MEETING THE DEMANDS OF A SHIFTING TREATMENT PARADIGM

OCT and OCTA facilitate earliest detection of PDR.

BY CAROLYN E. MAJCHER, OD, FAAO

Accurate staging of DR is incredibly important to enable us to manage patients appropriately according to standard-of-care recommendations, and it allows for prompt referral of eyes at high risk for vision-threatening complications. In my experience, clinical examination augmented with structural OCT and OCT angiography (OCTA) enables detection of proliferative diabetic retinopathy (PDR) earlier than is possible with a clinical examination alone.

CASE REPORT

A 51-year-old patient with an incoming diagnosis of severe nonproliferative diabetic retinopathy was referred to me by another optometrist for DR evaluation.

The fundus montage (Figure 1) shows extensive dot blot hemorrhaging extending into the midperiphery of all quadrants, with some exudates in the inferior macula and inferior temporal arcade. The only sign suggestive of PDR with clinical examination is a tiny area of neovascularization—resembling a small frond or sea fan—above the superior temporal arcade. When so many dot blot hemorrhages are present, however, I know the chance for PDR is high.

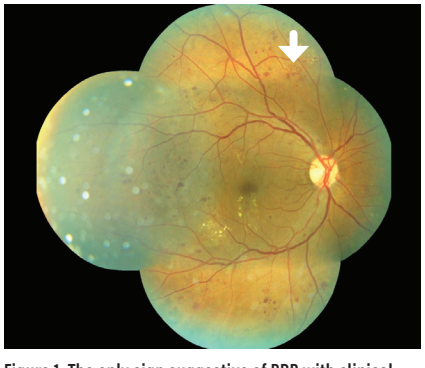

Figure 1. The only sign suggestive of PDR with clinical examination is a tiny area of neovascularization (see arrow) above the superior temporal arcade.

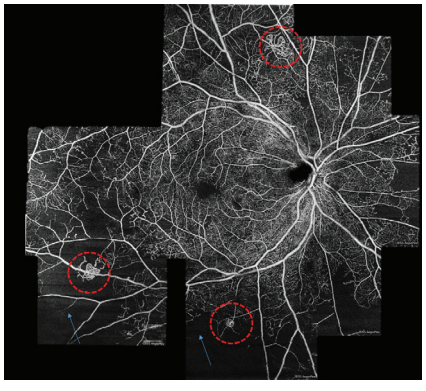

Figure 2. Note the three areas of preretinal neovascularization (see red circles), confirming the diagnosis of PDR.

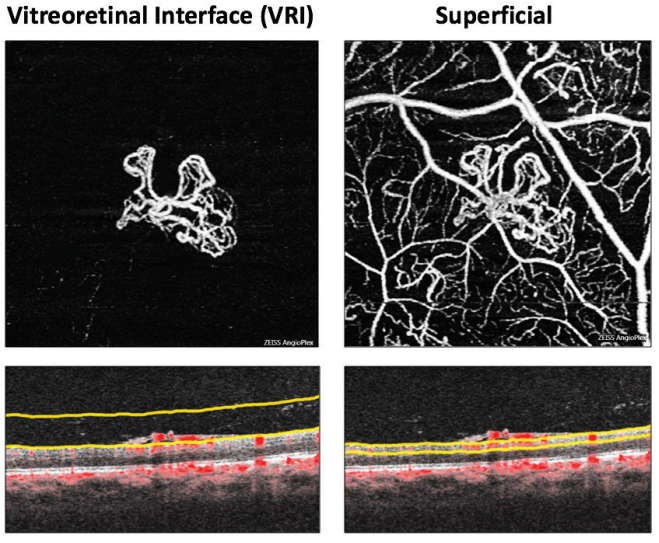

Figure 3. A magnified view of the preretinal neovascular membrane within the superior temporal arcade shows the exquisite detail that is possible with OCTA.

I routinely perform OCT and OCTA for all DR evaluations, and based on the appearance of the fundus, I know this eye is at high risk for proliferation. The OCTA montage (Figure 2) reveals three areas of preretinal neovascularization (red circles), confirming the diagnosis of PDR, and it reveals more severe proliferative disease than initially expected. The OCTA also highlights extensive retinal nonperfusion, particularly within the inferior temporal midperipheral fundus, which cannot be appreciated with ophthalmoscopy.

Figure 3 is a magnified view of the preretinal neovascular membrane within the superior temporal arcade. It shows the exquisite detail that is possible with OCTA, which is not

TAPPING THE UTILITY OF THE 1-LINE RASTER LIVE SCAN

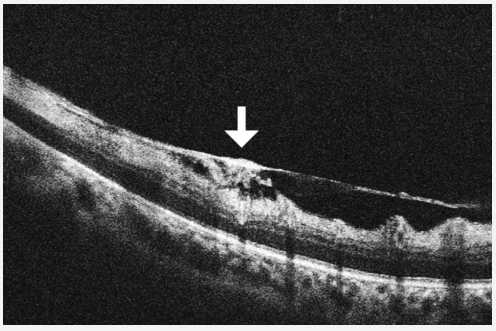

Figure 1. I live-scan the fundus to search for areas with tissue extending out above the retina (see arrow).

For all of my DR evaluations, particularly those at high risk for PDR, I drag the 1-line raster all around the posterior pole while in the acquisition mode to "live scan" the fundus. As I live scan, I search for areas with tissue extending out above the retina (Figure 1). Any area identified as having preretinal tissue, I scan with OCTA to determine whether it is neovascularization or just avascular fibrous tissue.

This live-scanning technique also gives me an idea of posterior vitreous detachment (PVD) status; eyes with complete PVD are at lower risk for proliferation or complications related to vitreoretinal traction (ie, vitreous hemorrhage, retinal detachment). Eyes with partial PVD are at highest risk for PDR, and live scanning allows me to see areas where the posterior hyaloid of the vitreous is just starting to detach from the retina. I believe these areas are at highest risk for proliferation.

possible with intravenous fluorescein angiography (FA). The vitreoretinal interface (VRI), a preset display on the CIRRUS HD-OCT 5000 with AngioPlex platform (ZEISS), was designed specifically to help detect and isolate preretinal neovascularization, which it did very well here. Typically, the VRI is totally black because there's no vascular movement in the vitreous. Anything that is visible there is likely to be preretinal neovascularization versus abnormal vasculature within the retina, such as intraretinal microvascular abnormalities (IRMA).

