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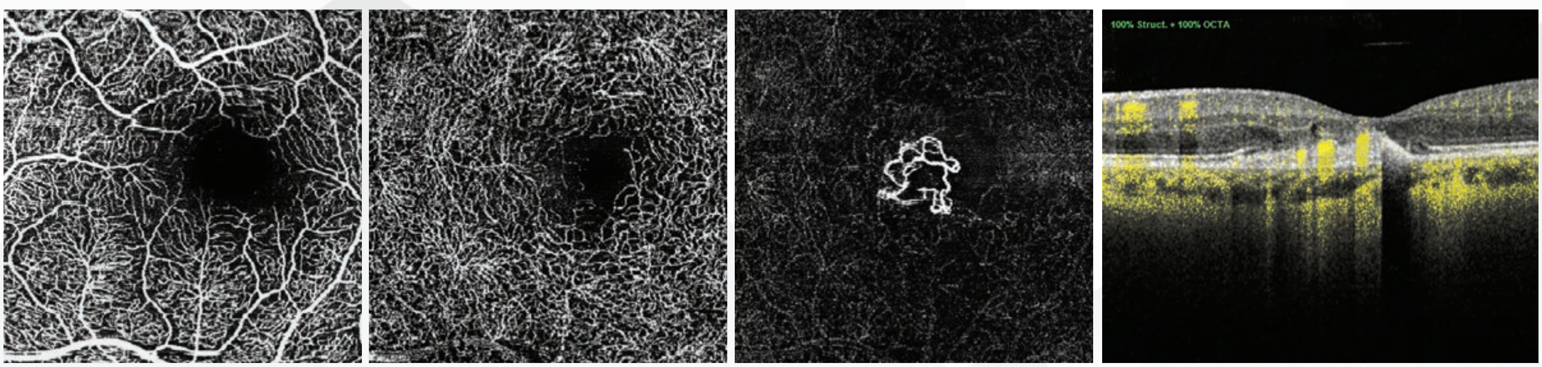
Evaluating OCT Angiography for Daily Clinical Practice

The SPECTRALIS OCTA Module breaks new ground in precision and diagnostic confidence.



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Evaluating OCT Angiography for Daily Clinical Practice

The SPECTRALIS OCTA Module breaks new ground in precision and diagnostic confidence.

The content for this supplement has been modified from the white paper, *SPECTRALIS Optical Coherence Tomography Angiography (OCTA): Principles and Clinical Applications*, with clinical information and retinal images provided by Marco Lupidi, MD. Read the white paper at Heidelberg Engineering: https://bit.ly/OCTAwhitepaper

To evaluate vascular disease in the retina and choroid, dye-based angiography has long been considered the gold standard. While fluorescein angiography (FA) and indocyanine green angiography (ICGA) allow for a dynamic widefield visualization of blood flow and patterns of dye leakage, pooling, and staining, they are invasive, lack depth information, and can cause side effects.[1] For routine diagnostic and progression applications, clinicians want a nonmydriatic, efficient, and noninvasive modality.

Optical coherence tomography angiography (OCTA) holds promise as a solution. Like FA and ICGA, the technology has limitations but also brings new diagnostic value to the table.

Noninvasive OCTA detects blood flow by acquiring multiple OCT B-scans at the same anatomic position and analyzing successive changes in OCT signal to identify movement (blood flow). By repeating this process at adjacent positions on the retina, clinicians are provided with three-dimensional views of perfused retinal and choroidal vasculature. This capability is why the use of OCTA is expanding in ophthalmic practices. Evidence is emerging that OCTA, as part of the multimodal imaging toolbox for retinal and choroidal vascular disease, can help clinicians to better diagnose and monitor ocular pathologies, and it may help to evaluate the effects of treatment. The SPECTRALIS OCTA Module provides clinicians with unique and clinically relevant benefits by producing high-resolution images with distinct image contrast, delivering OCTA on a truly multimodal imaging platform with confocal scanning laser ophthalmoscopy (cSLO) and addressing inherent challenges with the technology.

HOW OCTA WORKS

OCTA generates images of blood flow by differentiating the movement of erythrocytes from the surrounding tissues. All OCTA systems do this by analyzing changes in OCT signal on repetitive OCT B-scans at the same anatomic location. The SPECTRALIS OCTA Module excels because of the high-resolution of the SPECTRALIS B-scans, patented active eye-tracking technology, and the advanced probabilistic OCTA algorithm used to accurately discriminate between static tissue and blood flow.

OCT technology inherently loses some sensitivity at greater scan depths. This effect is called sensitivity roll-off. A reduction in sensitivity impacts the ability of OCTA to discriminate flow in the deeper vascular plexuses. To address this challenge, significant improvements were made to both the sensitivity and its roll-off (Figure 1) with the SPECTRALIS OCT2 Module, that offers about twice the scan speed compared to the SPECTRALIS OCT. SPECTRALIS OCTA was made possible by these improvements. The result: clinicians see quality, high-sensitivity scans with high image contrast, even at the maximum sampling depth.

OCTA devices available today use different algorithms to differentiate blood flow from other signal changes produced by static tissue, with varying levels of success.[2] Some algorithms only consider that static tissue, and perfused vasculature have different OCT signal variations, without sufficiently accounting for the different levels of signal variability in tissues. As a result, clinicians see less conclusive signal values overall due to reduced contrast and are presented with grayscale OCTA images.

