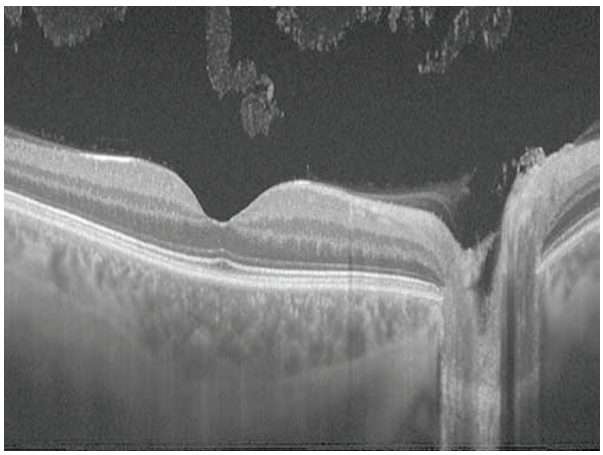
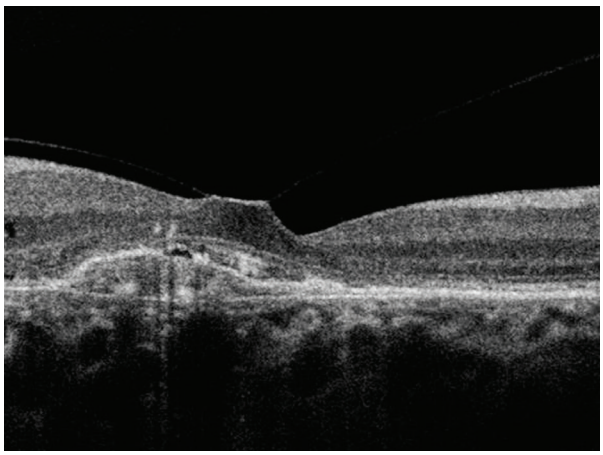
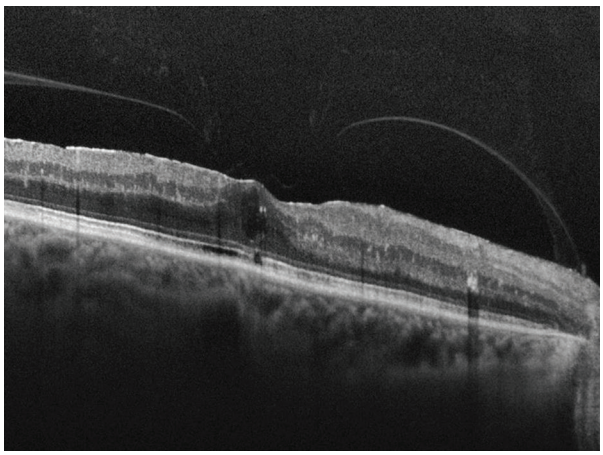
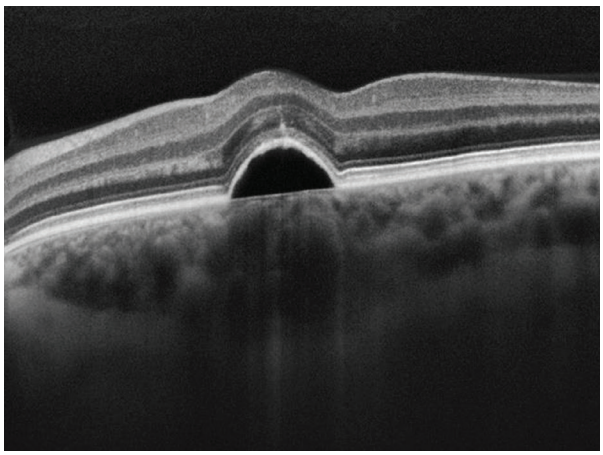
Retinal PHYSICIAN
APRIL 2020

OCT INTERPRETATION

A specialist's guide to optimizing the most frequently used imaging modality in ophthalmology

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ON THE COVER
Clockwise from top left: Swept-source OCT of a normal retina; choroidal neovascular membrane; exudative AMD with pigment epithelial detachment; vitreomacular traction. Images couresy of Darrin Landry

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*Study design: The efficacy of YUTIQ was assessed in 2 randomized, multicenter, sham-controlled, double-masked, phase 3 studies in adult patients (N=282) with noninfectious uveitis affecting the posterior segment of the eye. The primary endpoint in both studies was the proportion of patients who experienced recurrence of uveitis in the study eye within 6 months of follow-up; recurrence was also assessed at 12 months. Recurrence was defined as either deterioration in visual acuity, vitreous haze attributable to noninfectious uveitis, or the use of prohibited medications.[1,3]

INDICATIONS AND USAGE

YUTIQ® (fluocinolone acetonide intravitreal implant) 0.18 mg is indicated for the treatment of chronic noninfectious uveitis affecting the posterior segment of the eye.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

Ocular or Periocular Infections: YUTIQ is contraindicated in patients with active or suspected ocular or periocular infections including most viral disease of the cornea and conjunctiva including active epithelial herpes simplex keratitis (dendritic keratitis), vaccinia, varicella, mycobacterial infections and fungal diseases.