CONCLUSION

The earlier we detect PDR, the better. There is a huge paradigm shift right now toward earlier treatment of diabetic retinopathy with anti-VEGF agents even in the absence of macular edema. Anti-VEGF therapy may even prevent retinopathy progression to PDR, and eyes with extensive nonperfusion detected with OCTA may benefit from early treatment. ■

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WHEN TO REFER AND WHEN NOT TO REFER

How diagnostic modalities aid in clinical decision-making.

BY DIANA L. SHECHTMAN, OD, FAAO

Many clinicians may consider OCT one of the key ancillary modalities in ophthalmic practices. OCT provides high-resolution, cross-sectional images of the retina, helping in diagnosis and management of retinal disease. In today's era of early intervention, better prognosis relies on prompt diagnosis for proper referral to implement appropriate treatment.

STRUCTURAL OCT

Given that diabetic retinopathy (DR) is the major cause of blindness among working adults with diabetes, screening for DR is critical, particularly because the majority of patients who develop DR may be asymptomatic.[1] Therefore, screening guidelines for patients with diabetes include a dilated fundus examination to assess findings associated with DR. DR-related complications, such as proliferation and diabetic macular edema (DME), require a referral to a retina specialist for proper management. Although clinically significant macular edema may be assessed through a dilated fundus examination, OCT is regarded as the most sensitive method to detect and evaluate DME.

Another case in point would be the patient with age-related macular degeneration (AMD) findings, such as macular drusen or retinal pigmentary changes. In such cases, OCT helps identify signs of conversion toward wet AMD, which would require prompt referral for anti-VEGF therapy. Such findings include but are not limited to subretinal and intraretinal fluid, as well as hyper-reflective areas within the subretinal space (Figure 1).

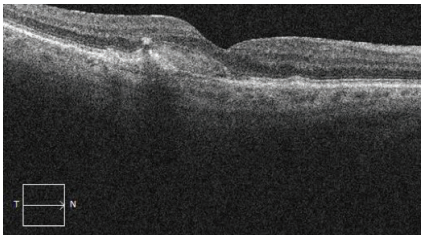

Figure 1. OCT helps detect signs of conversion toward wet AMD. Note the hyper-reflective areas within the subretinal space.

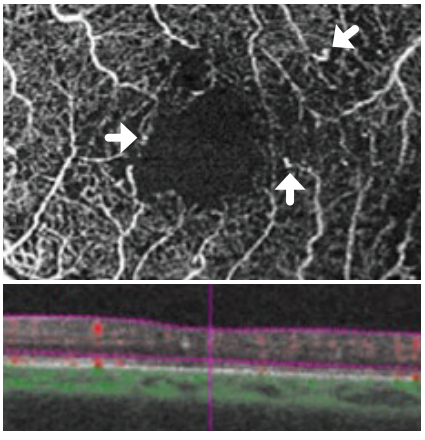

Figure 2. Small microaneurysms (as seen here), areas of nonperfusion, and foveal avascular zone remodeling can be easily assessed through the use of OCTA.

OCT ANGIOGRAPHY

The earliest changes of DR occur at the capillary vascular level. OCTA is an emergent noninvasive diagnostic tool that allows for exquisite capillary vascular network visualization. Small microaneurysms (Figure 2), areas of nonperfusion, and foveal avascular zone remodeling can be easily assessed through the use of OCTA. Such findings may help determine early DR changes that may not have been easily perceived during a dilated fundus examination alone.

Furthermore, OCTA has been shown to be valuable in the diagnosis

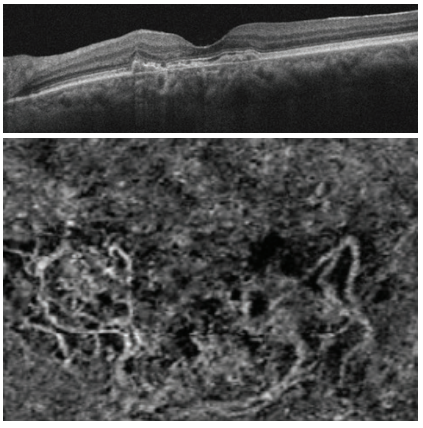

Figure 3. OCTA may help in the assessment of quiescent choroidal neovascular membrane.

of early choroidal neovascular membrane formation. Recent data have shown how OCTA may help in the assessment of quiescent choroidal neovascular membranes (Figure 3).[2] OCTA can clearly show the presence of a choroidal neovascular membrane, even though there is no fluid seen on OCT or fluorescein angiography.

CONCLUSION

I believe tools like OCT and OCTA help us become more confident with our diagnostic capabilities. ■

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INCREASING CLINICAL ACUMEN WITH INTEGRATED DIAGNOSTIC IMAGING

From static text and images to a dynamic diagnostic environment.

BY AARON E. LECH, OD

When managing ocular disease, our comfort level increases with our ability to see the disease process. Data-rich technologies, such as ultra widefield imaging, structural OCT, and OCT angiography (OCTA), provide invaluable insights about eye health. The new Integrated Diagnostic Imaging (IDI) platform (ZEISS) increases our efficiency by combining data from all of these, and other, modalities to give us a complete clinical picture.

TARGETED REFERRALS, ENHANCED PATIENT PERCEPTIONS

When we have excellent information from our diagnostics, our referrals are more detailed, and we can direct the subspecialist to a specific area of interest rather than offer a general impression. This facilitates an efficient flow between optometrist and subspecialist and creates a collegial network built upon the subspecialist's confidence in our diagnostic ability.

Our utilization of this technology also influences patients' perceptions. Being able to use Integrated Diagnostic Imaging to show patients visual representations of their disease, as well as changes or progression, assures them that they are receiving excellent care. This type of engagement helps them understand their condition and why adhering to therapy and follow-up appointments is so important.

