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TOPCON EURETINA 2018

Clinical Advances and Applications With Swept Source OCT and Angiography.

This supplement summarizes highlights from a lunch symposium held during the 2018 Euretina Congress in Vienna, Austria.

Thought leaders in ophthalmology shared their insights on the latest imaging technologies and their utility in clinical practice.

For more great lectures on Swept Source OCT and angiography, plan to attend the 3rd International Swept Source OCT and Angiography (ISSOCT) Conference on February 10 and 11, 2019, in Fort Myers, Florida.

CONTENTS

Swept Source OCT Angiography in the Diagnosis of Preophthalmoscopic Diabetic Retinopathy

A new study suggests OCT angiography detects early microvascular retinal changes not detectable in clinical examination.

BY JOSÉ M. RUIZ-MORENO, MD, PHD

Diabetic retinopathy (DR) affects approximately 93 million people worldwide and is the leading cause of blindness in working-age adults in developed countries.[1] Patients with DR do not experience visual symptoms until the later stages of the disease, thus, early detection of DR is critical for determining optimal management.

The first ophthalmoscopic sign of DR is the presence of microaneurysms in the posterior pole. While intravenous fluorescein angiography (IVFA) is more sensitive than ophthalmoscopy for detecting microaneurysms in the early stages of DR, it provides little information about the retinal capillary network. In addition, IVFA is invasive, costly, and time-consuming and, thus, is not an appropriate screening test for DR.

OCT angiography (OCT-A) is a rapid, noninvasive test that can be used to analyze the retinal microvasculature. The quality is at least as high as in IVFA, and OCT-A enables us to identify retinal vascular plexi separately. The high resolution of the microvascular details enables us to easily delineate the foveal avascular zone (FAZ) in diabetic eyes. Several studies have demonstrated quantitative differences of FAZ dimensions in DR compared to controls using IVFA.[2]

OCT-A reveals vascular changes associated with DR, such as microaneurysms, areas of capillary nonperfusion, tortuosity of the vessels, neovessels, and changes in FAZ.

With this technology, we can also accurately study the morphology of the neovessels that is the cause of blurred vision (Figure 1).

With the new DRI Swept Source OCT Triton (Topcon), we can perform 9 mm x 9 mm or 12 mm x 12 mm scans and obtain OCT-A maps to visualize vascular density. Figure 2 displays a case with cotton wool spots near the optic nerve. The vascular density map shows an absence of vascularization at this level.

Leakage is a usual sign of neovessels in IVFA, but it is not present in OCT-A; therefore, we must study the OCT at the same time with OCT-A to analyze and compare the presence of dark spaces to avoid a misdiagnosis of ischemia from a space occupied by fluid in macular edema, as in this case of diabetic macular edema (Figure 3).

We can also use OCT-A to quantify vascular density. Using maps of capillary perfusion density and mean perfusion density values, Agemy and colleagues found that patients with diabetes had significantly lower capillary perfusion density compared to normal controls, and they introduced the concept of color-coded perfusion density in OCT-A to quantify progressive retinal perfusion changes in DR.[3]

STUDY PURPOSE AND METHODS

The aim of our study was to determine if OCT-A can detect early microvascular changes not visible in the clinical examination, which until now is the usual procedure for DR screening. This was a prospective observational study of 34 eyes of 34 patients with diabetes mellitus without ophthalmoscopic DR and 20 eyes of 20 healthy patients (controls) matched in age and sex.

BCVA at the time of OCT-A imaging was 20/20 to 20/25. Images with poor signal or motion artifacts that were substantial enough to disrupt clear delineation of the FAZ were excluded.

We performed retinography and Swept Source OCT-A with the DRI Swept Source OCT Triton. Eyes with concomitant retinal diseases or other abnormalities of the vitreoretinal interface were excluded.

The variables studied included age, time of diabetes mellitus (DM), HbA1c, retinal thickness, retinal nerve fiber layer thickness, ganglion cell layer thickness, subfoveal and mean choroidal thickness, FAZ area and FAZ perimeter at the superficial (SP) and deep plexus (DP), vascular density at SP, DP, and choriocapillaris.

Acircularity index was defined as the ratio of the perimeter of the FAZ to the perimeter of a circle with equal area. Axis ratio was defined as the ratio between the major and minor axis of the generated ellipse. A perfectly circular FAZ has an axis ratio equal to 1.

Statistical analyses were performed as follows:

- The intraclass correlation coefficient with 95% confidence interval was calculated to assess inter-rater agreement.
- Correlation analyses were performed with a Spearman's

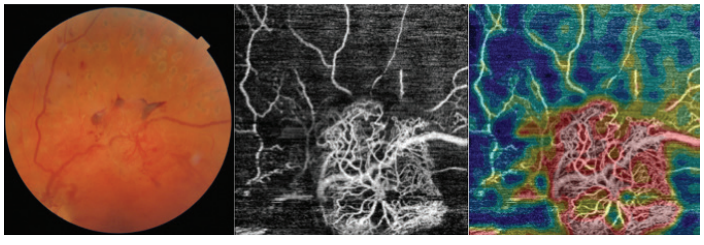

Figure 1. A young patient with proliferative diabetic DR. OCT-A shows the morphology of the neovessels growing.

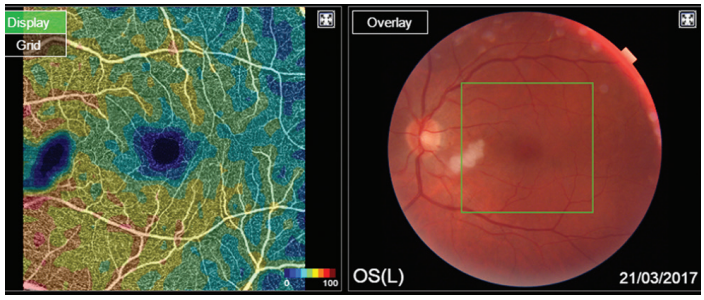

Figure 2. Retinography of the left eye of a young diabetic patient with cotton wool spots. OCT-A demonstrates the absence of blood circulation.

