Introduction

Optical coherence tomography (OCT) has revolutionized eye care by providing a fast, noninvasive method to visualize ocular structures in vivo since its development in 1991. It has since become one of the most important ophthalmic diagnostic tools, with an expanding number of applications that aid eye care providers in diagnosing and monitoring eye disease.

Recently, there has been great excitement in the development of a new OCT imaging technique called OCT angiography (OCTA). OCTA isolates microvascular circulation from OCT image data by specialized acquisition and processing techniques. This allows for visualization of blood flow in the retina without the need for intravenous injection of a contrast dye. Until now, clinical visualization of retinal vasculature has been limited to indocyanine green angiography (ICGA) and fluorescein angiography (FA), both of which require contrast dye injections. Despite their great clinical utility, these procedures are not without drawbacks. They are invasive, time consuming, and require a skilled photographer. The injected dye can sometimes cause adverse reactions...
including nausea, vomiting, and in rare occasions, anaphylaxis possibly leading to death\textsuperscript{1}. Additionally, indocyanine green dye is contraindicated in pregnant patients, or patients with kidney disease\textsuperscript{2}. With the introduction of OCTA, clinicians now have a fast, noninvasive method to visualize retinal microvascular perfusion.

**TECHNOLOGY**

OCTA works by scanning the same location on the retina multiple times consecutively. As the scanning beams enter the eye, areas with no movement will always reflect light the same way. However, moving structures (such as red blood cells) will reflect light differently between each B-scan. These B-scans are then compared against each other. After eliminating the effects of bulk motion such as head movements or saccades, any residual differences between the scans are thought to be due to blood flow, and hence indicate the location of a perfused blood vessel\textsuperscript{3}. Areas with blood flow appear bright, whereas dark areas indicate no flow (or flow that is too slow to detect). By combining the flow information in all B-scans, an \textit{en face} image of the microvascular circulation can be generated. These OCTA images can achieve an axial resolution of approximately 5 \(\mu\)m, which gives detailed views of fine capillaries (Figure 1).

![OCTA image](image)

Figure 1. OCTA \textit{en face} image of a healthy eye. Note that the foveal avascular zone can be clearly seen, as can the small retinal capillaries.
Currently, there are several different OCTA processing methods being used by different companies. These include phase-based techniques (Doppler shift or variance), magnitude-based techniques (speckle variance or decorrelation), or a combination of both. Each method utilizes a different part of the OCT signal to obtain flow information, but the goal of visualizing vasculature is the same, and the resulting images are similar. At the time of this article, Carl Zeiss Meditec and Optovue have received FDA clearance for their OCTA devices. Other companies are also actively developing their OCTA systems, and some have released products outside the US.

**CLINICAL APPLICATIONS**

One of the greatest advantages of OCTA is its ability to provide 3-dimensional, depth-encoded information. Because it is an OCT-based scan, the data obtained consists of multiple B-scans which are combined into a cube. By segmenting the cube into different layers or slabs, OCTA is able to isolate blood flow information at a specific retinal depth. Figure 2 shows OCTA *en face* images of a healthy retina at various depths. The superficial capillary plexus (SCP) can clearly be seen to have a different vessel pattern than the deep capillary plexus (DCP) and choriocapillaris, consistent with histological studies. This is the first imaging modality that allows noninvasive, in vivo visualization of individual capillary networks in the retina. In comparison, FA images are 2-dimensional, which means signals from all layers in the eye are projected in the same plane, thereby losing depth information.

![Figure 2. A) Superficial capillary plexus. B) Deep capillary plexus. C) Choriocapillaris.](image)

This unique capability of OCTA gives rise to new opportunities for studying the retina and understanding the pathophysiology of diseases. For instance, paracentral acute middle maculopathy (PAMM) is a condition characterized by intermediate and deep capillary plexus infarction, and has been hypothesized to affect...
patients with various retinal vascular diseases such as retinal vein occlusion and sickle cell disease \(^9\). A few papers have recently demonstrated with OCTA that the SCP and DCP are affected asymmetrically in PAMM, with more ischemia observed in the DCP (Figure 3), providing angiographic evidence of this condition \(^{10,11}\). Segmenting OCTA data also aids in highlighting vasculature in a specific area of interest. For example, neovascularization can develop in the setting of various diseases, and generally occurs at specific retinal depths depending on the disease. In wet age-related macular degeneration, OCTA segmentation can help isolate the choroidal neovascular membrane (CNVM) at the level of the RPE (Figure 4). In diseases such as retinal vein occlusions and proliferative diabetic retinopathy, neovascularization typically occurs in the preretinal space. By segmenting above the inner limiting membrane, OCTA allows visualization of the abnormal blood vessels independently from normal retinal vessels. Figure 5 shows FA and OCTA imaging of a branch retinal vein occlusion (BRVO) with neovascularization elsewhere (NVE). OCTA shows good agreement with FA in visualizing areas of ischemia. In addition, OCTA is able to isolate the NVE lesion by segmenting the preretinal space (Figure 5D), and the fine vessel details are not affected by dye leakage as in the FA image (Figure 5B). Isolating the lesion of interest enables clinicians to view only the information pertinent to the disease, potentially allowing a more detailed assessment of microvascular pathologies. It may also allow for easier comparison between visits to monitor for change.