The SPECTRALIS OCTA algorithm

is different. With an extensive understanding of OCT signal variability in static tissue and perfused vasculature, as well as variables such as sources of measurement noise, it makes use of two distinct signal distributions for non-vascular structures and blood flow. This produces high-resolution OCTA volumetric images presented in high-contrast black and white to make perfused vasculature very clear to the clinician.

The SPECTRALIS OCTA algorithm achieves this using a probabilistic approach, determining the probability that the signal variations represent static tissue or blood flow. Unlike some alternative methods, the SPECTRALIS OCTA algorithm allows you to avoid sacrificing axial resolution to improve the signal-to-noise ratio.[3] For the high-resolution and high-speed scan presets, the data is derived from the raw output at the original resolution, so no noise filters reduce resolution and contrast or introduce artifacts that can be hard to discern from real vascular structures.

KEY ADVANCE: CORRECTING FOR EYE MOVEMENT

Because OCTA detects blood flow by capturing repeated images at a precise location, it's essential that the technology can focus on that location accurately and efficiently as the eye moves, as well as identify the same location in subsequent sessions for accurate follow-up. OCTA systems can correct gradual eye movement over time (eye drift) using image post-processing techniques, such as image registration. Abrupt movements (saccades) or blinking present a tougher challenge because successive images do not show enough overlap. This makes the OCT scanning path deviate, creating geometrical distortions and lost data in OCTA volume scans (Figure 2).

Post-processing techniques alone cannot completely correct for saccades. The OCTA systems, which attempt to correct distortions this way, produce images that look accurate but may include geometrical distortions that look like vascular changes.[4,5] Image processing also can impair spatial resolution, making small vasculature unclear or inaccurate.[6]

The SPECTRALIS OCTA Module takes a different approach. SPECTRALIS TruTrack Active Eye Tracking technology continually monitors and controls the OCT scanning path live, using dual-beam active eye tracking to correct for movement and acquire images at the same location every time with less distortion and missing data. The dual-beam system works by re-positioning the second imaging beam in real time as it calculates displacements or torsional motion of the retina (Figure 3).

Using the SPECTRALIS OCTA Module with TruTrack Active Eye Tracking, clinicians can be confident that scans acquired over time will identify true changes without geometric distortions. The system produces a precise quantitative change analysis, with minimal post-processing.

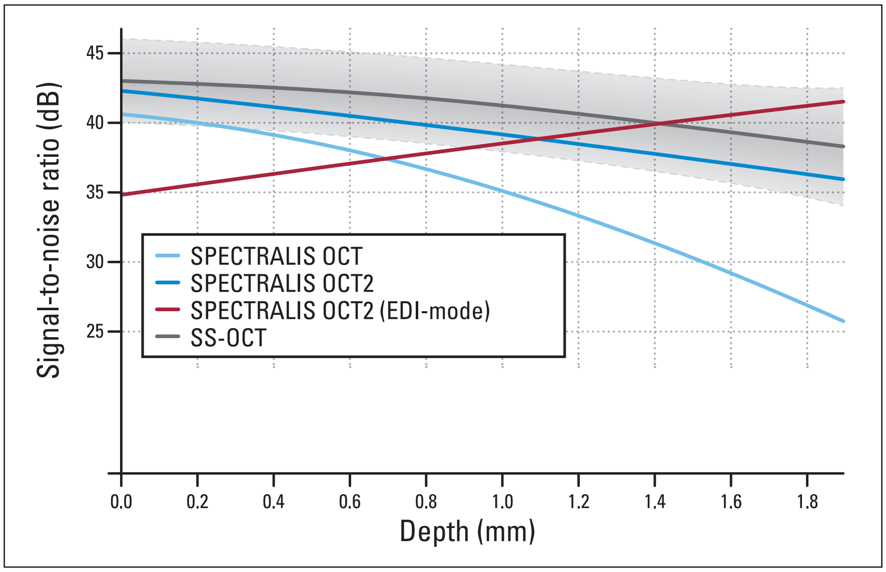


Figure 1. Roll-off curves for SPECTRALIS OCT and OCT2 in comparison to a hypothetical SS-OCT device. Within the depth range of the retina, illustrated by the B-scan, the sensitivity difference between the OCT2 in standard mode and an SS-OCT system is negligible. OCT2 EDI mode allows for even higher sensitivity for the deeper imaging range.

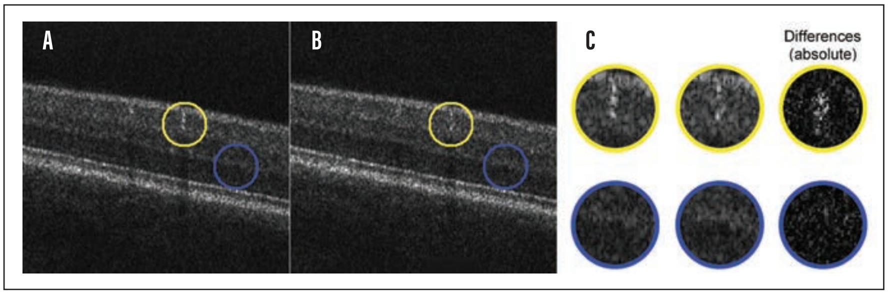


Figure 2. Example of how the OCT signal changes over time, after bulk motion correction. A, B: Structural OCT images were acquired with a time difference of 8 ms. The location of a larger blood vessel (yellow circle) and of static tissue (blue circle) is indicated in both images. C: Upon magnification of these areas and calculation of the differences, larger OCT signal changes can be seen within the blood vessel when compared with the static tissue. Note that this figure is not showing the SPECTRALIS OCTA algorithm results, but just the absolute differences between two single OCT scans (A and B) for illustration.