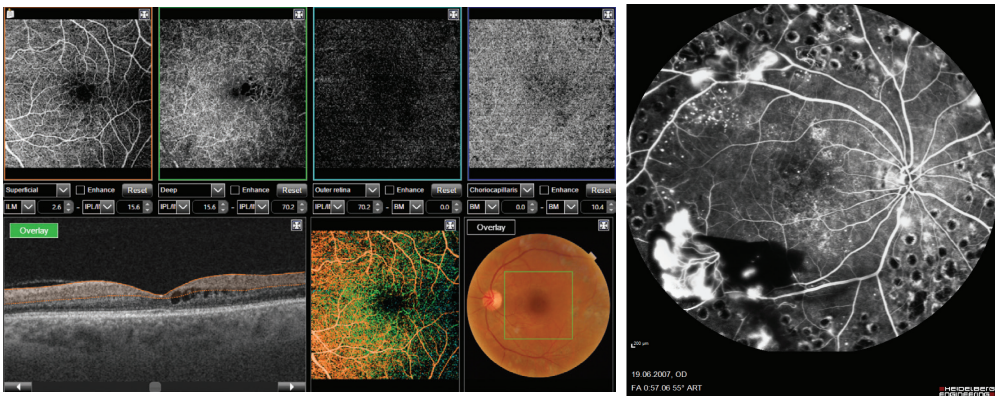

Figure 3. Right, IVFA showing leakage from neovessels in an eye with proliferative DR. Left, OCT-A in a case of diabetic macular edema; dark spaces correspond to intraretinal cysts, not ischemic areas.

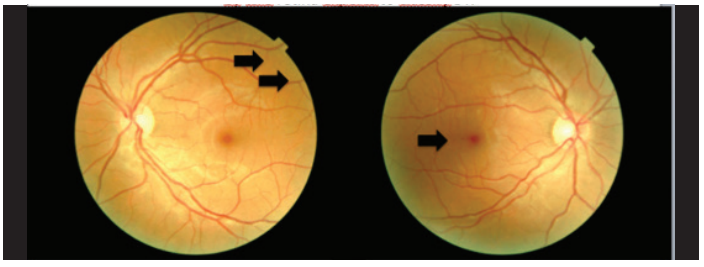

Figure 4. Masked examiners studied fundus retinography to classify DR.

rank correlation coefficient (q) if data did not demonstrate normality.

- The nonparametric Kruskal-Wallis and post hoc Mann-Whitney U tests with the Holm-Bonferroni correction for multiple comparisons were used to compare values between groups.
- P <.05 was considered significant.
- SPSS statistical software (IBM) was used.
- Fundus retinography was studied in a masked manner by two retina experts to classify DR (Figure 4).

STUDY RESULTS TO DATE

We found no statistically significant differences in retinal thickness, retinal nerve fiber layer thickness, ganglion cell layer, and subfoveal and mean choroidal thickness. We did find statistically significant differences in the perimeter of the FAZ at the DP and SP levels. We also found statistically less vascular density of the deep plexus in diabetic patients versus controls.

The acircularity index and the axis ratio in both plexi were statistically significantly different, as they were larger in the diabetic patients without DR versus the patients in the control group.

We have looked for the correlation of the seven statistically significant parameters with the HbA1c% and time of DM, finding no significant correlations with HbA1c% and significant correlations with the time of DM except for the axis ratio at DP.

STUDY CONCLUSION

We found that OCT-A can detect early microvascular retinal changes that are not detectable in the clinical examination in diabetic eyes without DR. Changes in the surface and morphology of the FAZ and the vascular density were more prevalent in diabetic eyes.

OCT-A is capable of detecting DR before the ophthalmoscopic diagnosis is made. It could be used as rapid, noninvasive screening for DR; however, the cost and the "necessary experts" are important limitations.

This is an ongoing study, which has yet to be published. ■

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Examining Vascular Flow Changes in Macular Telangiectasia Type 2

OCT angiography leads to deeper understanding.

BY CAREL HOYNG, MD, PHD

OCT angiography (OCT-A) is opening new windows in medicine, not only in ophthalmology but also in the study of small-vessel diseases in neurology and cardiology, as it enables physicians to see much smaller vessels than can be seen with angiography.

The following preliminary data are from a study of macular telangiectasia (MacTel). This report provides new insight into the disorder and also highlights the future utility of OCT-A.

ABOUT MACTEL

Type 2 MacTel is a rare, progressive disorder with characteristic changes temporal to the fovea. There are five disease stages, and VA decreases rapidly from about 50% to 10%. The cause of MacTel is unknown, and there is no treatment.

OCT-A relies on motion contrast to detect blood flow and registers the difference between two sequential B-scans. This noninvasive technology enables us to visualize 3D images of the deeper retinal layers.

According to the literature, OCT-A findings in MacTel type 2 include posterior displacement of retinal vessels, vascular invasion of the outer retina, loss of capillaries in all plexi, and reduced capillary density.[1-3]

STUDY PURPOSE AND DESIGN

The purpose of our study was to compare capillary density and fractal dimension in eyes with MacTel type 2, per MacTel stage and quadrant, versus healthy controls. Controls were defined as patients without retinal pathology in the study eye. For the quantitative analysis, 51 eyes of 33 MacTel patients met the inclusion criteria.