Hypersensitivity: YUTIQ is contraindicated in patients with known hypersensitivity to any components of this product.

WARNINGS AND PRECAUTIONS

Intravitreal Injection-related Effects: Intravitreal injections, including those with YUTIQ, have been associated with endophthalmitis, eye inflammation, increased or decreased intraocular pressure, and choroidal or retinal detachments. Hypotony has been observed within 24 hours of injection and has resolved within 2 weeks. Patients should be monitored following the intravitreal injection.

Steroid-related Effects: Use of corticosteroids including YUTIQ may produce posterior subcapsular cataracts, increased intraocular pressure and glaucoma. Use of corticosteroids may enhance the establishment of secondary ocular infections due to bacteria, fungi, or viruses. Corticosteroids are not recommended to be used in patients with a history of ocular herpes simplex because of the potential for reactivation of the viral infection.

Risk of Implant Migration: Patients in whom the posterior capsule of the lens is absent or has a tear are at risk of implant migration into the anterior chamber.

ADVERSE REACTIONS

In controlled studies, the most common adverse reactions reported were cataract development and increases in intraocular pressure.

References: 1. YUTIQ® (fluocinolone acetonide intravitreal implant) 0.18 mg full U.S. Prescribing Information. EyePoint Pharmaceuticals, Inc. October 2018. **2.** EyePoint Pharmaceuticals Receives FDA Approval of YUTIQ™ (fluocinolone acetonide intravitreal implant) 0.18 mg. Global Newswire. https://www.globenewswire.com/news-release/2018/10/15/1621023/0/en/EyePoint-Pharmaceuticals-Receives-FDA-Approval-of-YUTIQ-fluocinolone-acetonide-intravitreal-implant-0-18-mg.html. Accessed February 7, 2020. **3.** Data on file.

Please see next page for Brief Summary of full Prescribing Information.

EYEPOINT® PHARMACEUTICALS

480 Pleasant Street, Suite B300, Watertown, MA 02472

2/2020
US-YUT-2000020

YUTIQ™ (fluocinolone acetonide intravitreal implant) 0.18 mg, for intravitreal injection
Initial U.S. Approval: 1963

BRIEF SUMMARY: Please see package insert for full prescribing information.

1. INDICATIONS AND USAGE. YUTIQ™ (fluocinolone acetonide intravitreal implant) 0.18 mg is indicated for the treatment of chronic non-infectious uveitis affecting the posterior segment of the eye.

4. CONTRAINDICATIONS. 4.1. Ocular or Periocular Infections. YUTIQ is contraindicated in patients with active or suspected ocular or periocular infections including most viral disease of the cornea and conjunctiva including active epithelial herpes simplex keratitis (dendritic keratitis), vaccinia, varicella, mycobacterial infections and fungal diseases. **4.2. Hypersensitivity.** YUTIQ is contraindicated in patients with known hypersensitivity to any components of this product.

5. WARNINGS AND PRECAUTIONS. 5.1. Intravitreal Injection-related Effects. Intravitreal injections, including those with YUTIQ, have been associated with endophthalmitis, eye inflammation, increased or decreased intraocular pressure, and choroidal or retinal detachments. Hypotony has been observed within 24 hours of injection and has resolved within 2 weeks. Patients should be monitored following the intravitreal injection *[see Patient Counseling Information (17) in the full prescribing information]*. **5.2. Steroid-related Effects.** Use of corticosteroids including YUTIQ may produce posterior subcapsular cataracts, increased intraocular pressure and glaucoma. Use of corticosteroids may enhance the establishment of secondary ocular infections due to bacteria, fungi, or viruses. Corticosteroids are not recommended to be used in patients with a history of ocular herpes simplex because of the potential for reactivation of the viral infection. **5.3. Risk of Implant Migration.** Patients in whom the posterior capsule of the lens is absent or has a tear are at risk of implant migration into the anterior chamber.

6. ADVERSE REACTIONS. 6.1. Clinical Studies Experience. Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice. Adverse reactions associated with ophthalmic steroids including YUTIQ include cataract formation and subsequent cataract surgery, elevated intraocular pressure, which may be associated with optic nerve damage, visual acuity and field defects, secondary ocular infection from pathogens including herpes simplex, and perforation of the globe where there is thinning of the cornea or sclera. Studies 1 and 2 were multicenter, randomized, sham injection-controlled, masked trials in which patients with non-infectious uveitis affecting the posterior segment of the eye were treated once with either YUTIQ or sham injection, and then received standard care for the duration of the study. Study 3 was a multicenter, randomized, masked trial in which patients with non-infectious uveitis affecting the posterior segment of the eye were all treated once with YUTIQ, administered by one of two different applicators, and then received standard care for the duration of the study. Table 1 summarizes data available from studies 1, 2 and 3 through 12 months for study eyes treated with YUTIQ (n=226) or sham injection (n=94). The most common ocular (study eye) and non-ocular adverse reactions are shown in Table 1 and Table 2.