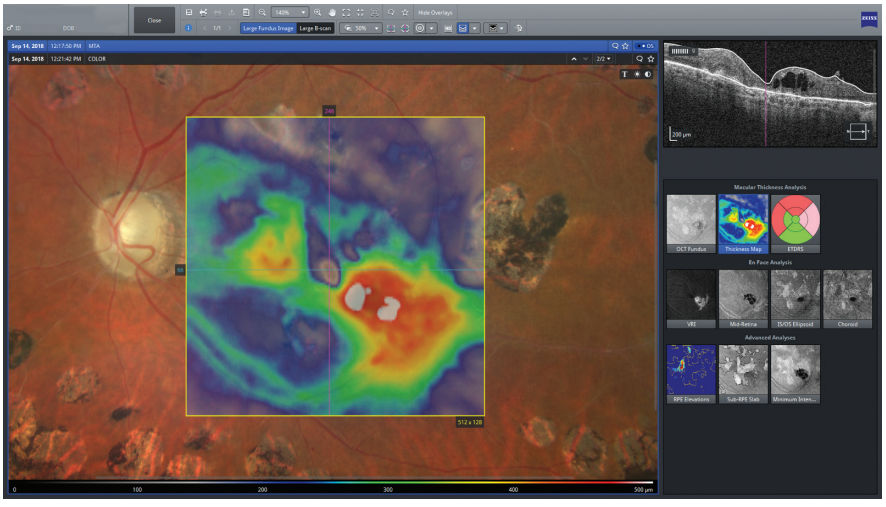

Figure 1. Case 1: A combination of OCT thickness mapping, demonstrating DME in a previously quiet eye.

TRUE DATA MANAGEMENT

When electronic medical records and electronic health records were introduced, the idea was to convert written notes to text-based, searchable fields. Images could also be stored and cataloged, but as static files, the data remained two-dimensional, missing an important clinical opportunity.

With the Integrated Diagnostic Imaging platform, data management is not just about entering information in the proper fields, but making sure the information in these little "packets" can be dissected and recombined with other diagnostic modalities to deliver a new piece of diagnostic data and clinical presentation. We now have report findings, trend analyses, comparisons, and so on, which were not available before.

In addition, photographs, OCTs, OCTAs, corneal topography scans, and other pieces of information, which in the past were stored locally on each device, are now automatically backed up to a central data archive that can also be accessed from each machine or any workstation in the office.

CASES: VALUE OF MULTIMODAL IMAGING

Case 1 demonstrates the value of multimodal analysis (Figure 1). We see a combination of OCT thickness mapping, which demonstrates diabetic macular edema in a previously quiet eye. With such an irregular macula, a photograph alone might not provide this information.

In case 2, the patient has 20/20 visual acuity but reports some metamorphopsia (Figure 2). The macula is

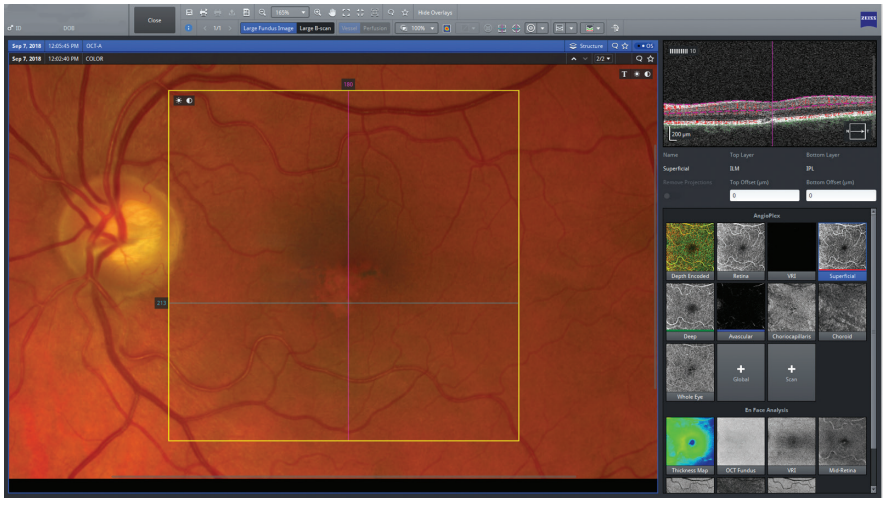

Figure 2. Case 2: Combining photographs and OCT enables visualization of the fundus in vivo and the B-scan to ascertain the level of damage to the underlying retinal structures.

irregular. Combining photographs and OCT enables us to visualize the fundus in vivo in the primary window at center and review the B-scan located at the top right of the image to ascertain the level of disruption or damage to the underlying retinal structures.

Each figure for case 3 (Figures 3 and 4) shows a fundus image with overlying blood flow and structural OCT analysis (side-by-side). To my knowledge, no other technology in the world can provide this analysis. Being able to coordinate blood flow and retinal structure is a dynamic educational tool and provides clinicians with an integrated clinical data set they could have only dreamed of. This enhances detection and may one day soon provide us with predictive values that will help us intercept a disease before it begins. ■

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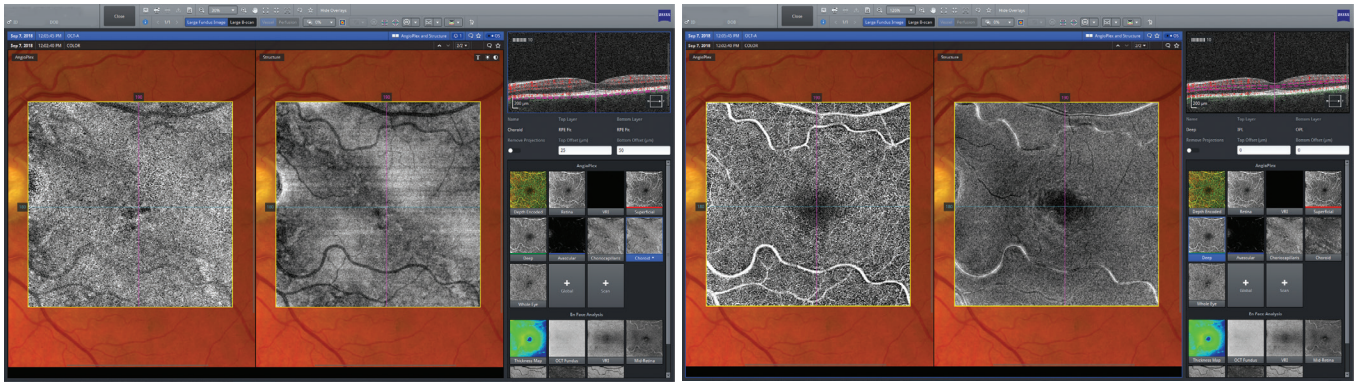