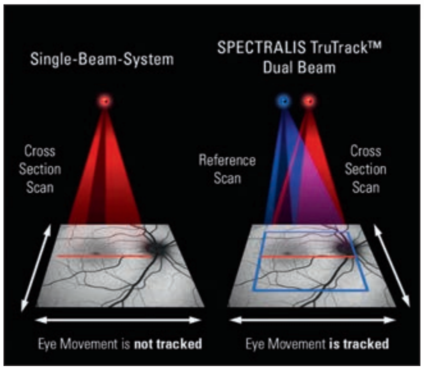
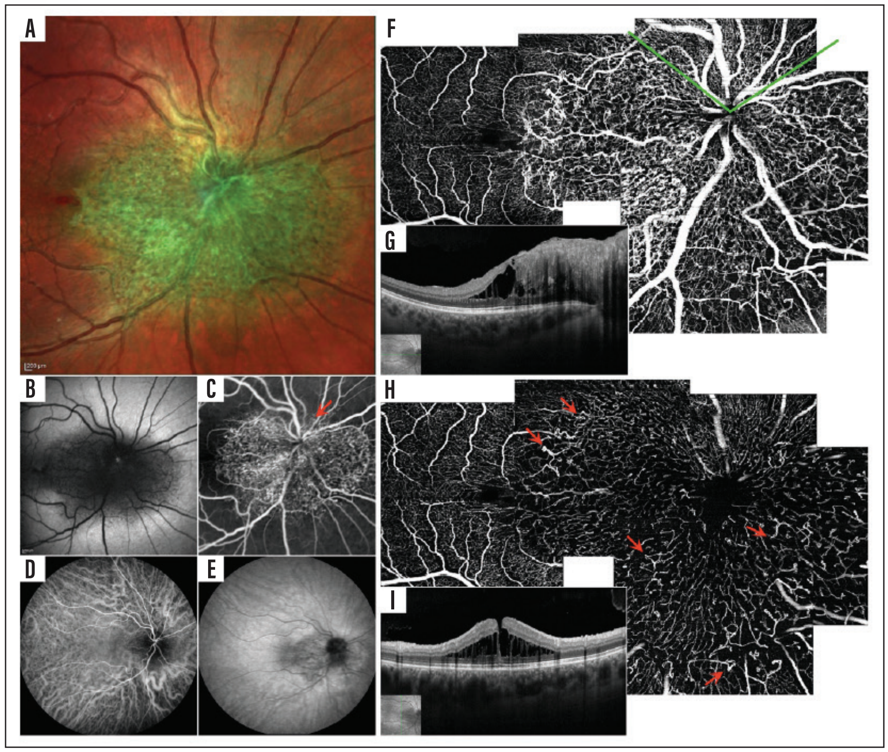


Figure 3. TruTrack Active Eye Tracking is a dual-beam tracking system that tracks the eye in real time, providing important clinical benefits such as retinal recognition, automated follow-up scanning, image averaging to improve image quality, and precise colocalization of fundus images with depth-resolved information in OCT scans.



Images provided courtesy of Dr. Marco Lupidi, Perugia, Italy.

Figure 4. Multimodal imaging of a 35-year-old woman with combined hamartoma of the retina and retinal pigment epithelium. The MultiColor cSLO image (A) reveals a large juxtapapillary retinal fibrotic lesion. Fundus autofluorescence (B) exhibits the masking effect of this proliferation but confirms an otherwise intact retinal pigment epithelium. Early-phase FA shows the vascular nature of the lesion as indicated by the arrow in C. ICGA indicates no choroidal involvement (D, E). The OCTA en face image, generated by a custom segmentation slab from the lower boundary of the ganglion cell layer to lower boundary of the inner nuclear layer, shows abnormal peripapillary vasculature in three quadrants caused primarily by structural changes associated with the lesion (F). The extent of the lesion is shown in the OCT structural scans (G, I). Another OCTA en face image (H), generated by a custom slab from retinal nerve fiber layer to ganglion cell layer, shows similar structural changes but also reveals 'hairpin' loops, indicating the vascular origin of this lesion.

Additionally, the OCTA images can be registered with dye-based angiography images to verify accuracy.[4,5,7,8]

OCTA AS PART OF THE MULTIMODAL IMAGING TOOLBOX

The same TruTrack technology used to correct for eye movement in the SPECTRALIS OCTA Module is applied across all modalities. That means that clinicians can precisely align OCTA and OCT images with cSLO fundus images. It's easy to compare OCTA with FA and ICGA for a hybrid approach to angiography, as well as with MultiColor and BluePeak fundus autofluorescence imaging.