Table 1: Ocular Adverse Reactions Reported in ≥ 1% of Subject Eyes and Non-Ocular Adverse Reactions Reported in ≥ 2% of Patients

Ocular		
ADVERSE REACTIONS	**YUTIQ (N=226 Eyes) n (%)**	**Sham Injection (N=94 Eyes) n (%)**
Cataract[1]	63/113 (56%)	13/56 (23%)
Visual Acuity Reduced	33 (15%)	11 (12%)
Macular Edema	25 (11%)	33 (35%)
Uveitis	22 (10%)	33 (35%)
Conjunctival Hemorrhage	17 (8%)	5 (5%)
Eye Pain	17 (8%)	12 (13%)
Hypotony Of Eye	16 (7%)	1 (1%)
Anterior Chamber Inflammation	12 (5%)	6 (6%)
Dry Eye	10 (4%)	3 (3%)
Vitreous Opacities	9 (4%)	8 (9%)
Conjunctivitis	9 (4%)	5 (5%)
Posterior Capsule Opacification	8 (4%)	3 (3%)
Ocular Hyperemia	8 (4%)	7 (7%)
Vitreous Haze	7 (3%)	4 (4%)
Foreign Body Sensation In Eyes	7 (3%)	2 (2%)
Vitritis	6 (3%)	8 (9%)
Vitreous Floaters	6 (3%)	5 (5%)
Eye Pruritus	6 (3%)	5 (5%)
Conjunctival Hyperemia	5 (2%)	2 (2%)
Ocular Discomfort	5 (2%)	1 (1%)
Macular Fibrosis	5 (2%)	2 (2%)
Glaucoma	4 (2%)	1 (1%)
Photopsia	4 (2%)	2 (2%)

(continued)

Table 1: Ocular Adverse Reactions Reported in ≥ 1% of Subject Eyes and Non-Ocular Adverse Reactions Reported in ≥ 2% of Patients

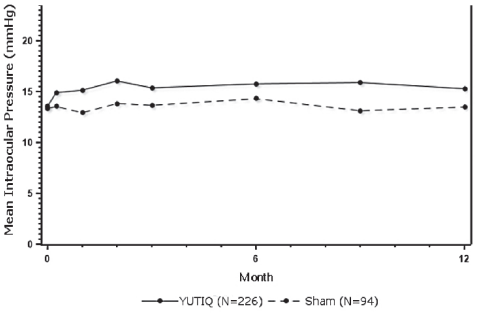
Ocular		
ADVERSE REACTIONS	**YUTIQ (N=226 Eyes) n (%)**	**Sham Injection (N=94 Eyes) n (%)**
Vitreous Hemorrhage	4 (2%)	0
Iridocyclitis	3 (1%)	7 (7%)
Eye Inflammation	3 (1%)	2 (2%)
Choroiditis	3 (1%)	1 (1%)
Eye Irritation	3 (1%)	1 (1%)
Visual Field Defect	3 (1%)	0
Lacrimation Increased	3 (1%)	0
Non-ocular		
ADVERSE REACTIONS	**YUTIQ (N=214 Patients) n (%)**	**Sham Injection (N=94 Patients) n (%)**
Nasopharyngitis	10 (5%)	5 (5%)
Hypertension	6 (3%)	1 (1%)
Arthralgia	5 (2%)	1 (1%)

1. Includes cataract, cataract subcapsular and lenticular opacities in study eyes that were phakic at baseline. 113 of the 226 YUTIQ study eyes were phakic at baseline; 56 of 94 sham-controlled study eyes were phakic at baseline.

Table 2: Summary of Elevated IOP Related Adverse Reactions

ADVERSE REACTIONS	YUTIQ (N=226 Eyes) n (%)	Sham (N=94 Eyes) n (%)
IOP elevation ≥ 10 mmHg from Baseline	50 (22%)	11 (12%)
IOP elevation > 30 mmHg	28 (12%)	3 (3%)
Any IOP-lowering medication	98 (43%)	39 (41%)
Any surgical intervention for elevated IOP	5 (2%)	2 (2%)

Figure 1: Mean IOP During the Studies



8. USE IN SPECIFIC POPULATIONS. 8.1 Pregnancy. Risk Summary. Adequate and well-controlled studies with YUTIQ have not been conducted in pregnant women to inform drug associated risk. Animal reproduction studies have not been conducted with YUTIQ. It is not known whether YUTIQ can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Corticosteroids have been shown to be teratogenic in laboratory animals when administered systemically at relatively low dosage levels. YUTIQ should be given to a pregnant woman only if the potential benefit justifies the potential risk to the fetus. All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the United States general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively. **8.2 Lactation.** Risk Summary. Systemically administered corticosteroids are present in human milk and can suppress growth, interfere with endogenous corticosteroid production. Clinical or nonclinical lactation studies have not been conducted with YUTIQ. It is not known whether intravitreal treatment with YUTIQ could result in sufficient systemic absorption to produce detectable quantities of fluocinolone acetonide in human milk, or affect breastfed infants or milk production. The developmental and health benefits of breastfeeding should be considered, along with the mother's clinical need for YUTIQ and any potential adverse effects on the breastfed child from YUTIQ. **8.4 Pediatric Use.** Safety and effectiveness of YUTIQ in pediatric patients have not been established. **8.5 Geriatric Use.** No overall differences in safety or effectiveness have been observed between elderly and younger patients.