Figure 3 and Figure 4. Case 3: Fundus images with overlying blood flow and structural OCT analysis.

THE CHANGING LANDSCAPE OF GLAUCOMA MANAGEMENT

Plus, a case demonstrating the utility of the ZEISS Integrated Diagnostic Imaging platform for efficient test correlation.

BY MURRAY FINGERET, OD, FAAO

Structural and functional tests are integral to the diagnosis of glaucoma and the monitoring of affected individuals for change over time. Structural testing involves optical coherence tomography (OCT) and analysis of the optic nerve with photography. Perimetry, or visual field testing, assesses function. Advancements in both types of testing are aimed at accurate clinical evaluations.

VISUAL FIELD TESTING EVOLVES

The automated Humphrey Field Analyzer (HFA) originally used a full threshold testing algorithm. The duration of the test was 8 to 10 minutes for a healthy eye and longer for an individual with glaucomatous field loss. The Swedish Interactive Thresholding Algorithm (SITA) was introduced in 1995. SITA Standard reduced the testing time by half from full threshold, and SITA Fast reduced the testing time as compared to FASTPAC. For many years, ZEISS recommended use of the SITA Standard test, while SITA Fast remained on the sidelines.

Studies have shown that SITA Fast is similar to SITA Standard, particularly for detecting glaucomatous progression, but SITA Fast takes 3 to 5 minutes, which is too long for some patients.[1,2] Efforts to make visual field testing more efficient resulted in SITA Faster. This test has the potential to reduce testing time by 30%, possibly without a loss of accuracy, which may make it the field test of choice, once validation studies are complete.

NEW TEST PATTERN

An issue that has plagued clinicians is the realization that we often see structural loss in the retinal nerve fiber layer (RNFL), optic nerve, and macular region, using optic nerve evaluation and OCT analysis before we see visual field loss. Some literature has shown that central field loss may appear very early as glaucoma is developing.[3,4]

Recently, Donald C. Hood from Columbia University championed testing the central region to detect visual field loss earlier.[3,4] This would include testing the macular region with OCT, as well as with perimetry.

For visual fields, the 10-2 pattern became the test of choice, because it assesses 65 points in the central 10° with 2-degree spacing, compared with 6-degree spacing with the 24-2.[5] Clinicians have had to grapple with several questions regarding these two test patterns. Which is more important? And, if they are going to perform both tests, when should they perform them?

Reimbursement issues also arise when multiple tests are performed on the same day and when testing patients with multiple tests at most visits. Thus, the question is not how applicable the 10-2 is to practice, but rather how to make the 10-2 and the 24-2 work in a practical, clinical sense.

The new 24-2C test pattern incorporates the 10 most commonly

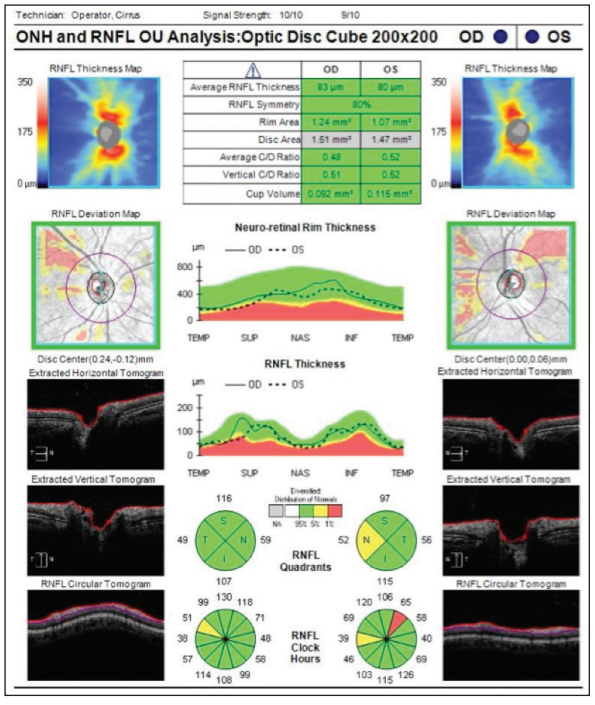

Figure 1. The patient's most recent OCT scan shows excellent image quality. The optic nerve is centered and evenly illuminated, and the B-scans are within the defined area with no segmentation errors present.

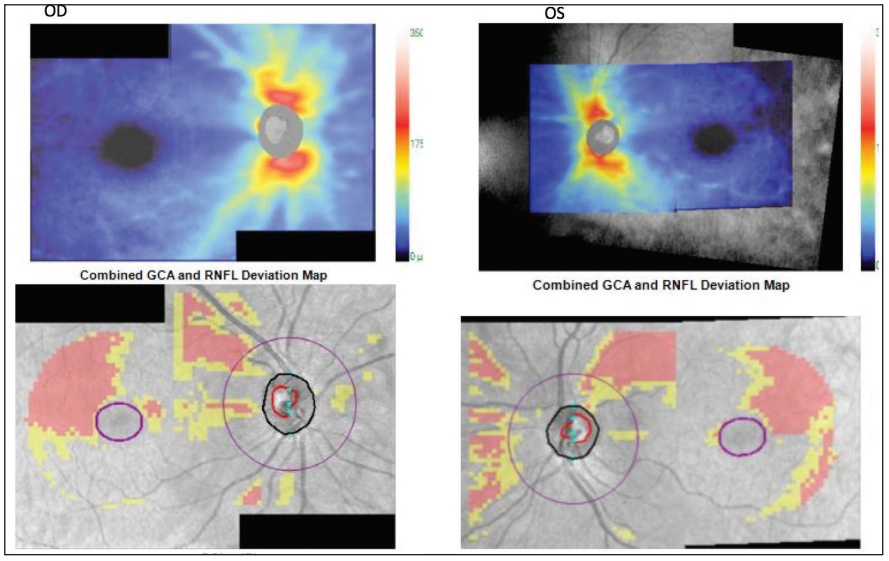

Figure 2. The PanoMap allows the RNFL and ganglion cell complex maps to be overlaid, providing a wide area for review.