Together, these modalities provide complementary diagnostic information—OCTA's three-dimensional views of structure and perfusion along with dye-based angiography's clear staining from vessel leakage—a clinical benefit unique to the SPECTRALIS platform (Figure 4).

Clinicians can focus OCTA imaging on a specific area of interest using the Scan Planning Tool. This tool allows clinicians to design an OCT structural scan or an OCTA scan based on a fundus image acquired on the SPECTRALIS. For example, if a patient with proliferative diabetic retinopathy (DR) shows pathology on FA, ICGA, and/or structural OCT, the clinician can use the Scan Planning Tool to guide the operator to acquire an OCTA image at the exact desired location (Figure 5). The SPECTRALIS precisely aligns the OCT modality with the cSLO fundus image for comparison and evaluation.

PRESENTING THE IMAGES CLINICIANS NEED

SPECTRALIS with OCT2 Module delivers exceptionally high-resolution and high-contrast scans that are ideal for advanced applications like imaging retinal and choroidal perfusion with, for example, the OCTA Module. Flexible scan sizes, patterns, and speeds, as well as dynamic multimodal visualization, maximize the clinical value of the technology and make the entire process seamless. OCTA stands out in its ability to accomplish the following:

- **Combine OCT and OCTA images.** OCTA volume scans combine a series of B-scans into a three-dimensional cube of data. The SPECTRALIS OCTA software breaks down that cube into three-dimensional slabs based on a set of boundaries that separate the vascular layers. The software can then be used to show the distinctive topography of each vascular layer by displaying a two-dimensional en face image from each slab.

Clinicians can view a "fusion image" where the OCTA flow information is displayed as a yellow overlay on the high-quality structural OCT B-scan image. A slider allows users to

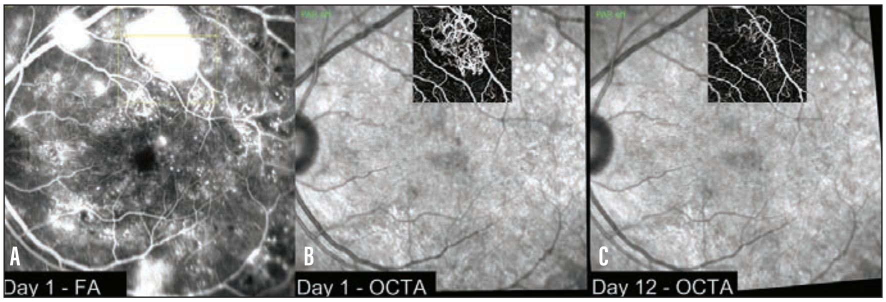


Figure 5. Multimodal integration of SPECTRALIS OCTA using the Scan Planning Tool. A: The patient was imaged with FA, presenting with proliferative DR. B: On the same day, an OCTA scan was acquired using the Scan Planning Tool in order to center the scan on the clinically relevant region. C: Treatment efficacy was visible via OCTA follow-up at the same exact location 12 days later.

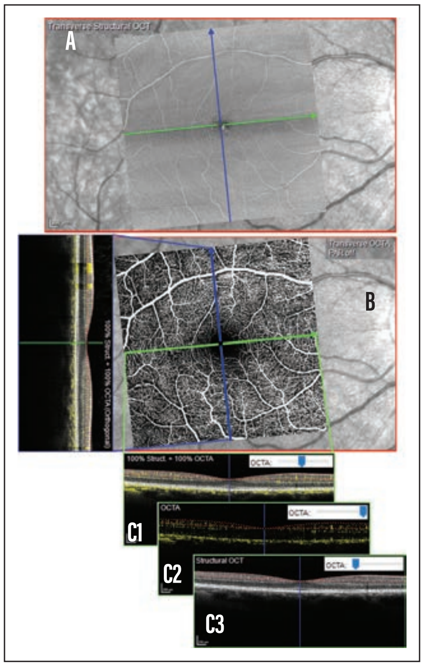


Figure 6. Review of OCTA data is mainly based on en face images and section images. A: En face image of the structural OCT data within the superficial vascular plexus. In the background, an infrared cSLO fundus image is shown. B: En face image of the corresponding OCTA data. C1-C3: OCT/OCTA fusion images of a section along the fast scanning axis (B-scan direction, green). C1: Section image shows structural OCT in the background and the OCTA data as yellow overlay. C2: Same as C1, but the structural OCT data is faded out via a slider. C3: Same as C1, but the OCTA data is faded out via a slider. D: OCT/OCTA fusion image where section is along the slow scanning axis (orthogonal to B-scan direction, blue).

adjust the relative transparency of the OCTA and the OCT information (Figure 6). Users can view both the original horizontal orientation and the corresponding orthogonal B-scan. By superimposing the data, clinicians get detailed, precise visual correlation between retinal microstructures and perfused vessels.

- **Provide a continuous view with no gaps.** All OCTA systems divide the original cube of data into slabs to produce images for analysis, but the methods they use to define those slabs produce different results. The challenge is to precisely define slabs within the retinal vascular network while ensuring that the assembled slabs offer an uninterrupted representation of retinal and choroidal vasculature.