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WITH OCT, QUALITY MATTERS

The importance of imager training for proper diagnostics

By Darrin A. Landry, CRA, OCT-C

Since its commercial introduction in 2006, optical coherence tomography (OCT) has restructured the landscape of ophthalmic imaging and practice patterns. Here was a technology that not only produced tomographic views of retinal anatomy, but offered quantitative data that was previously not obtainable—all in an easy-to-use diagnostic system.

As is the case with most diagnostic tools, the data produced is only as good as the effort and knowledge of the operator. The perception that producing quality images does not require extensive training of the imager may result in less-than-optimal images, which may then result in a missed diagnosis or erroneously alter the treatment plan.

PROPER TRAINING IS KEY

Proper, extensive training is critical for imagers. Along with learning how to utilize the software, the imager must also be acutely aware of ocular anatomy, disease pathology, and how the pathology affects the patient's vision.

For instance: All OCT systems are equipped with an internal fixation target. When a patient with a full-thickness macular hole (or other pathology that produces a central scotoma) is directed to fixate on the target, the system will scan the patient's subjective fixation. The resulting scan will be placed juxta-foveal, producing an image that does not reflect the pathology. A trained imager will recognize anatomical structures that indicate

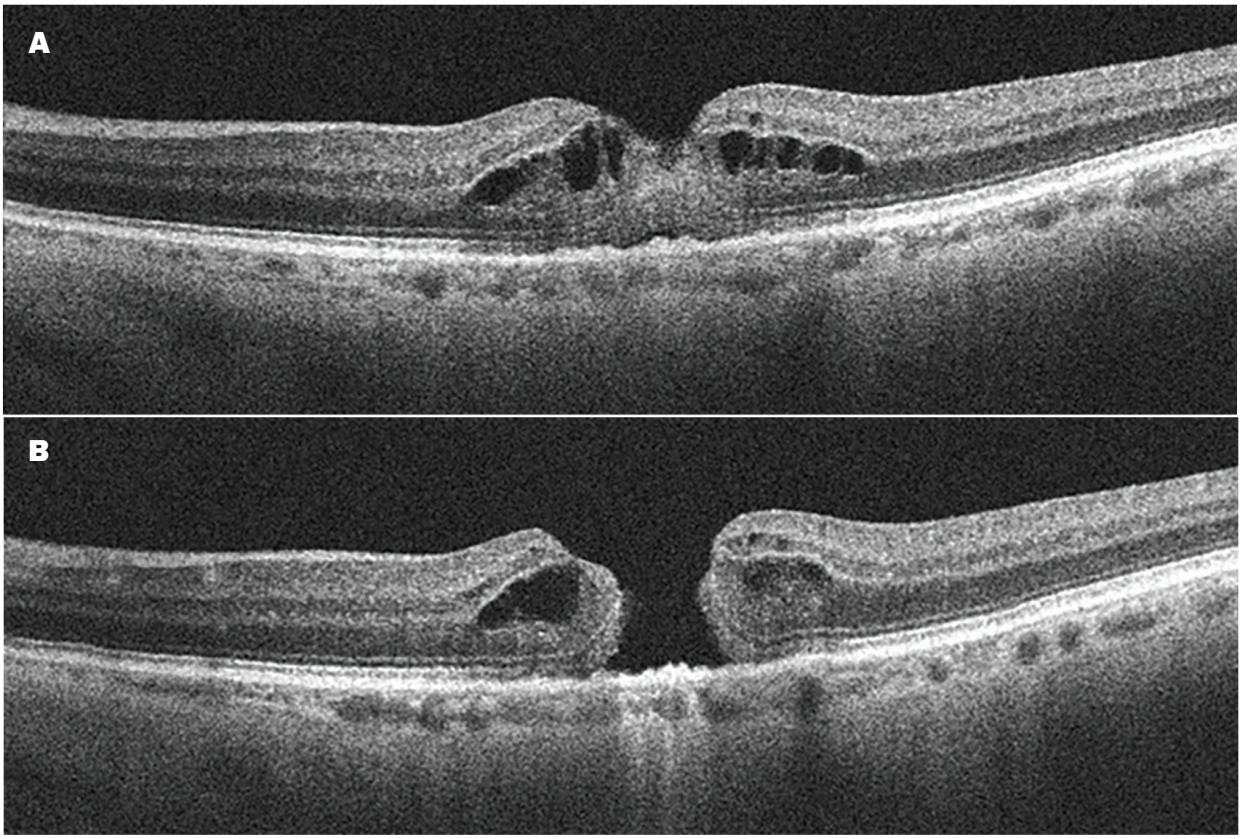

Figure 1. (**A**) The scan was acquired through the patient's subjective fixation, giving the appearance of intraretinal fluid. (**B**)The imager moves the scan to the patient's fovea, and a full thickness macular hole is revealed.

the patient is not fixating centrally and should adjust accordingly. In a busy clinical practice, this type of error may go unnoticed.

A trained imager also recognizes disease pathology and scans appropriately. A quality scan of the fovea is beneficial, but not all pathology is within the fovea or central macula. The imager should always consider what scan module to utilize, as well as what areas of the retina should be scanned.

