

A ROLE FOR OCTA IN DAILY RETINA PRACTICE

A review of practical applications and limitations of OCTA for the assessment of patients with diabetic retinopathy.

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Optical coherence tomography angiography (OCTA) is a relatively new method of visualizing blood vessels in the retina and choroid. OCTA uses variations in the phase and intensity of backscattered light to



detect moving objects, such as red blood cells, in the retinal tissue.¹ The motion contrast images produced noninvasively by OCTA are high-resolution (~10 µm), depth-resolved depictions of the retinal vasculature.

OCTA images are acquired in basically the same way as standard OCT images, and they take roughly 3 to 4 minutes to acquire under ideal circumstances. Neither patient nor physician would know the difference between a standard OCT scan and an OCTA scan simply by observing the procedure because OCTA images are generated using software algorithms to detect phase or intensity differences in the backscattered OCT signal. Therefore, OCTA is a fast, safe, noninvasive, and likely cost-effective method of imaging the retinal vasculature. It provides imaging at capillary-level resolution, much like OCT documents retinal thickness at micron-level resolution.

Nevertheless, the question remains: How do we use OCTA in our daily practice? In this article, we discuss the rapidly evolving practical applications and limitations of OCTA for the assessment of retinal vascular disease with an emphasis on diabetic retinopathy (DR).

OCTA OR FA?

OCTA is commonly compared with fluorescein angiography (FA), but this is not exactly a fair or desirable comparison. In fact, we would argue that each technique can play a role in the management of patients with retinal vascular diseases. The key is to understand when to use each platform.

When OCTA Is Indicated

The utility and potential of OCTA to resolve capillary-level detail has been demonstrated in the normal human retina.^{2,3} OCTA images demonstrate capillary detail that approaches the resolution of histological studies in human cadaver eyes.³⁻⁵ As a result, numerous studies, including those from our group, have suggested that OCTA images are at least equal to standard fluorescein angiograms for detecting macular complications of retinal vascular diseases, including DR^{6,7}; retinal vein occlusion (RVO)⁸; macular degeneration⁹⁻¹¹; macular telangiectasia¹²; and many others.

For example, it is well established that OCTA can detect areas of impaired perfusion or nonperfusion in both the superficial and deep capillary plexi, whereas FA cannot resolve the deep capillary plexus or superficial peripapillary capillary plexus at all.³ Therefore, OCTA provides a whole new dimension of depth information regarding the severity of impaired perfusion that we did not have with FA. The clinical relevance of this additional information remains to be determined, but, for now, OCTA allows us to assess the severity of ischemia with much more precision than is provided by FA. For example, OCTA has already been used to study diseases such as paracentral acute maculopathy¹³ and DR¹⁴ that are thought



AT A GLANCE

- OCTA represents a fast, safe, noninvasive, and cost-effective method of imaging the retinal vasculature at capillary-level resolution.
- OCTA and FA can each play a role in the management of retinal vascular diseases. The key is to understand when to use each one.
- There is mounting evidence that one of the most important applications of OCTA will be in detecting milder stages of DR when FA is not indicated or useful.



Figure 1. Images taken with AngioPlex OCT Angiography (Carl Zeiss Meditec), showing 3 x 3 mm (A), 6 x 6 mm (B), and 8 x 8 mm (C) fields of view.

to primarily affect the deep retinal layers.

OCTA can also detect intraretinal (eg, intraretinal microvascular anomalies) and extraretinal (eg, neovascularization of the disc or elsewhere) neovascularization with excellent reliability, as long as the pathology is within the field of view.^{6,7} Accordingly, one of the main limitations of OCTA is the field of view, although this is rapidly improving.

Commercially available devices have several field-of-view options, including 3 x 3 mm, 6 x 6 mm, and 8 x 8 mm (Figure 1). It is likely that larger fields will be available in the near future. Until then, physicians can direct their photographers to target a lesion or suspicious area that is outside the standard macular scan pattern. Users should be aware, however, that in most cases, as the field of view increases in size, the resolution of the scan decreases. This is because the same number of A-scans is used to scan a larger area. Nevertheless, the standard scan patterns of commercially available spectral-domain OCT (SD-OCTA) devices are likely sufficient to detect clinically relevant pathologic changes in DR and RVO.