We used the Swept Source DRI OCT Triton (Topcon) for OCT-A color photographs, and the Spectralis HRA+OCT (Heidelberg) for clinically indicated fluorescein angiography (FA). The photographs were graded according to the Gass and Blodi classification.[4]

Figure 1 describes how we processed our images, removing artifacts, for example, using software available from the internet. For quantitative analysis, we calculated the capillary perfusion density by dividing the area occupied by flow pixels by the total area. We also looked at fractal dimension, which is the measurement of complexity. Much like a snowflake, the more branches there are, the more complex the fractal dimension. Capillary perfusion density and fractal dimension provide the measurement of the vascular status.

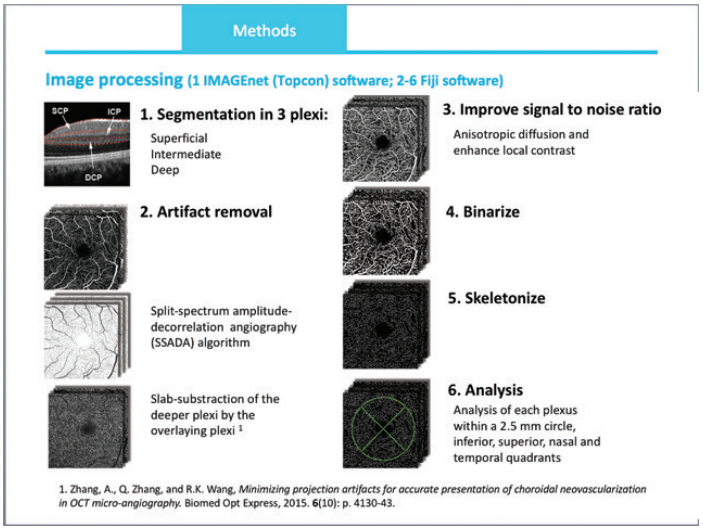

Figure 1. Image processing followed a specific protocol to ensure quality.

STUDY FINDINGS

As shown in Figure 2, FA reveals leakage in stage 1 MacTel, and OCT-A shows a typical hole in the foveal area, mostly temporal. Often, this finding is mistaken for cystoid macular edema. The retinal tissue has collapsed, and on OCT-A, we see ectatic vessels in the temporal quadrant of the intermediate deep capillary plexus.

In stage 2, FA shows more leakage, and OCT-A reveals more abnormalities.

In stage 3, the vessels cling together, and the vascular architecture is becoming more complex and abnormal. Some smaller vessels are missing, and new vessels have developed.

In stage 4, choroidal neovascularization is developing in the outer retina. With OCT-A, we can sometimes see peculiar flat, 2D choroidal neovascularizations in the outer retina. These can also be seen in other diseases, such as central serous chorioretinopathy and age-related macular degeneration.

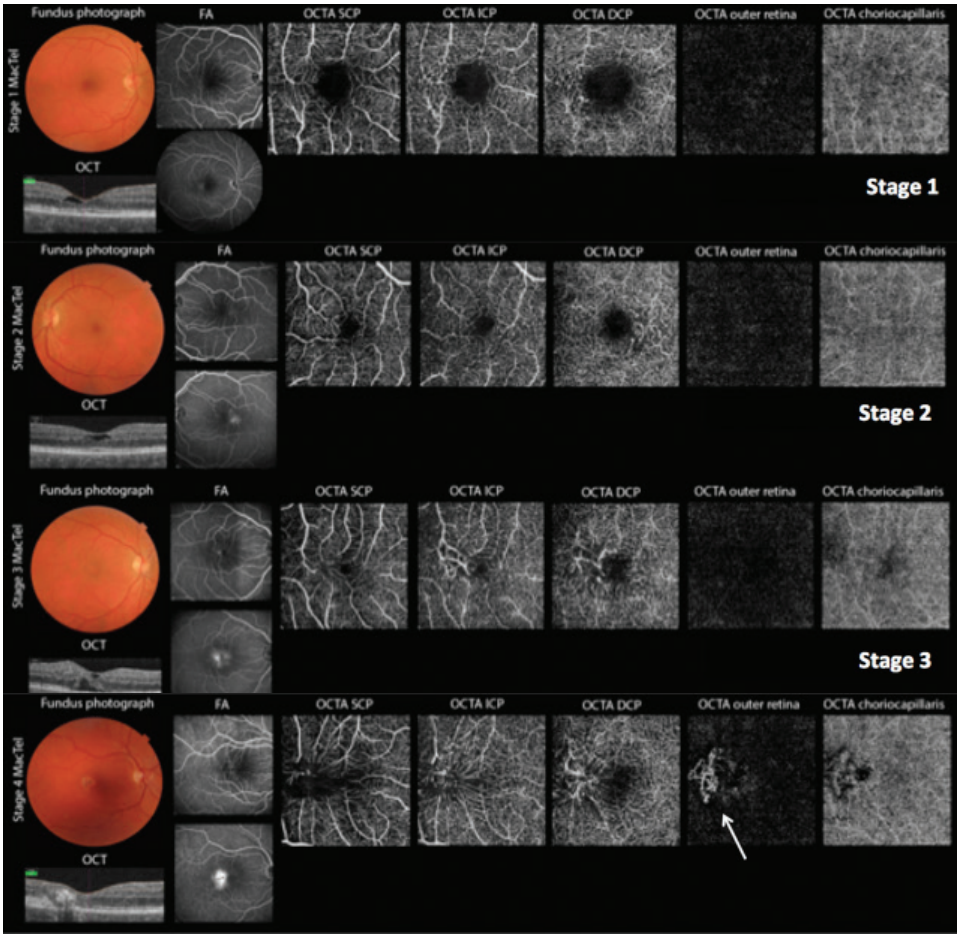

Figure 2. We studied 51 eyes at various stages of MacTel.