Figure 3. OCTA of a patient with sickle cell maculopathy. Note that while the SCP is relatively preserved (A), the DCP shows areas of ischemia temporal to the fovea (B).
Figure 4. A) FA image of a large, mature fibrovascular scar from type 1 CNV. Because of the extensive scarring of the macula, there is hypofluorescence centrally. B) OCTA image overlaid on FA. In this case, OCTA is able to image the CNV lesion in greater detail than FA, with the mature trunks of the CNV lesion clearly visible. C) The sub-RPE space was segmented to isolate the CNV lesion.
Figure 5. A) Early-phase FA of a BRVO. B) Mid-phase FA. C) OCTA en face image of the retina, with corresponding B-scan. D) OCTA en face image segmenting the preretinal space, with corresponding B-scan.
Another advantage of OCTA is its resolution. As mentioned above, OCTA can achieve an axial resolution of approximately 5 μm, which permits high definition imaging and clear visualization of microvascular capillaries that are difficult to view with current imaging methods. In Figure 6, areas of capillary nonperfusion can be seen clearly in a patient with diabetes. Several studies have shown early but promising results in the reliability of OCTA in imaging retinal ischemia in the setting of diabetic retinopathy. In particular, small pockets of ischemia seem to be visualized better on OCTA than FA. As research is being done on preventing or reversing macular ischemia, OCTA may serve as a useful tool in monitoring retinal perfusion changes over time. Figure 7 shows the SCP and DCP images of a patient with fovea plana. OCTA beautifully demonstrates the absence of the foveal avascular zone (FAZ) in the SCP. In the DCP, the FAZ can still be seen. Together with the structural B-scan which shows a lack of normal foveal depression, OCTA is able to easily confirm the diagnosis of fovea plana.

Figure 6. A) 3x3 mm scan and B) 6x6 mm scan of a patient with diabetic retinopathy. Areas of capillary nonperfusion can be seen as dark areas in the retina. A few microaneurysms are highlighted with yellow arrows.
The noninvasive nature and short scan duration also make OCTA easy for patients to tolerate. Image acquisition usually takes a matter of seconds, compared to FA which involves a series of photographs taken over minutes. In addition, since there is no need for dye injections, OCTA may be performed more frequently than FA. This enables clinicians to follow the patient more closely, and potentially detect changes earlier. All of these features make OCTA a promising tool for diagnosing and managing disease.

**LIMITATIONS / ARTIFACTS**

As with any test, interpreting OCTA images requires an understanding of the limitations of the technology, as well as being able to recognize artifacts that may confound the data. Because OCTA images are derived from OCT data, they are subject to the same artifacts. Any media opacity that blocks light from reaching the retina will cause the OCTA image to appear dark. Media opacities include cataracts, floaters, and even dry eyes. In addition, dense pigment within the retina (such as hemorrhages) can obstruct light from reaching deeper layers. When there are dark areas on the OCTA en face image, sometimes it is not possible to distinguish
between media opacities and true capillary nonperfusion based on the OCTA image alone. In these cases, it is important to reference the structural B-scans and structural en face image. Media opacities can be seen on the B-scan as a dark shadow, whereas capillary nonperfusion will not affect the brightness of the B-scan. In Figure 8A, there is a dark area nasal to the fovea on the OCTA en face image, which corresponds to a dark area on the structural en face image, as well as the B-scan in the corresponding location (Figures 8B, 8C). This confirms that the dark area on the angiogram is the result of a floater, not capillary nonperfusion.

Projection artifacts are the result of fluctuating shadows cast by blood flow in a more superficial layer of the retina onto deeper layers. These artifacts are detected as flow signals, and will have the same vessel pattern as the inner layer. Projection artifacts typically occur in reflective retinal layers, which appear bright on the structural B-scan, most strongly in the RPE\textsuperscript{13}. When evaluating deeper retinal layers for abnormal vasculature, it is important to rule out projection artifacts to avoid false positives. Currently, OCTA software have post-processing methods to reduce or eliminate these artifacts. In Figure 9, the SCP and DCP of a healthy eye are shown (Figures 9A, 9B). The DCP slab shows some projection artifacts from the SCP, which appear as vessels that replicate the pattern of the SCP. The same slab with projection artifacts removed is shown in Figure 9C. Figure 10 shows a subretinal, type 2 CNV. Because the CNV lesion is close to the level of the RPE, projection artifacts from both the SCP and DCP can be seen (Figure 10A). After removing the artifacts, the CNV lesion is clearly isolated.

