI, Hamilton P. Indocyanine green angiography in chorioretinal diseases: indications and interpretation: an evidence-based update. Ophthalmology 2003;110:15-21; quiz 2-3.
12. de Carlo TE, Bonini Filho MA, Chin AT, et al. Spectral--Domain Optical Coherence Tomography Angiography of Choroidal Neovascularization. Ophthalmology 2015;122:1228-38.
13. Moult E, Choi W, Waheed NK, et al. Ultrahigh--speed swept-source OCT angiography in exudative AMD. Ophthalmic Surgery, Lasers & Imaging Retina 2014;45:496-505.
14. Jia Y, Tan O, Tokayer J, et al. Split-spectrum amplitude-decorrelation angiography with optical coherence tomography. Optics Express 2012;20:4710-25.
15. Tokayer J, Jia Y, Dhalla AH, Huang D. Blood flow velocity quantification using split-spectrum amplitude--decorrelation angiography with optical coherence tomography. Biomedical Optics Express 2013;4:1909-24.
16. Dansingani KK, Naysan J, Freund KB. En face OCT angiography demonstrates flow in early type 3 neovascularization (retinal angiomatous proliferation). Eye 2015;29:703-6.
17. Ishibazawa A, Nagaoka T, Takahashi A, et al. Optical Coherence Tomography Angiography in Diabetic Retinopathy: A Prospective Pilot Study. American Journal of Ophthalmology 2015 [Epub ahead of print].
18. Jia Y, Wei E, Wang X, et al. Optical coherence tomography angiography of optic disc perfusion in glaucoma. Ophthalmology 2014;121:1322-32.
19. Jia Y, Bailey ST, Wilson DJ, et al. Quantitative optical coherence tomography angiography of choroidal neovascularization in age-related macular degeneration. Ophthalmology 2014;121:1435-44.
20. Jia Y, Bailey ST, Hwang TS, et al. Quantitative optical coherence tomography angiography of vascular abnormalities in the living human eye. Proceedings of the National Academy of Sciences of the United States of America 2015;112:E2395-402.
21. Thorell MR, Zhang Q, Huang Y, et al. Swept-source OCT angiography of macular telangiectasia type 2. Ophthalmic Surgery, Lasers & Imaging Retina 2014;45:369-80.