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EVALUATING THE EMERGING CLINICAL BENEFIT OF OCT ANGIOGRAPHY IN PRACTICE



OCTA Promising For Identifying Vascular Changes Earlier In Diabetic Patients

To more effectively direct sight-sparing treatments is the real goal of new technology.

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cular coherence tomography angiography (OCTA) is a new technology that allows for the identification of blood vessels in the eye noninvasively without the use of dye.1 Although for the past several decades fluorescein angiography (FA) and indocyanine green angiography have been the gold standard for evaluating retinal and choroidal vasculature, these tests have disadvantages. Drawbacks include the lack of depth resolution, a blurring of details from dye leakage, and the inability to selectively evaluate different levels of the retinal and choroidal microvasculature. Intravenous dye can cause nausea, vomiting, and rarely, anaphylaxis.²

In particular, for diabetic patients, it is extremely helpful to identify early deep vascular changes, for which depth-resolved OCTA is superior to FA.³⁻⁵ Having this information can help us as specialists tailor appropriate management for patients who are at risk of developing more severe disease. Patients can then be counselled regarding the need to maintain tighter glucose control, a clinical benefit I am already seeing from using OCTA. Of course, as further therapeutic advances occur, we can look forward to treating early diabetes-related changes.

The question to be answered as the technology is developed and improved is will OCTA's use in clinical practice provide the type of information that will allow specialists to improve patients' overall disease management, individualise treatment, and improve visual outcomes?

DEVICE SNAPSHOT

The PLEX Elite 9000 (ZEISS) is the company's most advanced platform for OCTA; it is a further development of and is quite similar to the company's AngioPlex, FDA cleared in September 2015 (Figures 1-3). I have been very pleased with my experience with the unit: the system is fast, the image quality is high, and it provides wide-field images,



Figure 1: Diabetic retinopathy with neovascularisation everywhere (AngioPlex, ZEISS).

especially important in diabetes. The PLEX Elite was FDA cleared in November 2016; the swept-source OCT and OCTA platform was designed for advanced retina research.

We have enjoyed a positive relationship with ZEISS as part of the Advanced Retina Imaging (or ARI network) for the PLEX Elite OCTA platform, and have forged a cooperative approach to its development. The network is led by Philip J. Rosenfeld, MD, PhD, and the global consortium of clinicians and scientists is focused on advancing OCT innovation to benefit more patients.

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CHALLENGES

Age-related macular degeneration presents a challenge for imaging modalities. To properly visualise the layers, which is key to identifying pathology, it requires a high amount of segmentation and interactive work on the part of the user.⁶ Future developments in OCTA will seek to improve the ability to identify pathological references and fine tune diagnoses.

The size and amount of data produced by advanced imaging modalities is a burden on information technology infrastructures to be sure. Technology, however, will likely render this a temporary problem as we learn what data we need and how to shrink and share it more efficiently.

The lack of standardisation among devices on the market presents a problem when it comes to research, data gathering, and comparison. For example, in our team's studies, we try to restrict our reading centre to one machine in a study; that does not always happen. I hope crosstalk among the manufacturers can lead to perhaps a basic platform from which to have a standard for comparison. This technology continues to evolve and the endpoint is unknown!

BRINGING IT BACK TO PATIENT MANAGEMENT

OCTA looks ready to signal a significant change in how specialists diagnosis retinal disease. Keeping the focus squarely on how ever-improving technology ultimately benefits patients in the real world is the way to ensure that we use of the best diagnostic tools in clinical practice.



Figure 2. AngioPlex image of branch retinal vein occlusion.



Figure 3. Wet age-related macular degeneration with choroidal neovascularization lesion imaged with AngioPlex.

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Emerging Clinical Value Of OCTA

The new technology may ultimately guide earlier treatment.

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CT angiography (OCTA) will have a major impact on the way retina specialists practice. It is likely OCTA will supplant the use of fluorescein angiography (FA) in the next five years or so, leading to a closed chapter in history. OCTA allows us to learn more about vessels and the true nature of neovascularisation—a living natural history of angiogenesis.¹

FA remains the gold standard for the detection of choroidal neovascularisation (CNV), although it is an invasive and timeconsuming test that requires IV administration of dye and imaging. The resulting scans provide 2-D images that allow for a wideview, dynamic visualisation of blood flow. The images are not depth resolved, however, making it more challenging to identify the axial location of pathology.² Dye-associated complications, although rare, do occur.

NEOVASCULAR AMD

OCTA provides a level of sensitivity not seen with previous tests. For example, OCTA allows visualisation of drusenoid pigment



Figure 1. AngioPlex (ZEISS) images can illustrate the presence of microaneurysms and areas of ischaemia in diabetic retinopathy. Clockwise from top left: full-depth colour-encoded image, superficial retinal layer, deep retinal layer, and the superficial layer overlaid on to FA.