**Figure 8.** A) OCTA en face image with a dark area caused by a floater (yellow dashed circle). B) The structural en face image shows the same artifact in the same location. C) B-scan through the area shows dark shadow through all layers of the retina, suggesting that this is a vitreal floater.
Areas with slow flow are also more difficult to image with OCTA. Due to the fast scanning speed of OCT, areas with slower flow may not have enough difference between successive B-scans to meet the OCTA detection threshold. Therefore, any flow that is slower than the detection threshold will not be shown on OCTA images, and will appear dark. Examples of areas with slow flow include intraretinal fluid, some microaneurysms, and hemorrhages. However, many of these areas can be visualized on the B-scan, such as in Figure 11.
Finally, segmentation errors can be a source of artifacts. The appearance of the OCTA en face image is dictated by its corresponding slab, whose upper and lower boundaries are defined by segmentation lines. Therefore, any errors in segmentation will cause the en face angiogram to be displayed incorrectly. Figure 12 is an example of a patient with multifocal choroiditis. In Figure 12A, there appears to be an area within the
inflammatory lesion that looks suspicious for choroidal neovascularization. However, a closer look at the B-scan reveals an error in segmentation in that same area. After the segmentation is corrected, the bright area on the angiogram is no longer present (Figure 12B). Checking segmentation is important when evaluating OCTA images, and gives the clinician more confidence in the angiogram’s findings.

Figure 12. A) Choriocapillaris with segmentation error. B) Choriocapillaris without segmentation error.

**OCTA vs. FA**

Because they both have the word “angiography” as part of their names, it is natural for clinicians to draw comparisons between the two imaging modalities, and even explore the possibility of replacing FA with OCTA. It is important to note that while both OCTA and FA aim to image blood flow, they are different technologies, and will therefore image vascular features differently. Although OCTA generally shows good agreement with FA, it does not, at least presently, serve as a replacement for FA.

As mentioned above, OCTA is not able to image leakage. In addition, staining, pooling, and vessel filling time are also not features of OCTA. However, this also means that vasculature below an area of fluid, which would otherwise be obscured by dye leakage with FA, can be seen on OCTA. Since they each have their strengths and weaknesses, determining which test is indicated for the patient should be based on clinical need. Most
likely, OCTA will serve as a complementary test to FA, giving clinicians additional information for assessing retinal vasculature.

CONCLUSION

Although OCTA is a technology that is still in its infancy, it has already shown to have great potential for the future. The ability to provide depth-encoded information at very high resolution makes it a valuable tool for both clinicians and researchers. Its noninvasive nature also makes it readily accessible to optometrists to utilize.

Future developments in OCTA technology will further optimize its clinical utility. Automatic quantification of vessel density may be useful in monitoring diseases such as diabetes and glaucoma\textsuperscript{14,15}; wider fields of view and improved resolution will allow clinicians to utilize OCTA in more situations; there is also much research currently ongoing to explore the potential new applications of this imaging method. OCTA is a promising new technology which is generating great interest, and is likely to become more popular in clinical practice over the next few years.

REFERENCES


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1. The following are methods to generate OCTA images except:
   A. Speckle variance
   B. Doppler Shift
   C. Autofluorescence
   D. Decorrelation

2. What is the approximate axial resolution of OCTA?
   A. 0.5 µm
   B. 5 µm
   C. 50 µm
   D. 500 µm

3. OCT angiography is able to image all of the following clinical features except:
   A. Choroidal neovascular membranes (CNVM)
   B. Retinal capillary nonperfusion
   C. Neovascularization elsewhere (NVE)
   D. Intraretinal fluid

4. Projection artifacts in a given layer of the retina...
   A. ... result from fluctuating shadows cast by vessels in a more superficial layer.
   B. ... result from fluctuating shadows cast by vessels in a deeper layer.
   C. ... originate from the highly-reflective RPE.

5. With the introduction of OCTA, FA is no longer needed because all features on FA can be clearly visualized with OCTA.
   A. True
   B. False

6. Why are microaneurysms not imaged well on OCTA?
   A. There is no blood flow within microaneurysms because they are not blood vessels.
   B. Microaneurysms occur too deep in the retina for the OCT scanning light to reach.
   C. The flow speed within some microaneurysms is slower than the detection threshold of OCTA.
   D. Dense pigment within microaneurysms usually cast shadows in the retina, which

7. Artifacts on OCTA images can originate from all of the following EXCEPT:
   A. Floaters
   B. Contact lens wear
   C. Dry eye
   D. Segmentation errors

8. What is a possible reason a CNV lesion is not visualized on OCTA?
   A. Blood flow within the CNV is too fast for OCTA to image.
   B. Leakage from the CNV obscures the vessel details, preventing OCTA from adequately imaging the lesion.
   C. The blood vessel walls of CNV lesions are too thick, preventing the OCT scanning light to pass through, thereby blocking flow signal.
   D. The segmentation lines are incorrectly defined, and pass through an area that does not contain the CNV.

9. Which slab on the OCTA is best suited for visualization of diabetic neovascularization?
   A. Above the ILM
   B. ILM to OPL
   C. OPL to RPE
   D. RPE to choroid

10. Which of the following clinical features can be visualized on both FA and OCTA?
    A. Neovascularization of the disc (NVD)
    B. Subretinal fluid in central serous chorioretinopathy
    C. Diabetic macular edema
    D. Isolated ischemia of the DCP in sickle cell maculopathy
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