The bottom line is that physicians still need to perform FA to detect extramacular lesions of any sort, including neovascularization and peripheral nonperfusion in DR. Follow-up examinations for assessing macular ischemia can be done with OCTA.

Our group has also shown that OCTA can demonstrate novel pathologic features that do not correlate with features on FA or OCT.^{6,8} For example, certain types of intraretinal edema are detected very well on OCTA, but these regions do not correlate with typical intraretinal fluid pockets on OCT or with late staining regions on FA (Figure 2).^{6,8} This finding has been demonstrated by our group in patients with DR⁶ and in patients with RVO.⁸ We have postulated that this finding occurs because even trace amounts of particulate debris (lipid and extracellular protein deposits such as hard exudates) within retinal tissue can generate OCTA signal from Brownian motion. The clinical significance of this finding is not yet clear, but it is the subject of ongoing investigation (unpublished data).

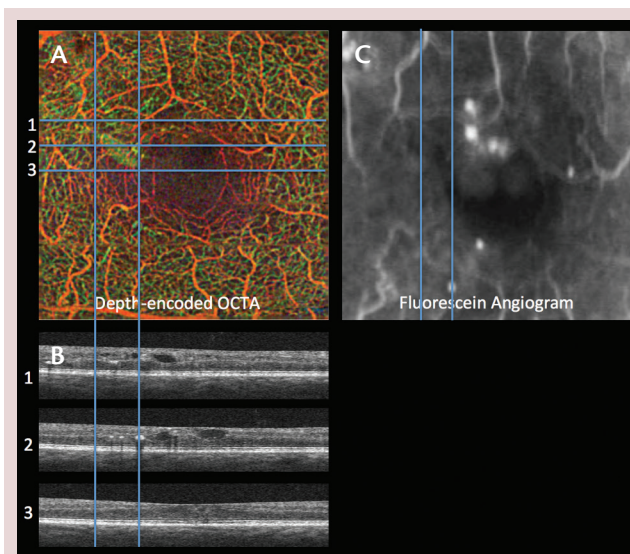


Figure 2. OCTA of a 77-year-old patient with DME. Pseudo-colored, depth-encoded OCTA (red = superficial, green = deep, yellow = overlay) image shows mild capillary loss and foveal avascular zone (FAZ) abnormalities in the superotemporal quadrant (A). An area of green-colored reflectivity, delimited by vertical blue lines (A1, A2, A3), does not correlate with the bulk of hyporeflective intraretinal fluid spaces shown on OCT B-scans (B). These regions of hyperreflectivity have been noted in patients with DR and in patients with RVOs and do not correlate with the region of staining on late FA (C). We hypothesize that these areas correspond to regions of particulate debris (eg, hard exudate) with Brownian motion that is detected with OCTA. OCTA images obtained with AngioPlex. FA obtained with Spectralis (Heidelberg Engineering).

Another novel finding with OCTA is subclinical vascular changes that are noted in patients with minimal or no DR (Figure 3). We have observed many diabetic patients with

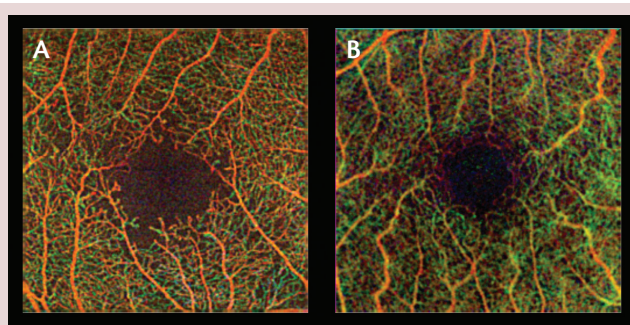


Figure 3. OCTAs in an asymptomatic patient with mild non-proliferative DR (A) and a healthy individual (B), showing the central 3 x 3 mm. Note the mild loss of capillaries and the incomplete FAZ in A, compared with the healthy eye in B. The subtle areas of impaired perfusion in the superotemporal and inferonasal quadrants (A) are suggestive of subclinical disease.

excellent vision but subclinical variations in the appearance of macular capillaries. Although the clinical significance of these variations is not known, it is possible that OCTA is detecting vascular changes before clinically detectable disease has occurred. If this were shown to be the case, then OCTA would become a very powerful tool to detect DR before clinically evident changes occur.