To provide a continuous picture without the data gaps seen in some OCTA devices, the SPECTRALIS OCTA Module follows a concept developed by Campbell et al., which showed that two distinct capillary plexuses within the deep vascular complex could best be separated by defining slab boundaries based on the minima of the flow density profiles (Figure 7).[9,10] A subsequent study using SPECTRALIS OCTA by Hirano et al. made use of this concept. The results were used to define the appropriate boundaries to separate the intermediate and deep capillary plexus for SPECTRALIS.[11] The precise slab definitions differentiate the distinct geometric vascular patterns of the intermediate capillary plexus and deep capillary plexus and separate the nerve fiber layer vascular plexus from the superficial vascular plexus. The result is that clinicians can rely on accurate data in each slab, and

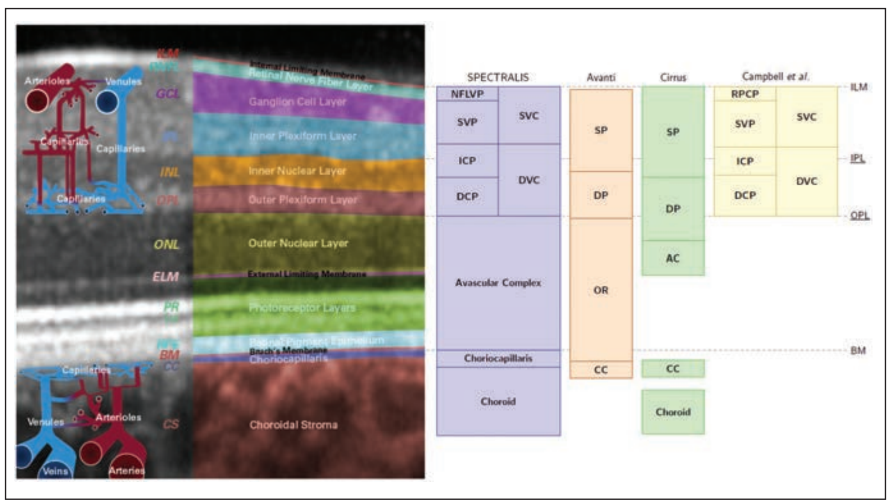


Figure 7. Definition of the slab boundaries. Left: Schematic figure of the layers and vessel networks in the human retina (Download here: www.he-academy.com/ Retinal-Layers-Interactive). Right: Schematic figure of the slab definitions of SPECTRALIS, Avanti,[10] Cirrus, and Campbell et al.[9]

Abbreviations: SVC: Superficial Vascular Complex; NFLVP: Nerve Fiber Layer Vascular Plexus (part of SVC); SVP: Superficial Vascular Plexus (part of SVC); DVC: Deep Vascular Complex; AC: Avascular Complex; ICP: Intermediate Capillary Plexus (part of DVC); DCP: Deep Capillary Plexus (part of DVC); CC: Choriocapillaris/Choroid Cap; RPCP: Radial Peripapillary Capillary Plexus; SP: Superficial Plexus; DP: Deep Plexus; OR: Outer Retina.

Sources:

SPECTRALIS: Heidelberg Engineering. OCT Angiography Module User Manual, Software Version 6.9. 2017.

Cirrus: Carl Zeiss Meditec Inc. CIRRUS HD-OCT User Manual Models 500, 5000, 2016. Campbell et al.[9]

Avanti: Avanti Optovue. Optovue RTVue XR OCT Avanti System User Manual, Software Version 2016.1.0.26. 2016.[10]

they will not experience gaps in between the slabs that could lead to missed vascular abnormalities and hindered diagnosis.

• **Use scan patterns to visualize either broad areas or the smallest capillaries.** The SPECTRALIS OCTA Module has adjustable scan patterns, so clinicians have the flexibility to customize the density and field of view for various pathologies. For example, a high-speed 30° x 15° (~8.8 mm x 4.4 mm) scan pattern with a lateral resolution of 11 µm/pixel provides a large overview of retinal and choroidal circulation—ideal for detecting large vascular abnormalities or problems outside the central macula, as well as for evaluating capillary dropout in retinal conditions. A high-resolution 10° x 10° (~ 2.9 x 2.9 mm) scan pattern with a lateral resolution of 5.7 µm/pixel gives clinicians the resolution needed to visualize the smallest capillaries, which are about 8 µm (Figure 8).[12]

The SPECTRALIS OCTA Module also applies a contrast function to improve the visibility of small capillaries (Figure 9). At higher contrast, small capillaries are seen more clearly, while lower contrast resembles FA, with enhanced visualization of thicker vascular structures such as superficial arteries or larger neovascularizations.

MAKING PROGRESS ON OCTA'S RECOGNIZED LIMITATIONS

OCTA has known limitations in how it images unusual structural pathologies and how it delivers data to clinicians. Several features of the SPECTRALIS OCTA Module are designed specifically to maximize practical use of the data it captures, regardless of whether the pathology is common or rare.