flagged points on the 10-2 and the 24-2 patterns. The hope is that clinicians will need to run only one test pattern to evaluate the central region, as well as the regions previously tested with the 24-2. Studies are needed to document how well this performs, but there is optimism that this may become the default test pattern. The 24-2C runs under the SITA Faster mode, so testing takes the same time as the 24-2 SITA Fast.

LIQUID LENS

In perimetry, trial lenses provide the refractive correction needed so the patient can see clearly during the test. This is an inefficient method, as the trial lenses may be in the wrong position, leading to artifacts, or you may not have the correct power.

In the Humphrey Field Analyzer 3 (HFA3; ZEISS), the old manual process has been replaced with a Liquid Trial Lens, which automatically delivers the appropriate refractive correction using measurement information entered into the instrument. This eliminates the need for trial lenses and creates a more efficient testing environment.

STREAMLINING WORK FLOW

The following case illustrates some of the advances in glaucoma diagnostics that are streamlining work flow, making these technologies faster, more efficient, and better able to detect loss, possibly at an earlier point in time.

CASE: STABLE OR PROGRESSING?

- 47-year-old black female
- Primary open-angle glaucoma of 4 years duration
- Family history of glaucoma
- Initial therapy: latanoprost; switched to bimatoprost (Lumigan, Allergan); currently using brinzolamide/brimonidine tartrate (Simbrinza, Alcon)
- IOPs: 14 mm Hg OD, 15 mm Hg OS
- Pachymetry: 508 µm OD, 509 µm OS
- Gonioscopy: open angles with ciliary body visible 360°

Figure 1 shows the patient's most recent OCT scan. The RNFL deviation maps show loss superior temporal in both eyes. The average RNFL is 83 µm OD and 80 µm OS, with sectors flagged in the right eye (yellow at 10 o'clock) and the left eye (red at 1 o'clock). The TSNIT curve shows superior temporal thinning.

The PanoMap allows the RNFL and ganglion cell complex maps to be overlaid, providing a wide area for review (Figure 2). The loss extends superior temporal from the optic disc in both eyes to beyond the fovea.

The question for this patient is not whether glaucoma is present, but whether the disease is stable or worsening.

DISCUSSION

With the FORUM (ZEISS) software, also called the Integrated Diagnostic Imaging platform, data from the HFA3 and the CIRRUS HD-OCT (ZEISS) are displayed together on one screen, facilitating comparison of structure and function tests.

Figure 3 shows two different views of how the Structure-Function Guided Progression Analysis (GPA) is displayed. On the left at the top,

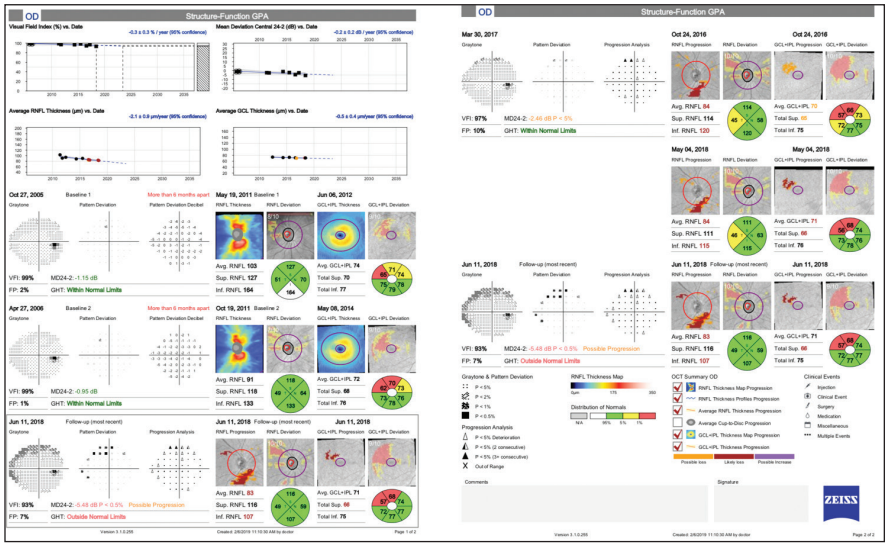

Figure 3. Two different views of how the Structure-Function Guided Progression Analysis is displayed.

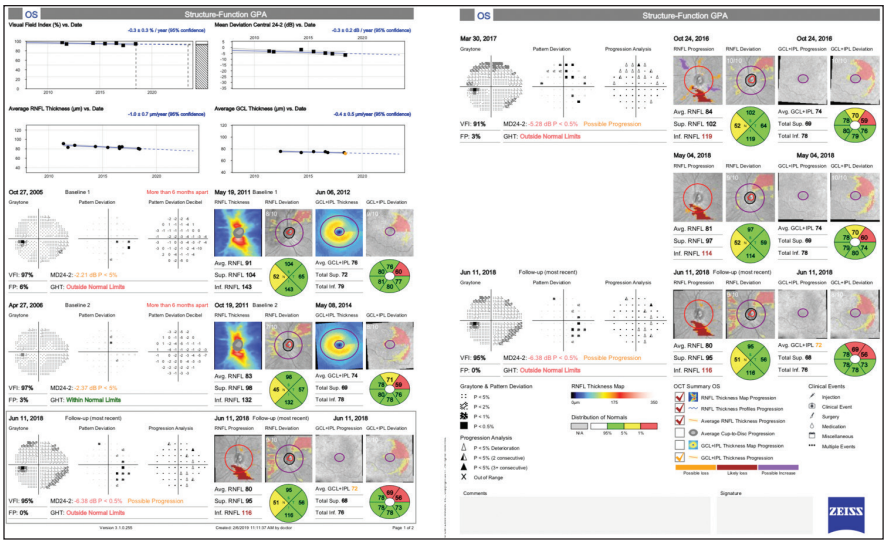

Figure 4. The OCT change analysis for the left eye shows a defect has enlarged inferior temporal, which is in addition to the defect already present superior temporal.