We found the capillary perfusion density was decreased in all plexi, and it was significantly reduced in MacTel stage 3 and stage 4 (Figure 3). We also found the capillary perfusion density was reduced significantly in all quadrants of the deeper plexus (Figure 4), and the fractal dimension was reduced significantly in the superficial plexus (Figure 5). The fractal dimension was significantly reduced in the superficial plexus in MacTel stages 3 and 4 (Figure 6).

STUDY CONCLUSION

Based on our preliminary data, we believe the capillary perfusion density is reduced in MacTel eyes, predominantly in the deeper plexus. One theory is that MacTel is a disease of the Müller cells, and our findings appear to be in line with that theory. In addition, the fractal dimension in MacTel eyes is reduced in the superficial plexus, most likely because of collapsed layers in later stages.

SUMMARY

With this study, my colleagues and I provided some insight into this rare disease, utilizing OCT-A with applications available from the internet. Most importantly, we

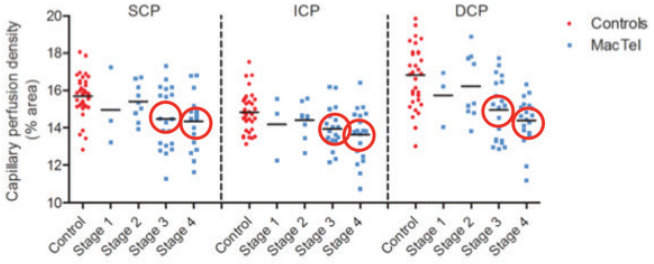

Figure 3. Capillary perfusion density was significantly reduced in eyes in MacTel stages 3 and 4.

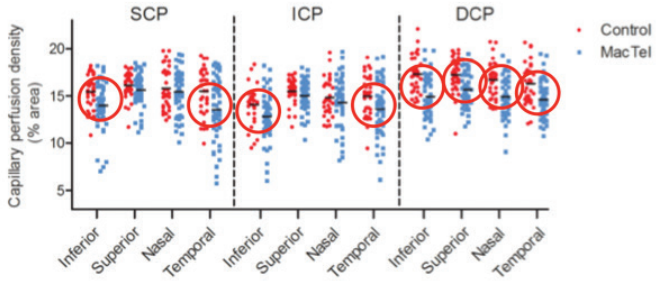

Figure 4. Capillary perfusion density was significantly reduced in all quadrants of the deep plexus.

	MacTel group (n=51)	Control group (n=33)	P-value
D_f superficial plexus	1.780 (± 0.014)	1.791 (± 0.009)	<0.001
D_f intermediate plexus	1.783 (± 0.014)	1.788 (± 0.009)	0.052
D_f deep plexus	1.790 (± 0.012)	1.794 (± 0.009)	0.105

Mean (± SD)

Figure 5. Fractal dimension was significantly reduced in the superficial plexus.

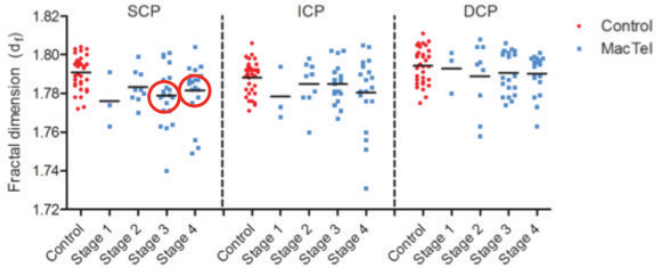

Figure 6. Fractal dimension was significantly reduced in the superficial plexus in MacTel stages 3 and 4.

demonstrated what can be done with this machine and what the future may hold for this technique. In our opinion, OCT-A will open a whole new era of retinal analysis in the future. ■

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Gain a Better Understanding of Optic Nerve Pathology With OCT Angiography

Advanced imaging technology offers new insights noninvasively.

BY LUISA PIERRO, MD

The vasculature of the optic nerve is well-identified using OCT angiography (OCT-A). Spaide and other authors found that the OCT-A examination of the retinal vasculature, especially around the optic nerve, without dye injection, may aid clinical evaluation in healthy individuals and patients with diseases.[1] My focus is the area of the optic nerve that corresponds to the radial peripapillary capillary network. Investigation of this area is important because various optic neuropathies involve this part of the optic disc. For OCT-A imaging, we use the DRI Swept Source OCT Triton (Topcon). In order to have a better understanding of optic nerve pathology we integrated the OCT-A with the B-scan retinal nerve fiber layer analysis.

GLAUCOMA

In a glaucomatous eye, we see capillary dropout and focal perfusion defects associated with retinal nerve fiber layer thinning (Figure 1).

In addition to the disc excavation, OCT-A reveals a thinning of the vessels that corresponds to an area of reduced ganglion cells in the glaucomatous eye. We can readily see the different vascularization in this particular glaucoma case compared to the control (Figure 2).

NONARTERITIC ANTERIOR ISCHEMIC OPTIC NEUROPATHY

In a case of nonarteritic anterior ischemic optic neuropathy (Figure 3), we can observe black areas that correspond to the

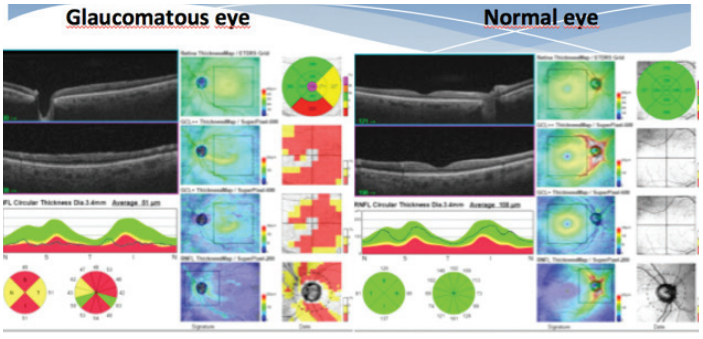

Figure 1. Note capillary dropout and focal perfusion defects associated with retinal nerve fiber layer thinning in the glaucomatous eye.