Take diabetic retinopathy and macular edema, for example. A single horizontal line scan that intersects the fovea may appear normal, but if the imager also scans vertically, pathology above and below the fovea may be found. This is also true with the scan modality—protocol should always include a volumetric, or cube scan that covers the entire macula.

With most OCT systems, the software allows for scans to be set as references, which the imager can use to ensure the same scan placement every time the patient is scanned. However, if the initial scan is incorrectly placed, subsequent scans will also be misplaced. This further emphasizes the need for the imager to be trained properly.

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4 OCT IMAGING TIPS

1. FINE FOCUS.
The OCT scan has a corresponding fundus image, usually taken in infrared. This helps to orient the imager and viewer, and to illustrate where the scan line is placed on the retina. Having fine focus on the fundus image is critical—the imager should ensure the finest focus on the smallest structure in the center of the frame. Once focus is achieved, then concentrate on the B scan image.

In the case of glaucoma nerve fiber layer scans, focus is even more critical. Focusing deeper than the nerve fiber layer will result in erroneous nerve fiber layer thickness measurement.

2. ID ARTIFACTS.
Learn what artifacts look like. Anything that affects light will affect the image. Therefore, if the patient has a cataract, some of the returning light from the retina will be scattered and not read. Using a composite function on the OCT will help, but the imager needs to work to find the clearest view in the patient's optical path.

One of the biggest issues affecting images is dry eyes. To produce the best image possible, the patient's tear film should be uniform. Dry eye artifacts appear on the fundus image as circular "spots," and the OCT B scan will appear hazy or out of focus.

Imaging the patient prior to workup is ideal. The effect of drops and applanation will affect the tear film. Always keep artificial tears handy.

If the final image is degraded due to lens or cornea, the imager should take an anterior image reflecting the reason the image is not optimal. This not only helps the viewer understand why the image is not ideal, but also helps the imager when taking future scans of that patient.

3. CLEAR COMMUNICATION.
This applies to communication with clinicians, staff, and the patient. Clinicians need to be clear about OCT protocol they need to diagnose and decide treatment. Not all patients are the same, just as not all retinal disease is the same. Having a clear protocol keeps everyone on the same page, especially if multiple staff members are imaging patients.

Communication with staff is also key. For example, technicians who do not image need to understand how drops and applanation disrupt the optimal optical pathway for imaging.

The imager also must communicate efficiently with the patient. Explaining what is required of the patient and what they can expect during the process will only make the imager's job easier. Remind the patient that they should blink normally, unless instructed otherwise. Indicating where they should focus, and what not to focus on, will elicit a much more cooperative patient.

4. KEEP LEARNING.
Technology is changing constantly, and even if the hardware or software used in your practice doesn't change, imagers are finding new and better techniques all the time. Stay in touch with other imagers. Join organizations such as the Ophthalmic Photographers' Society or one of the communities on social media. These can be perfect venues for voicing issues with technique, artifacts, and other helpful advice from users all over the world.

INTEGRATED IMAGING DELIVERS

How integrated data aids efficiency and better patient care

By Eric W. Schneider, MD

With the population aging and the success of anti-VEGF therapies, retina specialists are seeing and treating more patients than ever. Coupled with the increasing availability of new and more sensitive diagnostic imaging devices, this creates a "data overload" problem that can overwhelm a practice's ability to function efficiently. Thankfully, integrated image review has arrived as a possible solution.

New platforms and software suites allow visualization and interpretation of data from different imaging modalities all on a single screen. Switching among various instrument software and waiting for multiple programs to load while seeing patients are now chores of the past. Integrated imaging not only improves day-to-day clinic efficiency, but also has the potential to drive better patient care through greater analytic capabilities and improved patient education.

SEEING WHAT WE'VE BEEN MISSING

For our image integration needs, our practice chose the Integrated Diagnostic Imaging (IDI) platform from ZEISS. We had the ambitious goal of being able to review any image obtained at any of our nine office locations. With the necessary IT infrastructure in place, the server-based IDI platform accomplishes that for us. We also preferred the platform's advanced data analytics compared with that of others we considered.

ZEISS IDI consists of two pieces of software: FORUM review and Retina Workplace. We also have a dedicated FORUM server that serves as a single repository for images obtained with any DICOM-compliant instrument.

FORUM review interacts with the server to give me a quick and easy review, using just a few clicks, of all current and historical images from a single patient. I can click between and compare optical coherence tomography (OCT) scans with fundus photography, fluorescein angiography (FA), OCT angiography (OCTA), and any other imaging modality I've utilized for a given patient.