the trend analysis for the visual field's Visual Function Index (VFI) and mean deviation (MD) is shown. A small amount of change is noted (dip) toward the end of both lines. Just below this is the trend analysis for average RNFL and average ganglion cell layer thickness. In particular, the RNFL line (OD) is going down over time, indicating progression at a rate of 2.1 µm per year. This is a significant loss that has been confirmed by the colored circles on this trend line.

Below that, fields on the left show a recent loss superior. Adjacent to this are OCT printouts from 2011 to 2018 with an inferior temporal RNFL defect that was not present in 2011. The average RNFL value has decreased from 103 µm in 2011 to 83 µm in 2018. On the right are views of the progression analysis with relative stability from 2016 to 2018. Note that in 2016, brinzolamide/brimonidine tartrate was added to bimatoprost, further lowering the eye pressure.

Figure 4 shows the Structure-Function GPA for the left eye. On the left, both the MD and the VFI show little change, with the OCT average RNFL changing 1 µm per year. The OCT change analysis for the left eye shows a defect has enlarged inferior temporal, which is in addition to the defect already present superior temporal. The GPA for the visual fields shows progression inferior, which correlates with the superior RNFL defect. The majority of change occurred between 2011 and 2016, at which time a change to the medical regimen reduced IOP. Since then, visual fields and OCT appear stable also in the left eye.

SUMMARY

This case shows the utility of the Integrated Diagnostic Imaging platform (ZEISS) Structure-Function GPA in which the OCT and visual fields are shown side by side, allowing changes to be correlated between tests. Because structural and functional losses often do not occur at the same time, it is useful to see them both on one screen to better understand the temporal relationships. ■

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DETECTING PROGRESSION IN THE GREEN ZONE: GREEN DISEASE

Modern OCTs can detect glaucomatous changes in eyes that are still in the normal range.

BY MARK T. DUNBAR, OD, FAAO

Results of an OCT scan of the retinal nerve fiber layer (RNFL) are displayed in an easy-to-read, color-coded format that enables us to quickly decide if an eye is normal (the green zone), suspicious (yellow), or abnormal (red). In the context of a patient who is a glaucoma suspect, it stands to reason that if the visual field is normal and the OCT is normal, the patient probably does not have glaucoma. However, there is a large range of "normal" before the RNFL reaches the tipping point (Figure 1). As with perimetry, a patient can lose a third of his or her RNFL and still be within the normal range.

Fortunately, modern OCTs provide highly reproducible measurements, enabling us to identify patients who are losing ground, even while they are still in the green zone. A study by Kuang et al. found that assessment of RNFL thickness with OCT could detect glaucomatous damage before the appearance of visual field defects on standard automated perimetry.[1] In many patients, significantly large lead times were seen when applying OCT as an ancillary diagnostic tool.

The following is a case in point.

CASE: GLAUCOMA SUSPECT

- 50-year-old male, initially seen July 2012
- BCVA: 20/20
- IOP: 32 mm Hg OS
- OCT RNFL scan, ganglion cell analysis, and visual fields were normal
- Monitored as glaucoma suspect with ocular hypertension.

Follow-up scans in December 2013 appeared normal and were essentially the same as those taken in 2012 (Figure 2). However, when scans from November 2015 are compared with the December 2013 scans, we can see progression (Figure 3).

By March 2016, a visual field defect had developed in

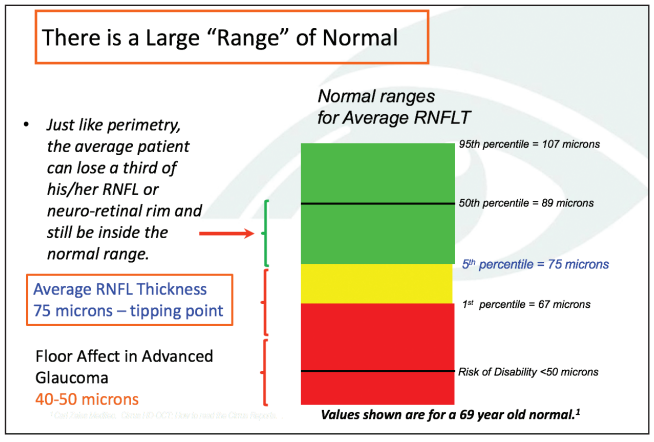

Figure 1. Highly reproducible measurements enable us to identify patients who are losing ground, even while they are still in the green zone.