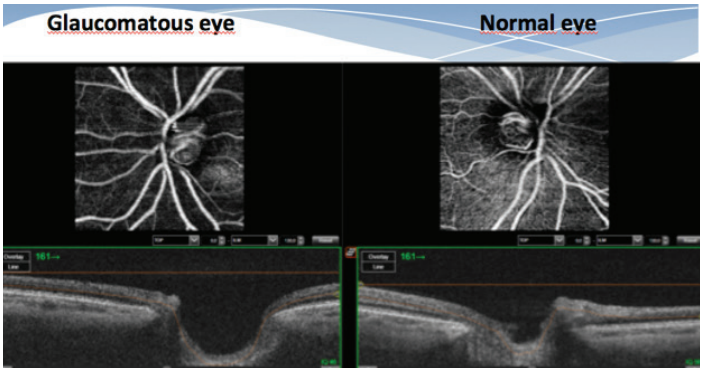

Figure 2. In the glaucomatous eye, OCT-A reveals a thinning of the vessels that corresponds to an area of reduced ganglion cells.

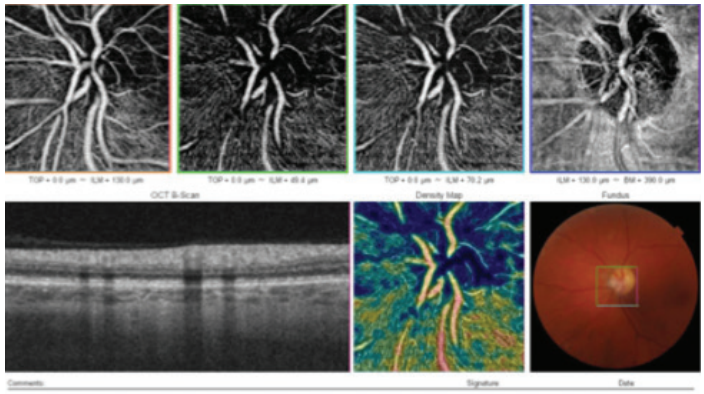

Figure 3. Black areas correspond to the blue color that shows the reduced vascularization in this area.

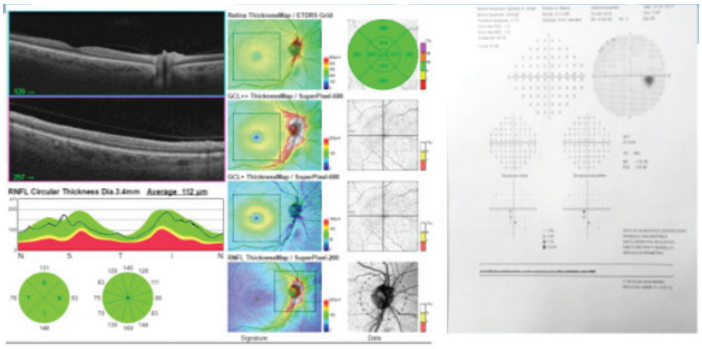

Figure 5. Note the difference between the affected eye (Figure 4) and the contralateral eye, which is normal.

blue color in the flow map that shows reduced vascularization in this area.

OCT-A reveals the reduced blood supply around the optic nerve. In addition, the same area corresponds to an area of reduced ganglion cells in accordance with the visual field (Figure 4). The aspect of the contralateral eye is different from the other eye, which is normal (Figure 5).

OPTIC NERVE DRUSEN

Optic nerve drusen are frequently seen in clinical practice. We can confirm the diagnosis using echography. Using OCT-A, we can observe different vascular features in each eye. In Figure 6, we observe disc overcrowding with altered vascularization in one eye, but this result is stronger in the other eye, where the drusen are more evident and push up the vascularization.

LEBER HEREDITARY OPTIC NEUROPATHY

In Leber hereditary optic neuropathy, OCT-A reveals microangiopathic alterations (Figure 7). In the contralateral eye, ischemic areas are less prominent but visible.

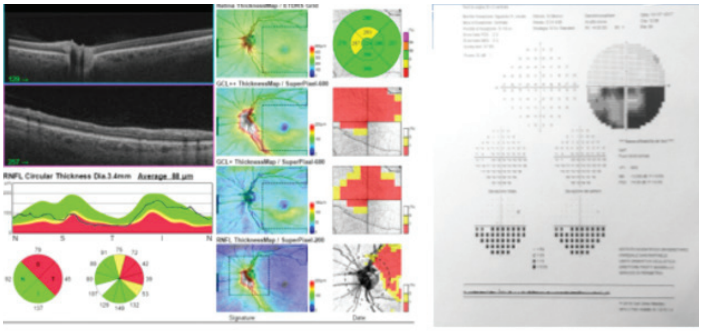

Figure 4. OCT-A reveals the reduced blood supply around the optic nerve.