Figure 2. AngioPlex images illustrate the presence of CNV in AMD. Clockwise from top left: full-depth colourencoded image, superficial retinal layer overlaid on to FA, B-scan, and custom layer revealing CNV below the retinal piament epithelium. epithelial detachments that are not seen on FA or structural OCT.^{3,4} Thus, treatment can be initiated sooner with better outcomes. OCTA can also rule out a blood vessel, which allows adjustment to a patient's follow-up schedule accordingly. These are tangible benefits for managing patients' care that are already being seen in clinical practice.

It is important to remember that the patient's treatment burden is the overall process involved with coming to the office for an injection. OCTA can help surgeons implement more sustainable strategies for treating patients with neovascular AMD and diabetic macular edema. See Figures 1 through 3 for examples of images obtained using the AngioPlex from ZEISS.

PROTOCOLS

Top-line data from a phase 3 trial of brolucizumab versus aflibercept in neovascular AMD showed brolucizumab allowed patients to extend the time between treatments to 12 weeks.⁴ Importantly, the time frame determined in the study was based on a disease-activity assessment plan. This is the first of its kind used in a comparable study that allows for the use of a validated criteria based on certain parameters.

This type of criteria will likely be applied more commonly. In conjunction, having better data from OCTA would add to specialists' confidence when extending patients. Its use will likely be part of such criteria in the future, as specialists seek to optimally treat patients who exhibit a wide variability in response to anti-VEGF therapy.

FUTURE DIRECTIONS

OCTA is allowing specialists to better understand the pathophysiology of angiogenesis. Neovascularisation is part of a wound-healing response, and some welltreated AMD patients can have a blood vessel present with excellent outcomes. Patients with eradicated blood vessels can develop atrophy, the biggest cause of long-term visual loss.⁶

A certain level of neovascularisation may be a treatment goal. If this is found to be the case, OCTA will allow specialists to monitor not only the existence of but also understand the exact nature of neovascularisation.

WHERE WE ARE

One of the barriers to more widespread use of OCTA currently is a lack of standardisation. Each device uses a different proprietary algorithm, making it difficult to perform a correlational study. Also needed is improved quantifying data to allow for normative analyses of ischaemia using numeric values. In a 35-yearold diabetic patient, it is extremely valuable to be able to visualise, for example, an enlarged foveal avascular zone thus signaling ischaemia.⁷ We lack, however, standardised normative foveal avascular zone measurements.⁸

The final challenge is reimbursement. Once reimbursement strategies are mapped out, OCTA's use will become more widespread.



Figure 3. AngioPlex images clearly delineate the location of the occlusion and affected areas of ischaemia superior to optic nerve head in branch retinal vein occlusion. Clockwise from top left: full-depth colour-encoded image (6 x 6 mm), full-depth colour-encoded image (3 x 3 mm), superficial retina layer overlaid on to LSO fundus image, and superficial retina layer.

CONCLUSION

OCTA will soon allow retina specialists to have more detailed information on which to base disease-treatment strategies, allowing for improved outcomes and better management for patients' everyday lives. OCTA is poised to match the game-changing nature of structural OCT.

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Adding OCTA To Your Practice

Invest in the future with today's technology.

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ptical coherence tomography angiography (OCTA) brings a completely new diagnostic modality into specialists' routine. With OCTA, physicians can meticulously examine the retinal and choroidal vasculature. Compared to invasive fluorescein and indocyanine green angiography, OCTA has obvious advantages.¹⁻³

All ophthalmologists seek to provide optimal care to their patients using stateof-the-art equipment. OCTA represents one of those instruments. The images it provides allow more insight into blood flow variations with disease in the choroid and retina (Figure). OCTA allows the user even to differentiate various capillary plexus in the neurosensory retina —which has not been possible before— so there is huge interest in the technology.^{1,4,5}

CHALLENGES

In many fields of medicine, specialists face a challenge when choosing to incorporate new products into practice. Until the use of a device is regularly reimbursed, there may always be a time gap before its widespread adoption. Of course, this situation varies country by country; in Germany, about 90% of patients are covered by insurance that does not yet pay for this new imaging modality.

Another important aspect of OCTA technology is the need for normative data and reference points for comparison. Comparative studies among devices are needed to see what is best for certain clinical conditions. Although still in its early days, there are very dynamic developments occurring in OCTA.

An aspect of advanced digital technology like OCTA that must be addressed is the size and quantity of data it produces. Improved IT infrastructure and software solutions to compress files are needed to allow for moving, sharing, and storing such massive amounts of information.

CONCLUSION

OCTA technology requires additional systematic and prospective studies to see how it can best be implemented in the routine management of patients. No doubt still in its infancy, the diagnostic modality has huge potential. I predict it will, in many



OCTA image with perifoveal capillaries (A). PLEX Elite 9000 Swept-Source OCT auch wide-angle OCTA imaging (B). C und D: choroidal nevosacularization due to age-related macular degeneration. In the B-Scan (D) blood flow is indicated in red at the retinal level and green in the sub-RPE compartment. This is obviously an occult CNV.

instances, replace the use of invasive technology allowing for advanced imaging to be less of a burden on patients and on busy clinical practices.

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