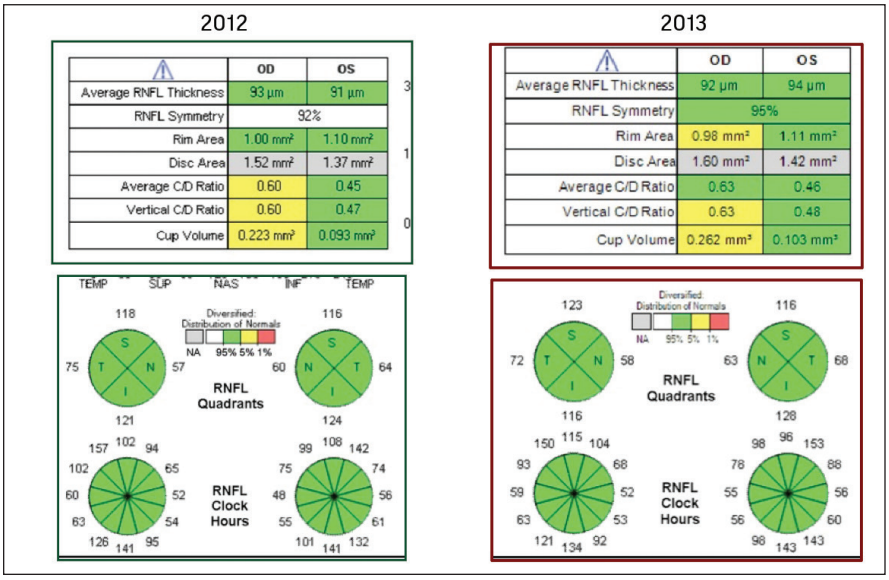

Figure 2. The scans from 2012 to 2013 are essentially the same. If anything, the 2013 scans are better. Note the clock hours at 11 o'clock on both right-eye scans.

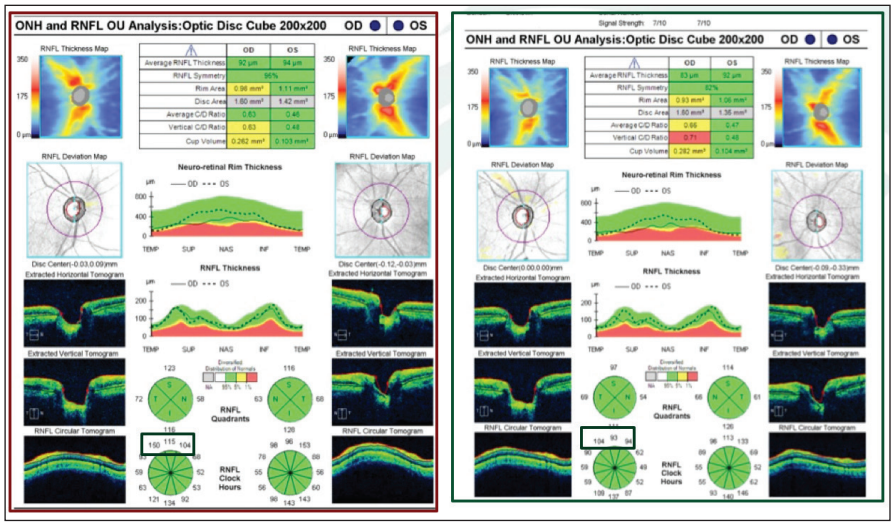

Figure 3. Progression is evident when scans taken in 2013 are compared with those taken in 2015.

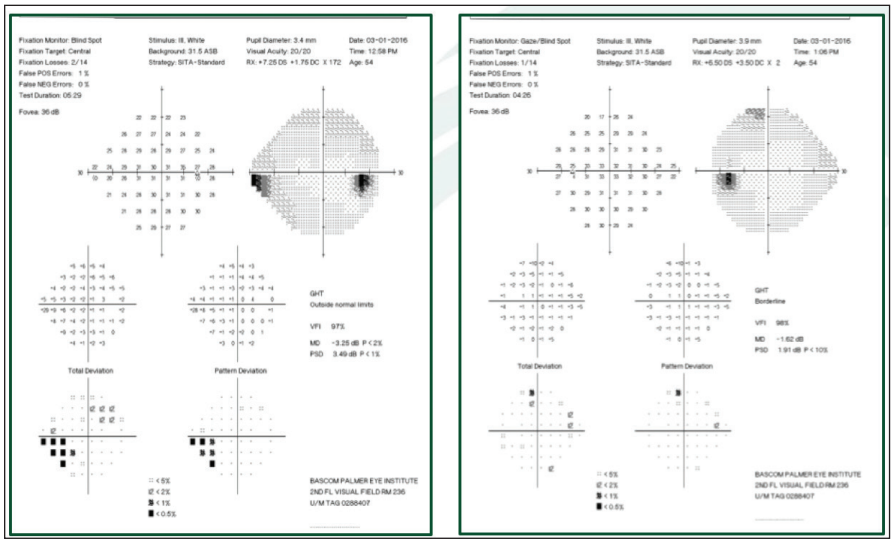

Figure 4. Ultimately, a visual field defect developed in the right eye.[1]

the right eye (Figure 4), and by March 2017, OCT showed clear progression. The right eye was changing while it was still "normal."

DISCUSSION

The average person has about 107 µm of RNFL, and the tipping point between normal and abnormal is at about 75 µm. In other words, it is possible for a patient to lose a third of RNFL or neuroretinal rim and still be inside the normal range. That was the message with this patient. He was a glaucoma suspect with normal fields, and at multiple visits, OCT showed he was in the normal range. In retrospect, we were able to highlight statistically significant changes that were occurring. Therefore, it appears the OCT is sensitive enough to pick up those statistically significant changes while patients might still be in the normal range. I think we have enough longitudinal data to show that OCT has that sensitivity.

CONCLUSION

None of these technologies or tests exists in a vacuum, and we cannot rely on any single test for diagnosing and managing glaucoma. I believe we now recognize that OCT has the sensitivity to pick up change, maybe even better than a visual field. Kuang et al. could detect change in more than a third of the patients before it became apparent on their visual fields, which has always been the gold standard. We have had this technology for a dozen years or so, and we are learning to trust and utilize it properly to be able to show change before it is significant.

It is important to pay attention to the indicators of normal/suspicious/abnormal that the OCT test results provide; however, it is paramount for clinicians to pay attention to the value differentials within each of these categories from visit to visit to ensure that there are no dramatic changes and losses in a patient's RNFL. ■

1. Kuang TM, Zhang C, Zangwill LM, et al. Estimating lead time gained by optical coherence tomography in detecting glaucoma before development of visual field defects. *Ophthalmology*. 2015;122(10):2002-2009.

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INTEGRATED DIAGNOSTIC IMAGING SOLUTIONS STREAMLINE WORK FLOW

Appreciating the value of the Structure-Function Report.