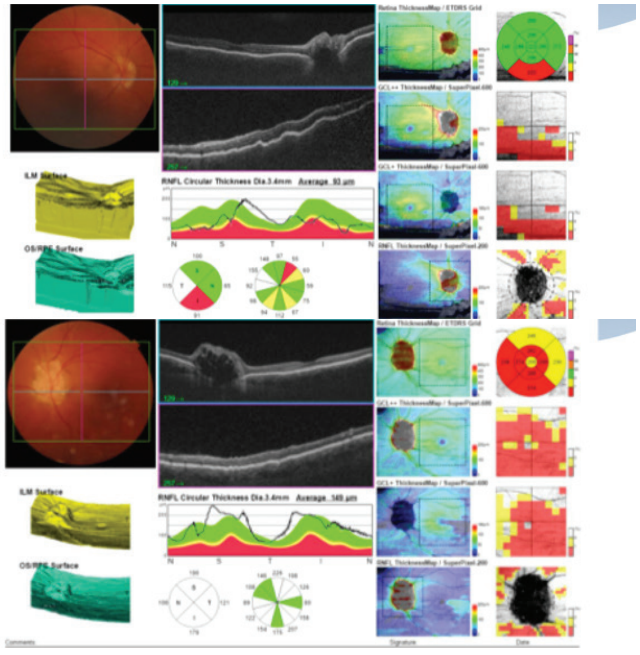

Figure 6. In one eye, disc overcrowding with altered vascularization is evident; in the other eye, drusen are more evident and larger.

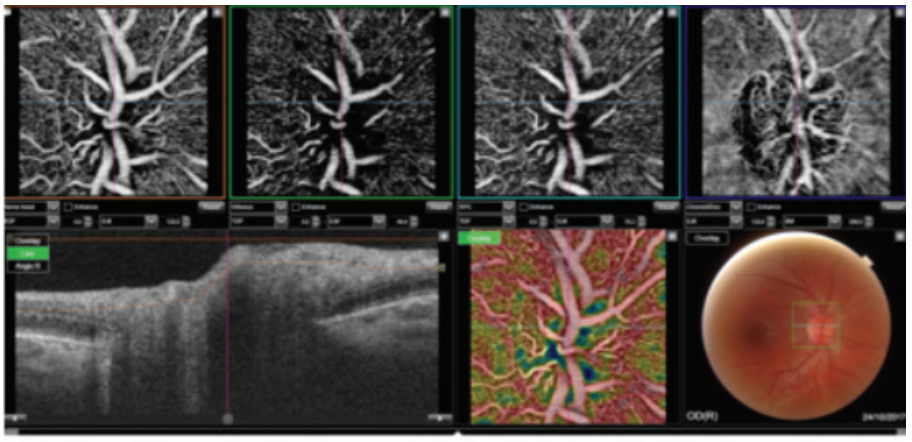

Figure 7. OCT-A reveals microangiopathic alterations in acute Leber hereditary optic neuropathy.

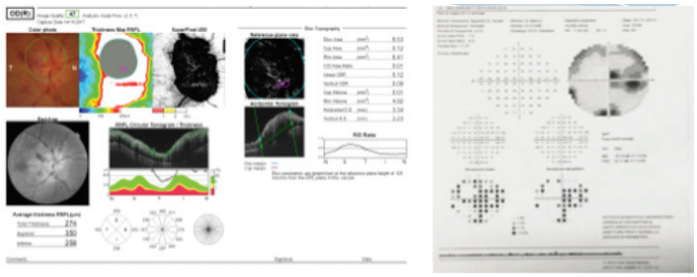

Figure 8. Hemorrhages and alterations of the retinal layers can be observed.

PAPILLEDEMA IN SYSTEMIC HYPERTENSION

The presence of papilledema in systemic hypertension involves not only the optic nerve itself but also the retina and choroid. Hemorrhages and alterations of the retinal layers can be observed, and there is a diffused but not significant alteration of the visual field (Figure 8).

SUMMARY

Thanks to OCT-A, we are now able to obtain useful information about optic nerve diseases without employing an invasive procedure. A new chapter of investigation is now open using not only OCT-A but also Topcon OCT wide field compared to visual field. Multimodal imaging is the gold standard in the diagnosis process in optic nerve diseases. ■

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Swept Source OCT Angiography for Managing Proliferative Diabetic Retinopathy

OCT angiography and the value of wide-field scans to monitor regression.

BY PEARSE A. KEANE, MD

OCT angiography (OCT-A) is an exciting technology that has huge potential in academic research. Today, however, I will discuss why I cannot live without OCT-A in my clinic, particularly when managing severe nonproliferative diabetic retinopathy (NPDR) and proliferative diabetic retinopathy (PDR).

MY STANDARD IMAGING PROTOCOL

For all patients with severe NPDR or PDR, my standard protocol with the DRI Swept Source OCT Triton (Topcon) includes:
- high-definition line scans,
- 12 mm x 9 mm 3D volume scans, and
- 6 mm x 6 mm AngioDisc scans.

Although wider fields can be obtained, the 6 x 6 works nicely for me, as it is quick and easy to obtain, and it provides the clinically relevant information I need.

Because of my high case volume, I have found that obtaining these scans before I see these patients is the most efficient approach, rather than sending patients back and forth to the photographers for additional imaging. We have imaged nearly 100 PDR eyes using this protocol over the last 18 months. Keep in mind, however, this technology is evolving so rapidly that this protocol may need to be adjusted based on new advancements.

The following case—a typical situation in most clinics—illustrates the utility of OCT-A.

CASE OF SEVERE NPDR

A 57-year-old woman with poorly controlled type 1 diabetes came to our clinic in October 2013. Her VA was 6/6 OD and 6/9 OS, and it appeared she had severe NPDR. Unfortunately, the patient did not keep her follow-up appointments and therefore, received no treatment. We next saw her in September 2017. In the interim, she had undergone anterior segment refractive laser procedures on both eyes.