The real strength of FORUM review, however, is its ability to use point-to-point registration technology to

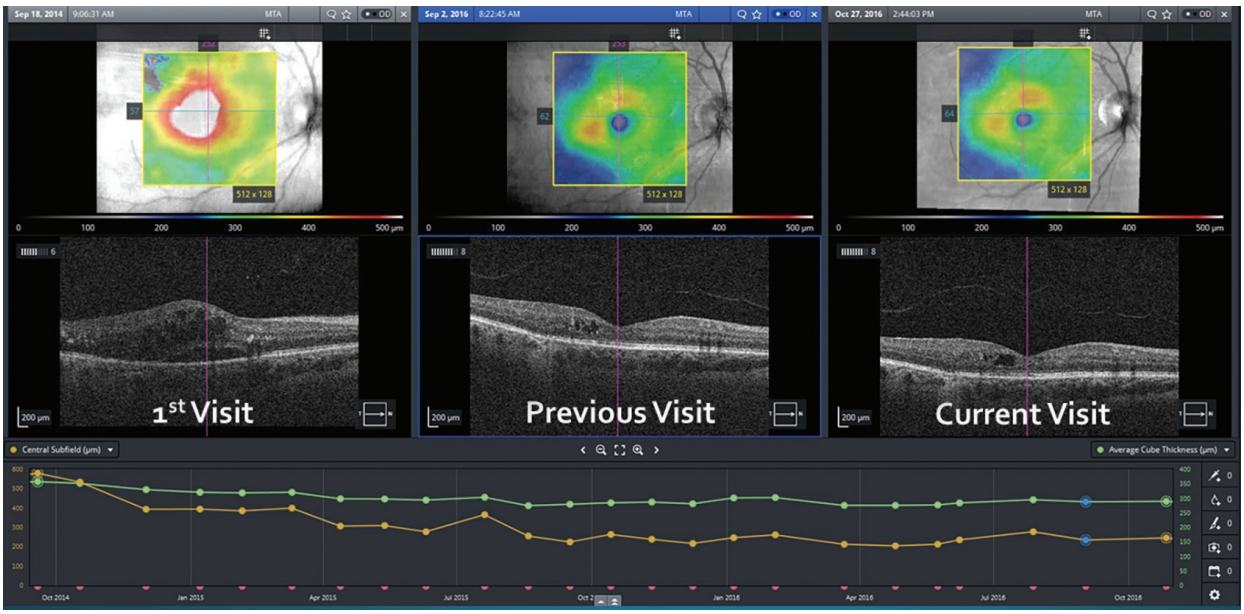

Figure 1. Retina Workspace software from ZEISS allows viewing and manipulation of three sets of OCT scans at once, from any three different dates. In addition, a variety of measures (such as central subfield thickness and average cube thickness, as shown here) can be automatically plotted over time to reveal trends and insights.

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create multimodal overlays. This allows me to review all of a patient's images on a single screen that's easily navigable. Additionally, I can ensure I'm evaluating the same location on clinical exam or photographs as I am on OCT scans. I can also see the vascular structure, imaged by OCTA, that underlies leakage on FA or visualize choroidal blood flow changes or ischemia on OCTA before changes appear on FA or fundus photographs, as often occurs in certain forms of inflammatory chorioretinitis.

While FORUM review integrates OCT with other imaging modalities, Retina Workplace analyzes OCT data over time, quickly revealing insights that would otherwise be difficult to detect without spending an inordinate amount of time reviewing innumerable historical scans. Instead of comparing only a patient's current scans with the prior visit's scans as is typically done, I can view and manipulate three sets of scans at once, from any three different dates.

Furthermore, imaging data from the entirety of a patient's history with our practice, which in many cases is 5-10 years, can be macroscopically reviewed in line graph format (Figure 1). A variety of measures can be viewed in this manner, including OCT thickness metrics (central subfield thickness, macular cube volume), advanced retinal pigment epithelium analyses (geographic atrophy area and distance to fovea), and angiometrics (foveal avascular zone size, total vessel density, and so on). These can be automatically plotted over time so trends are easily recognized.

It's easy to imagine how advanced analytics inform patient management decisions. For instance, I can clearly see whether improvement in a patient's retinal thickness with a new anti-VEGF medication is due to a switch in medication or perhaps following his or her typical pattern of variation in response to treatment over time. Similarly, the analysis of historical data can reveal the most effective treatment interval for patients on a treat-and-extend regimen.

MOVING RETINA PRACTICES INTO THE FUTURE

Image integration already makes our practice more efficient and optimizes the vast amount of data we have collected in a manner that allows us to actually apply it to real-world clinical decision-making, and this is only the beginning.

Having all imaging in one place nicely positions our practice to take advantage of potential artificial intelligence algorithms capable of extracting deeper insights and correlations. In this coming paradigm shift, we'll have even more advanced analytics that will further elevate and individualize patient care.

Dr. Schneider is a vitreoretinal specialist with Tennessee Retina. His clinical and research expertise and interests include diseases of the vitreoretinal interface and novel applications of ophthalmic imaging technology.

With OCT, Quality Matters *continued from page 6*

"A single horizontal line scan that intersects the fovea may appear normal, but if the imager also scans vertically, pathology above and below the fovea may be found."

BETTER TECHNOLOGY CALLS FOR BETTER TRAINING

With the advent of newer technology that allows for more data and faster scans, it is imperative that the imager have proper training to ensure a knowledge base that can be relied upon to make the decisions that lead to correct diagnosis and treatment plans.

Constant vigilance and communication on the part of both the imager and the clinician is critical to success.

WHAT MAKES A GOOD IMAGER?