BY DANICA J. MARRELLI, OD, FAAO; DIPLOMATE, GLAUCOMA SECTION, AAO; DIPLOMATE ABO

The following case exemplifies the value of the Integrated Diagnostic Imaging (IDI) platform through FORUM (ZEISS) for data-driven glaucoma diagnosis and management. With this platform, we can store all diagnostic tests in a single computer and view reports that integrate both structure (OCT, fundus photos) and function (visual fields), enhancing efficiency in the clinic.

CASE: GLAUCOMA EVALUATION

- 61-year-old male referred for glaucoma evaluation because optic nerves appeared abnormal
- BCVA: 20/20
- IOPs: 18 mm Hg OD, 15 mm Hg OS
- Central corneal thickness: 542 µm OD, 557 µm OS
- Gonioscopy and pachymetry: normal
- Average retinal nerve fiber layer (RNFL): 107 µm OD, 121 µm OS
- Optic nerves: large

Diagnostic testing included fundus photographs, OCT, and visual fields. Individually these test results are important, but I find real benefit in interpreting them all together, and that is the value of the Integrated Diagnostic Imaging platform with Structure-Function Report (Figure 1).

Looking at the RNFL TSNIT curve, with the right RNFL superimposed on the left, you can see that, even though the superior RNFL is thick, the RNFL of the right eye is substantially thinner than that of the left eye. On the RNFL thickness map, a small slit in the superior RNFL correlates well with the inferior nasal step on the visual field. If you were to look at the OCT and see greens and whites on the quadrants and clock hours, you would think this patient is golden, but the Structure-Function Report presents a more complete picture.

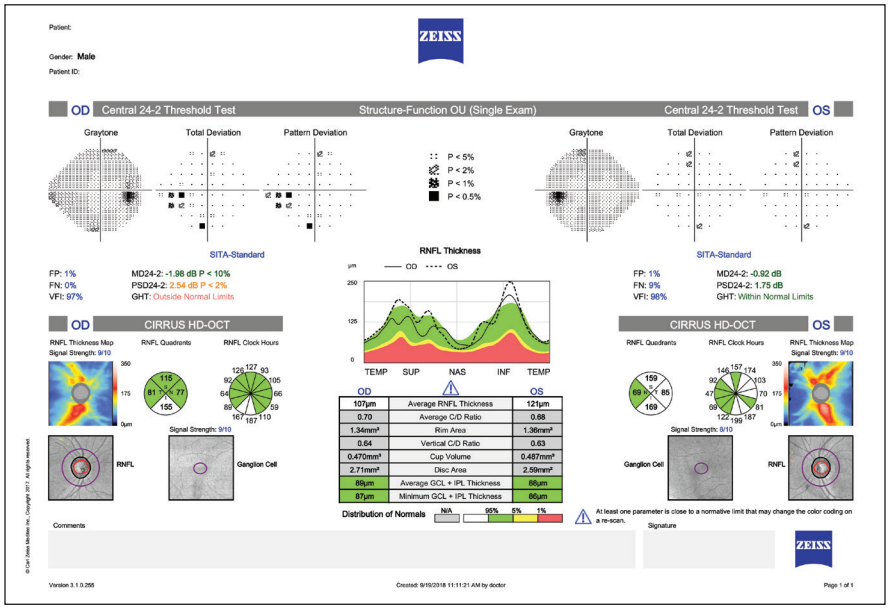

Figure 1. While individual test results are important, the FORUM IDI Structure-Function Report is valuable for interpreting them all together.

Looking at the optic nerve photograph (Figure 2), you can see a tiny disc hemorrhage, as well as a subtle defect in the RNFL. The defect looks almost like a blood vessel, but it is real and visible on OCT. I think this is the type of OCT that could lead some clinicians to say, "Oh, this looks great," but in fact, the patient has early glaucoma.

DISCUSSION

If we look at any one piece of this patient's data—his IOP, his initial OCT, even his initial visual fields—nothing is diagnostic of glaucoma at first glance. Silos of data are difficult and inefficient to organize, compare, and correlate. FORUM enables us to create structure-function plots so we

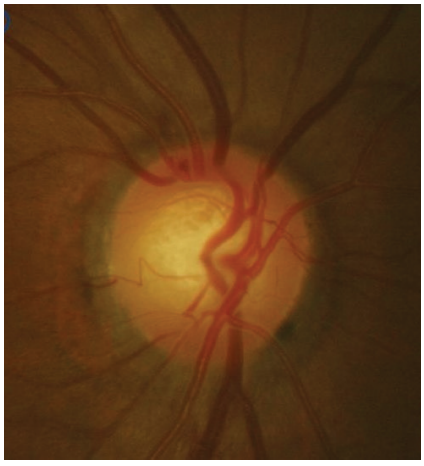

Figure 2. The optic nerve photograph shows a tiny disc hemorrhage and a subtle defect in the RNFL.

can view OCTs, visual fields, and photographs on a single screen and start to put the pieces together.

One of my favorite features of Integrated Diagnostic Imaging platform is being able to see all of the data together instead of having four windows open at one time on my computer or needing to move from one instrument to another within the building to view the tests. I also appreciate that once I enter a patient's data, essentially linking all of my instruments in FORUM, every test I have ever performed for that patient is imported into the program.

FORUM performs some functions in terms of disease progression that would be much more difficult to do without it. Although progression software is available on the individual instruments, it is also included in Integrated Diagnostic Imaging platform. If a patient completed a visual field test today, I do not have to go to the instrument to use the progression analysis. It is in Integrated Diagnostic Imaging platform already. I can adjust progression analysis to reflect clinical instances that occurred, or remove outliers from a bad test. Let's say a visual field from 2 years ago is an outlier and is skewing the progression information. I can remove it from the analysis in Integrated Diagnostic Imaging platform, and, if necessary, I can undo what I just did. Having these options at my fingertips improves my efficiency.

CONCLUSION

The ZEISS FORUM—Integrated Diagnostic Imaging platform enables clinical decision-making with more data, fluidity in data access, and seamless management of disease over time, thus streamlining our workflow. ■

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