In the left eye, standard OCT revealed macular edema (ME) and a partially detached posterior hyaloid with

vitreous hemorrhage dispersed throughout (Figure 1). Some neovascularization was also present.

The line scan of the right eye showed a neovascular complex on top of the disc and a tractional element elsewhere in the scan (Figure 2).

We also obtained a 12 x 9 volume scan but moved straight to the center of it with the 6 x 6 AngioDisc scan (Figure 3).

Note that when viewing the *en face* images, you may see beautiful delineation of the neovascular complex, but often, you will not see it. The key point is that the *en face* imaging is less interesting than turning on the flow so that it is superimposed on the B-scan. One reason why these images may not look pristine is because a massive neovascular complex is present and the segmentation gets confused. What you can do is look at the perfusion of the neovascular tissue.

In this case, on the projection OCT image (Figure 3), a massive frond of neovascular tissue is visible. We can see the vessels using the detached posterior hyaloid as a scaffold to climb through the vitreous.

Aside from the neovascularization shown on the AngioDisc images, we also have a sense that the normal retinal vasculature of the disc is engorged and more torturous (Figure 3).

Perhaps observing how those parameters change over time will also be a good indicator of regression following treatment.

The line scan of the other eye reveals the vitreous hemorrhage within the detached posterior hyaloid and the ME (Figure 4). When we look at the volume scan and take different cuts, we can see the posterior hyaloid pulling up.

A nice advantage of the Triton OCT-A machine, particularly when I am working with residents and fellows, is that I can scroll back and forth in the 12 x 9 images and quickly get a sense of the severity of the disease. In this case, the AngioDisc revealed active neovascularization, and we immediately began treatment with panretinal photocoagulation (PRP) and anti-VEGF therapy.

To date, the patient has received five anti-VEGF injections and PRP. Her VA is 6/9 and 6/24. On the volume scan, some laser scars are still visible, and the fibrous tissue is still present. Looking at the OCT-A, we see that the frond vessels have disappeared (Figure 6). When we turn on the flow, we see perfusion of the neovascular complex has disappeared, as have the invasive red blood vessels.

Of course, because we are breaking new ground, we need to be cautious and base our treatment decisions on the current

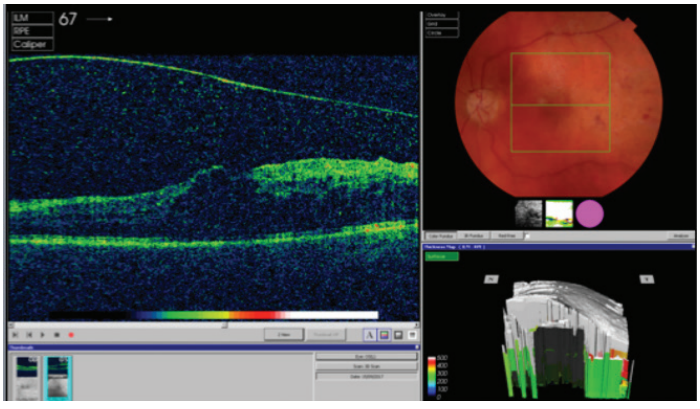

Figure 1. A standard OCT revealed ME and a partially detached posterior hyaloid with vitreous hemorrhage dispersed throughout.

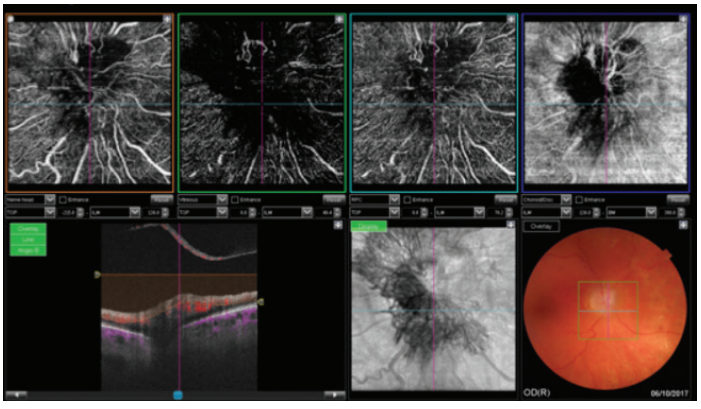

Figure 3. Aside from the neovascularization, the normal retinal vasculature of the disc appears engorged and more torturous.

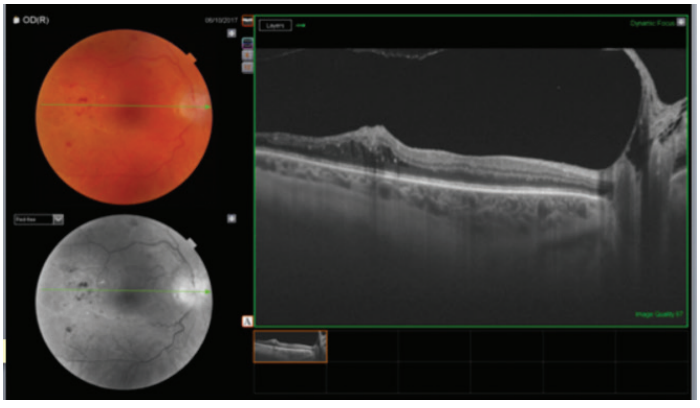

Figure 2. The line scan showed a neovascular complex atop the disc and a tractional element elsewhere in the scan.