The OCT imager must possess certain qualities to ensure high-quality scans:

1. Knowledge of ocular anatomy
2. Understanding of the effect of disease pathology on vision
3. Recognition of disease pathology, both anatomically and how it presents on OCT
4. Communication with the clinician
5. Constantly critiquing their images
6. Understanding of how OCT technology works
7. The desire to continue learning

Mr. Landry is the co-founder of Bryson Taylor Inc., an ophthalmic and management consulting firm, and is diagnostic imaging manager at Eyecare Medical Group in Portland, Maine. An ophthalmic photographer since 1990, he has been an expert advisor in the development of certification for OCT for the Ophthalmic Photographers' Society and has written three books on retinal imaging as well as multiple peer-reviewed articles.

THE GOLD STANDARD OF DME TREATMENT

OCT's role in the diagnosis and management of diabetic eye disease

By SriniVas R. Sadda, MD

The extent to which optical coherence tomography (OCT) has transformed how retina specialists diagnose and manage diabetic eye disease is impressive. This workhorse technology is now the gold standard for diagnosing diabetic macular edema (DME), monitoring treatment response, and determining when to re-treat. As a clinical tool, OCT is evidence-based. Its use is driven and supported by large clinical studies, many conducted by the Diabetic Retinopathy Clinical Research Network (drcr.net).

In the era of anti-VEGF therapy, we no longer decide whether to treat patients based on "clinically significant macular edema (CSME)" as seen on clinical exam, ophthalmoscopy, and fundus photographs. Instead, the CSME criterion has been replaced by whether increased retinal thickness as measured by OCT is center-involving. Once we make the decision to treat, we use OCT to monitor the response. Following drcr.net and other trial protocols, our focus is normalizing central retinal thickness on OCT to the greatest extent possible. When that is achieved, we continue to use OCT to watch for recurrence and determine the best interval between treatments.

UTILITY BEYOND RETINAL THICKNESS

OCT potentially has a role in DME management beyond assessment of retinal thickness. It identifies other retinal abnormalities that may be helpful for informing our expectations of treatment outcomes and patient prognosis. A number of potential biomarkers can be assessed.

Disorganization of the retinal inner layers (DRIL), for example, seems to be a sign that ischemia is likely present and visual outcomes may not be as good (Figure 1A).[1] OCT also shows the integrity of the outer retinal bands, i.e., the ellipsoid zone and external limiting membrane. Solid data that have been published indicate that eyes with disrupted outer retinal bands may have inferior vision recovery after treatment.[2]

Hyper-reflective spots are another OCT-visualized biomarker being evaluated for prognostic value.[3] Commonly, these spots or dots are evidence of lipid exudates. When we see a significant number of such exudates, especially if they're tracking toward the foveal center, we increasingly interpret it as a negative prognostic sign. Furthermore, hyper-reflective spots are a reminder to make sure the patient is working with his or her internist on lipid level control. It has also been theorized that even very small hyper-reflective spots may be significant, possibly indicating activated microglia or migrating RPE cells, and/or markers of inflammation.

Larger prospective trials will determine just how closely DRIL, disruption of the outer retinal bands, and hyper-reflective spots are associated with poorer visual outcomes and less-than-desired response to anti-VEGF therapy and how we should use the findings in day-to-day practice.

Other OCT biomarkers, such as diffuse vs. focal/cystoid DME and the presence of subretinal fluid, were previously thought to be relevant to how an eye would respond to therapy. However, they haven't proved to be important in terms of anti-VEGF therapy or how patients should be managed.

OCTA: A NEW FRONTIER

OCT angiography (OCTA) is one of the newest diagnostic technologies available to retina specialists, and it will likely prove to be of value in the realm of DME. For example, OCTA can detect lesions relevant to DME, such as microaneurysms.

That said, it's important to note that we can't rely on OCTA alone in cases where part of the plan is to treat with focal laser. First, not all microaneurysms are visible, only a subset. There's indication that the more hypo-reflective microaneurysms visible on structural OCT are less likely to be detected on OCTA.[4] Second, OCTA doesn't discern which microaneurysms are leaking. Therefore, it doesn't indicate which ones to treat.

OCTA can be a potent and useful tool for evaluating macular ischemia, which is quite relevant given what we know about DRIL, which leads us to suspect it. OCTA has shown us that ischemia may involve different retinal layers (Figure 1B-C). Following its extent may be useful from a prognostic standpoint.

Finally, OCTA appears to be much more sensitive than fluorescein angiography for assessing macular perfusion. This is likely to be very helpful as we collectively continue to monitor what impact anti-VEGF therapy may or may not have on macular perfusion.