• **Adaptive retinal slab.** One key area for improvement is OCTA's ability to adapt to pathological disruption of the retinal layers. When a condition causes extensive disruption of the retinal layers, it confounds the OCTA slab definitions. To address the problem, the SPECTRALIS OCTA Module introduced an adaptive retinal slab, which allows clinicians to see a continuous interactive display of structure and flow between the internal limiting membrane (ILM) and Bruch's membrane (BM). The adaptive slab changes shape according to the proximity of its upper and lower boundary, to the ILM and BM respectively, which can help to visualize individual vascular layers even in cases of disrupted retinal boundaries. Clinicians can change the thickness and location of the adaptive retinal slab based on pathology, allowing them to see this customized view in the corresponding en face images as well (Figure 10).

• **Segmentation propagation tool.** Pathological changes can affect OCTA's segmentation of retinal layer boundaries. Clinicians treating patients with intraretinal fluid or certain atrophic changes need to review the segmentation to be sure en face projections are accurate. With some OCTA devices, clinicians need to correct each B-scan manually, which is cumbersome. The SPECTRALIS OCTA Module's segmentation propagation tool enables clinicians to correct only a few evenly spaced B-scans and then takes over to correct the rest.

• **Projection artifact removal.** OCTA systems continue to face the issue of projection artifacts. Since the OCT beam passes through the superficial layers before reaching and being reflected in the deeper layers, large superficial vessels create OCT signal fluctuations in the deeper layers, even if nothing is moving. Most OCTA algorithms cannot differentiate between these artifactual signal fluctuations and fluctuations caused by blood flow in the deeper layers.[6,13] Some systems use algorithms that mask the regions below larger superficial vessels, resulting in dark areas and seemingly disrupted vasculature appearing in deeper layers.[14,15] The SPECTRALIS OCTA Module, on the other hand, uses a projection artifact removal algorithm to minimize artifacts without affecting visualization of deeper-layer vasculature. Additionally, the clinician has the option to toggle the projection artifact removal tool on and off to confirm the integrity of the displayed data.

ENHANCING THE SPECTRALIS OCTA MODULE FOR THE FUTURE

By imaging vascular networks in greater detail than ever before and providing new information as part of a multimodal approach to imaging, OCTA has the potential to improve how clinicians diagnose, monitor, and treat vascular and inflammatory diseases. OCTA's depth-resolved retinal vascular information can be used to evaluate a spectrum of retinal vascular diseases, including DR, retinal vein occlusion, uveitis, retinal arterial occlusion, and age-related macular degeneration, as well as neurodegenerative diseases, such as glaucoma, Alzheimer's disease, and Parkinson's disease.

A key area for improvement of OCTA remains retinal perfusion. Today, as dye-based angiography remains the clinical standard for this purpose, Heidelberg Engineering is pursuing the goal of enabling OCTA to precisely detect and quantify retinal perfusion with three-dimensional vessel segmentation. In addition, the company is actively developing functional improvements to the SPECTRALIS OCTA Module in other key areas, including:

• **Speed.** SPECTRALIS offers the highest lateral and axial resolution OCTA scans on the market, accompanied by high-lateral and axial resolution structural OCT scans with flow overlay. For high-resolution OCTA images to be anatomically and geometrically accurate, precise TruTrack Active Eye Tracking is essential. Live eye tracking acquires more data, which does take more time than a structural OCT scan, but is a significantly faster solution to collect angiographic information when compared to dye-based angiography.

To increase OCTA acquisition speed, Heidelberg Engineering plans to release OCTA scanning protocols in the near future that are significantly faster. With faster, high-resolution OCTA scanning protocols, practices will be able to improve workflow without sacrificing quality.

• **Reference database.** Not all improvements to a diagnostic technology can be made by engineers. Only clinical research can provide the data needed to enhance the reference databases and analytics that support clinical diagnosis. For the SPECTRALIS OCTA Module, research is underway to develop and visualize reference data for capillary density measurements.[9,11]

• **Analytics.** Based on research on how vascular changes relate to thickness changes in the retinal nerve fiber layer and ganglion cell layer, Heidelberg Engineering is also working to develop OCTA analytics for glaucoma diagnosis. High-resolution SPECTRALIS OCTA images will help provide analytics for morphological changes such as vessel tortuosity and loops, interconnectivity, foveal avascular zone size and shape, and microaneurysms. In addition, artificial intelligence is being explored for its potential ability to facilitate early and automatic detection of vascular changes that may indicate a disease or predict its progression.

• **Visualization enhancements.** Heidelberg Engineering is making efforts to enhance visualization as well. To make it easier for clinicians to assess vascular changes of the peripheral retina seen in diseases such as DR, Heidelberg Engineering is working to expand the OCTA field of view. In addition, the development of three-dimensional vessel segmentation will improve three-dimensional visualization of blood vessels and enhance analytics.