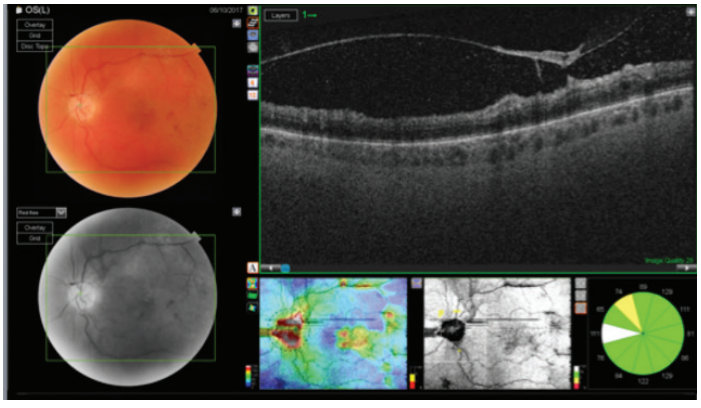

Figure 4. The line scan of the other eye reveals the vitreous hemorrhage within the detached posterior hyaloid and the ME.

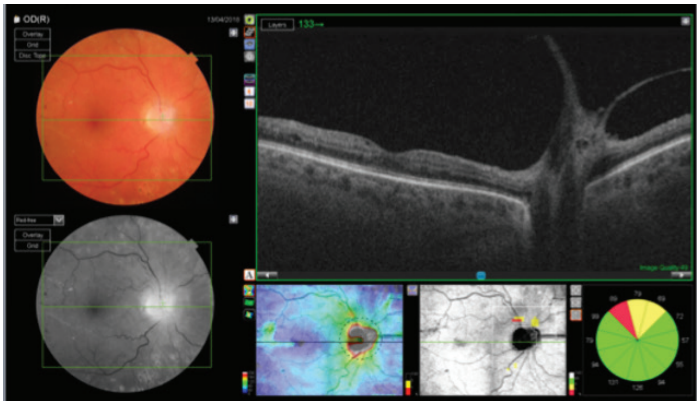

Figure 5. Posttreatment, some laser scars are still visible, and the fibrous tissue is still present.

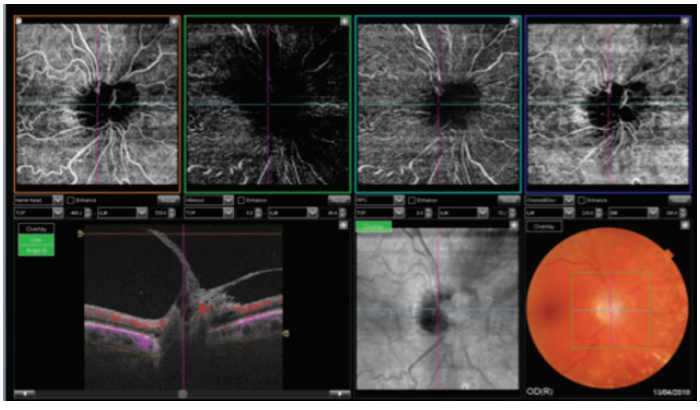

Figure 6. Posttreatment, the frond vessels have disappeared; when we turn on the flow, we see perfusion of the neovascular complex has disappeared.

gold standard. I am always somewhat concerned that we may be seeing an effect of the anti-VEGF. We should make sure that the PRP is sufficient and that we are closely monitoring these patients.

In the other eye, some vitreopapillary traction is visible (Figure 7). On the AngioDisc scan, there is no evidence of perfusion of the neovascular complex at the disc. We are continuing to closely monitor this patient.

It will be interesting to see how this case progresses over time, because I have other patients who have had similar situations. When they returned 2 months later, after a decision to closely monitor had been made, the frond of neovascularization had recurred, and we had to reescalate all treatments. This is exciting because it was captured beautifully using OCT-A, but we still need to be very cautious.

CONCLUSION

I believe widefield OCT is key to advancing the objective, quantitative treatment and monitoring of patients with PDR.

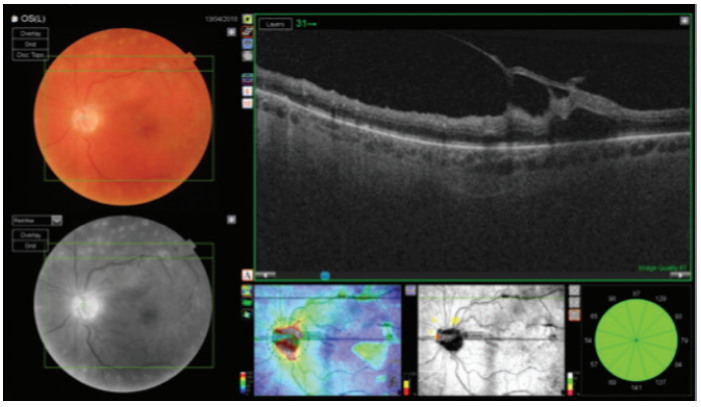

Figure 7. In the other eye, some vitreopapillary traction is visible, but there is no evidence of perfusion of the neovascular complex at the disc.

I have many cases where little bits of neovascularization start to emerge. We need to be able to scroll up and down through the volume scans, looking for tissue on top of the internal limiting membrane and looking for hyperreflective material growing just above. It can be quite subtle. I believe we, as a community, will need to reprogram ourselves to search for that sort of finding.

The posterior pole is the danger area, and the 12 x 9 volume scan facilitates quick review of this area, particularly in a context where I have 60 patients and cannot perform a bespoke examination of every one of them, in addition to that already provided by the resident or fellow in the clinic.

Judging flow is key to judging activity, particularly when studies suggest that anti-VEGF is a good treatment for neovascularization, and that we may be able to give three loading doses and then treat prn as determined by the absence or presence of activity.[1,2] We may be entering an era similar to that of the PrONTO study of wet age-related macular degeneration, when OCT becomes our go-to diagnostic tool to determine whether or not we reinject some eyes.[3] ■

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