When FA Is Indicated

Microaneurysms have been demonstrated on OCTA, but they are not identified as frequently with this technology as with FA.^{6,7} We postulate that this is because microaneurysms have a life cycle, and histology studies have shown that microaneurysms can be patent, clotted, or sclerosed. Therefore, any microaneurysm that does not have blood flow (ie, that is sclerosed) is unlikely to show up on an OCTA scan but will still stain with fluorescein dye. Also, the flow rate of blood in microaneurysms can vary and may be below the threshold of detection for current OCTA devices. In general, users should be aware that regions that lack OCTA signal may have blood flow that is too slow for OCTA to detect. It is not known what the threshold flow rate is for detection of blood flow using SD-OCTA. Additional studies using OCTA may allow us to revisit the relevance of microaneurysms in diabetic macular edema (DME).

COMPLAINTS AND ADVANTAGES

Some clinicians have noted that OCTA images do not show the hyporeflective intraretinal fluid pockets that are typically seen on OCT in patients with DME. Physicians should be using OCTA in conjunction with standard OCT to detect intraretinal fluid, so this should not be an issue. The additional time it takes to perform an OCTA scan is negligible, and viewing the OCT concurrently with OCTA also takes little more effort than viewing the OCT by itself.

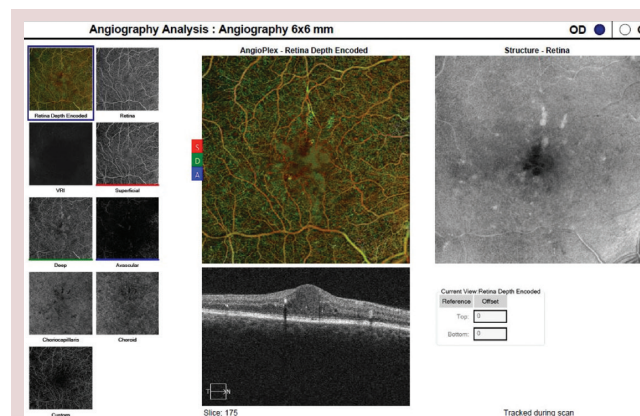


Figure 4. Representative PDF screenshot of one panel from the AngioPlex output for use in clinic. In the center is a large pseudocolored, depth-encoded image, which provides a global view of vascular changes. The structural intensity scan, at right, can be used to assess the quality of the OCTA and also to rule out image artifacts. Below the top center image is a B-scan that shows one slice from the OCTA in profile. The small icons on the left are other images that can be individually saved as PDFs.

Another common complaint is a lack of reimbursement for performing OCTA. This certainly is a problem that must be addressed.

Some clinicians have noted that OCTA images are not always easy to interpret. In our practice, we use a PDF export of the pseudocolored perfusion map (Figure 4) to view the OCTA results for patients on our image management system, just as many clinicians use the OCT Thickness Map PDF. This takes little time and is therefore manageable in a busy practice setting. As our understanding of OCTA interpretation continues to mature, more detailed analysis of the images may be necessary, but for now this is a reasonable approach to adopting OCTA in a practice for the first time.

OCTA can be advantageous for follow-up in patients in whom a baseline FA has already been performed and a diagnosis is confirmed. In such a case, noninvasive OCTA is preferable to FA, which can take 15 to 30 minutes and requires an intravenous injection. Unlike FA, OCTA does not visualize dye leakage. This can be a limitation for assessing vascular permeability, but it can also be an advantage because fluorescence can obscure DR features.

CONCLUSION

There is mounting evidence that one of the most important applications of OCTA will be in detecting clinically relevant changes in milder stages of DR, when FA is not indicated or useful. The noninvasive nature of OCTA makes it possible to perform this test without significant risk to patients.

Our group and others have shown that subtle subclinical changes on OCTA are not uncommon in patients with mild

nonproliferative DR. We are developing quantitative metrics to objectively capture these subtle changes to provide objective evidence of DR severity. Our pilot studies show that OCTA-based metrics of capillary density, branching complexity, and capillary diameter correlate well with the clinical severity of DR,¹⁴ the severity of RVO (unpublished data), and the diagnosis of uveitis.¹⁵

Larger scale studies are under way, aimed at determining whether OCTA can detect subclinical DR changes. If these studies are successful, this could pave the way for earlier interventions and allow clinicians to prevent vision loss and disease progression, rather than treat vision loss. ■

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