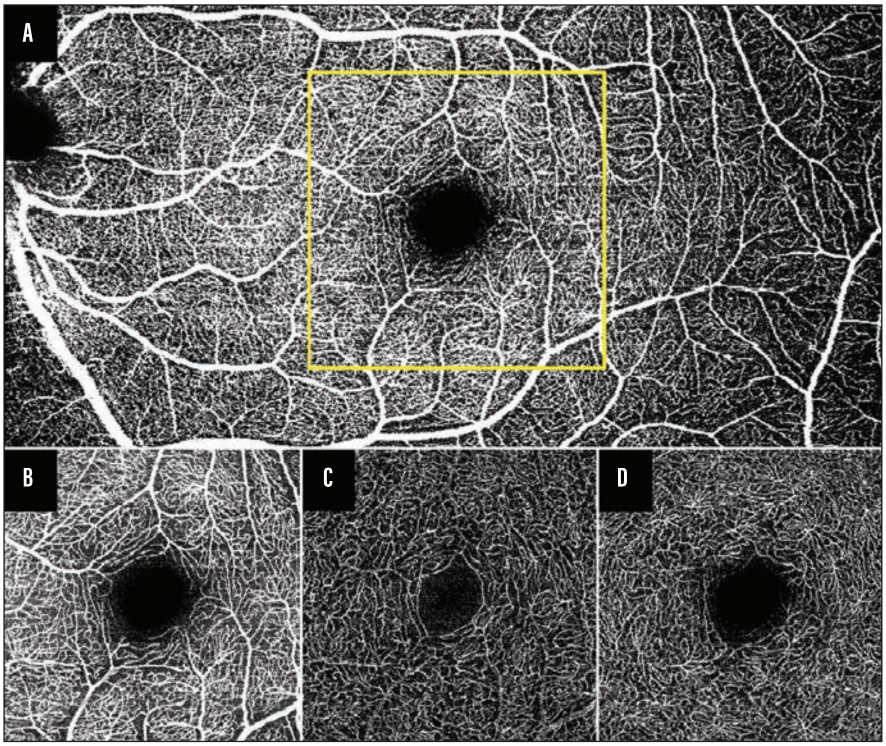


Figure 8. Comparison of two examinations of the same eye. A: En face image of the SVP from 30° x 15° scan acquired in high-speed and high-resolution mode (11 µm/pixel) providing a large field of view. B, C, and D: En face images acquired from a 10° x 10° scan in high-resolution mode (5.7 µm/pixel). B: The small capillaries are better resolved in the SVP en face image of the high-resolution scan. Compare B to the yellow outline in A which shows the same region of the same eye. C: The ICP can be clearly distinguished from the DCP (D) due to the high axial resolution (~3.9 µm/pixel) of SPECTRALIS OCTA. The ICP and DCP vessel networks show clearly distinct geometric structures. In the DCP, star-like vascular intersections can be discerned, which likely represent connection to the venous superficial network.

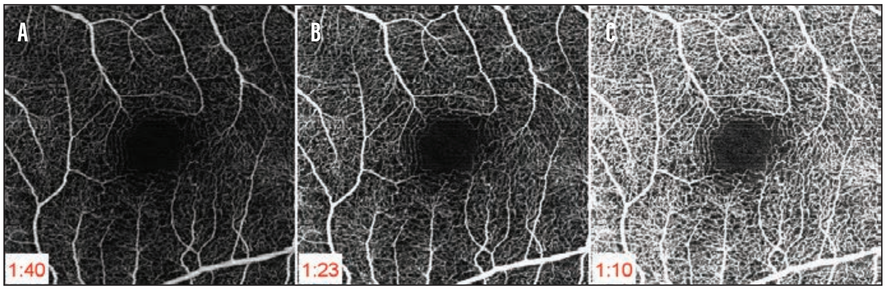


Figure 9. OCTA en face images (sum projection) of the full retina slab (from ILM to basement membrane) with different contrast settings. A: The contrast is set to 1:40, producing a low contrast OCTA image that resembles an FA image. B: The contrast is set to 1:23, producing an OCTA image with more contrast that highlights smaller capillaries. With this setting, the brightness of larger vessels begins to saturate. C: The contrast is set to 1:10, producing an OCTA image with even more contrast where the en face image is becoming saturated since the full retina slab includes both the SVC and the DVC.

• **Depth.** Collaboration with key opinion leaders revealed that resolution in the z direction (depth) allows clinicians to make better diagnostic decisions when evaluating various retinal vascular diseases. Based on this feedback, Heidelberg Engineering developed a dense B-scan OCTA protocol that takes advantage of SPECTRALIS TruTrack Active Eye Tracking, allowing for the quick acquisition of multiple OCTA scans

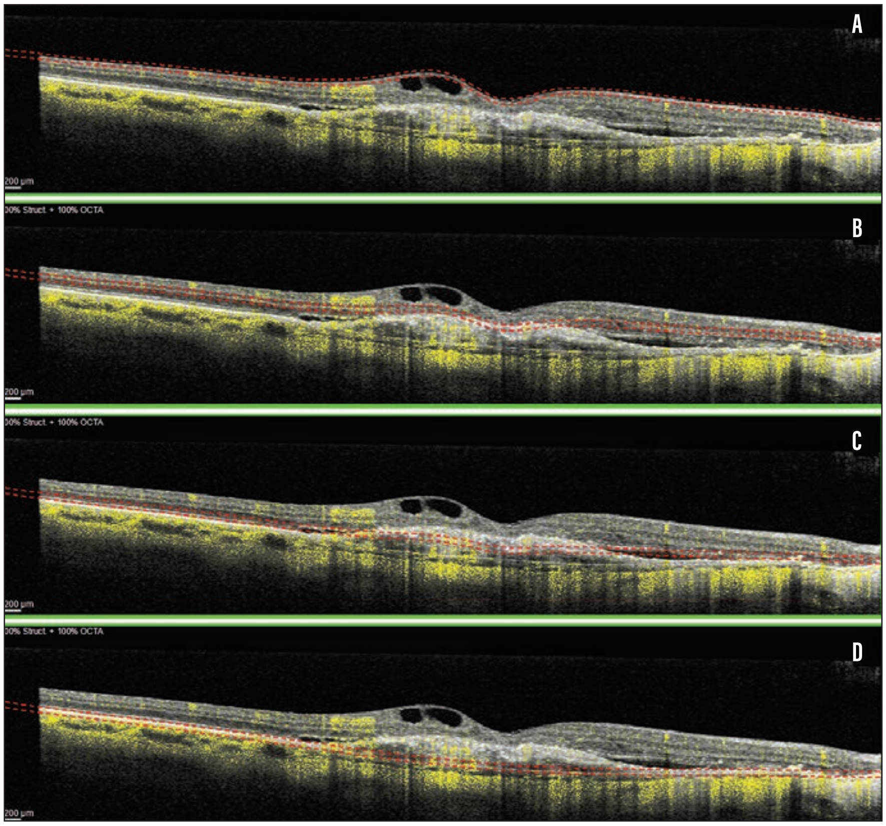


Figure 10. OCTA section images showing the adaptive slab feature. The shape of the slab is automatically adjusted to fit the ILM (A), demonstrated by dashed-red lines, and changes progressively (B, C) to adopt the shape of BM (D). The thickness of this slab can also be customized.

within a small region of the retina. The combination of live eye tracking and dense OCTA scan patterns delivers the highest axial resolution OCTA on the market. The software produces structural OCT and OCTA images with less speckle and noise.[16] With this dense B-scan OCTA, clinicians will be able to precisely correlate retinal microstructures and blood flow, allowing them to refine and enhance their understanding and clinical management of vascular diseases.

CONCLUSION

Taken together, these improvements represent a very deep, long-term commitment to deliver the best OCTA technology possible. This extensive research and development—speed, depth, field of view, new reference data, and analytics—will ultimately benefit patients by driving diagnosis earlier in the disease process. ■

1. De Carlo TE, Romano A, Waheed NK, et al. A review of optical coherence tomography angiography (OCTA). *Int J Retina Vitreous*.2015;1:5.
2. Zhang A, Zhang Q, Chen CL, et al. Methods and algorithms for optical coherence tomography-based angiography: a review and comparison. *J Biomed Opt*. 2015;20(10):100901.
3. Gao SS, Liu G, Huang D, et al. Optimization of the split-spectrum amplitude-decorrelation angiography algorithm on a spectral optical coherence tomography system. *Opt Lett*. 2015;40(10):2305-2308.
4. Jia Y, Tan O, Tokayer J, et al. Split-spectrum amplitude-decorrelation angiography with optical coherence tomography. *Opt Express*. 2012;20(4):4710-4725.
5. Kraus M, Mayer MA, Bock R, et al. Motion artifact correction in OCT volume scans using image registration. *Invest Ophthalmol Vis Sci*. 2010;51:4405-4405.
6. Spaide RF, Fujimoto JG, Waheed NK. Image artifacts in optical coherence tomography angiography. *Retina*. 2015;35(11):2163-2180.
7. Kraus MF, Potsaid B, Mayer MA, et al. Motion correction in optical coherence tomography volumes on a per A-scan basis using orthogonal scan patterns. *Biomed Opt Express*. 2012;3(6):1182-1199.
8. Kraus MF, Liu JJ, Schottenhamml J, et al. Quantitative 3D-OCT motion correction with tilt and illumination correction, robust similarity measure and regularization. *Biomed Opt Express*. 2014;5(8):2591-2613.
9. Campbell JP, Zhang M, Hwang TS, et al. Detailed vascular anatomy of the human retina by projection-resolved optical coherence tomography angiography. *Sci Rep*. 2017;7:42201.
10. Avanti: Avanti Optovue. Optovue RTVue XR OCT Avanti System User Manual, Software Version 2016.1.0.26. 2016.
11. Hirano T, Chanwimol K, Weichsel J, et al. Distinct retinal capillary plexuses in normal eyes as observed in optical coherence tomography angiography axial profile analysis. *Sci Rep*. 2018;8(1):9380.
12. Tan PE, Yu PK, Balaratnasingam C, et al. Quantitative confocal imaging of the retinal microvasculature in the human retina. *Invest Ophthalmol Vis Sci*. 2012;53(9):5728-5736.
13. Spaide RF, Fujimoto JG, Waheed NK, et al. Optical coherence tomography angiography. *Prog Retin Eye Res*. 2018;64:1-55.
14. Liu L, Gao SS, Bailey ST, et al. Automated choroidal neovascularization detection algorithm for optical coherence tomography angiography. *Biomed Opt Express*. 2015;6(9):3564-3576.
15. Zhang A, Zhang Q, Wang RK. Minimizing projection artifacts for accurate presentation of choroidal neovascularization in OCT micro-angiography. *Biomed Opt Express*. 2015;6(10):4130-4143.
16. Freund KB, Gattoussi S, Leong BC. Dense B-scan optical coherence tomography angiography. *Am J Ophthalmol*. 2018;190:78-88.