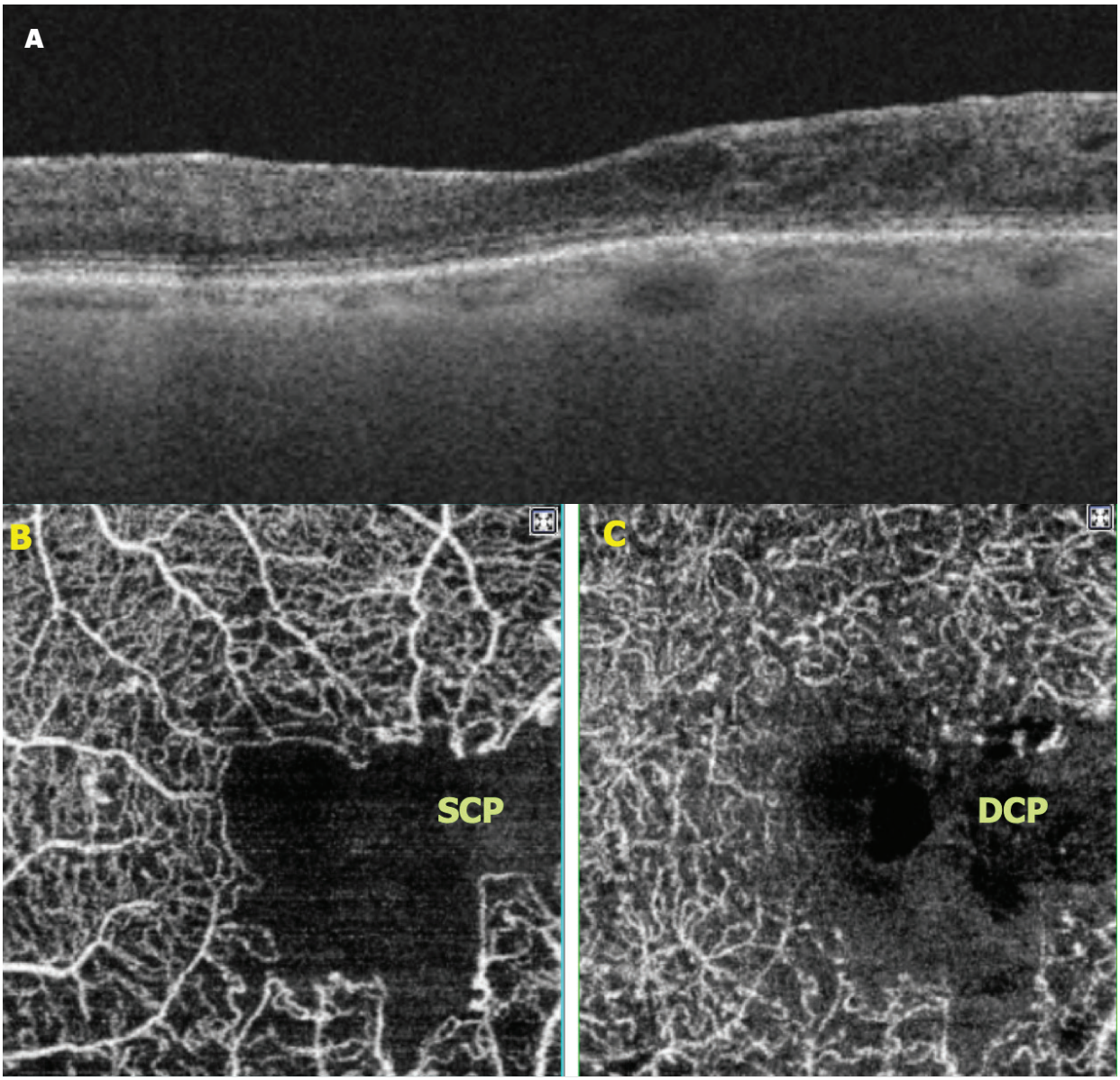

Figure 1. Spectral domain OCT B-scan (**A**) of a 74-year-old patient with diabetic retinopathy with evidence of disorganization of the retinal inner layers (DRIL). Note that to the right of the foveal center adjacent to the cystoid spaces, there is poor delineation of the retinal layers consistent with DRIL. OCT angiography of the macula shows extensive capillary nonperfusion in both the superficial capillary plexus (**B**) and deep capillary plexus (**C**).

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TODAY'S OCT PLATFORMS DRIVE PERSONALIZED AMD CARE

OCT is helping retina specialists improve their diagnostic ability in this critical area

By Peter A. Karth, MD, MBA

Optical coherence tomography (OCT) has so revolutionized the diagnosis and management of age-related macular degeneration (AMD) that it is now not only standard of care but also the foundation of personalized care for our patients.

Per our current diagnostic paradigm, we rely on OCT to detect and measure intraretinal and subretinal fluid and pigment epithelial detachments, i.e., all the markers of active choroidal neovascularization (CNV). OCT data informs treatment strategies and response to medications. It's my firm opinion that the OCT-guided approach has led to earlier detection and better outcomes. Furthermore, as we choose from among an increasing array of anti-VEGF medication options and adopt today's treatment protocols—primarily treat and extend—OCT allows us to evaluate the aggressiveness of each patient's CNV, which guides us to more precise, personalized treatment plans.

What treatment interval we set, and when and by how much we can extend it, are questions we can only fully answer with OCT.

OCT IN PRACTICE

In my practice, ensuring I'm using this crucial technology to its fullest potential for the benefit of my patients means adhering to the following practices.

• **OCT in both eyes, every visit.** I order bilateral OCT scans at every visit for all AMD patients I'm monitoring, which are those with higher-risk dry AMD and those with CNV in at least one eye. This includes "injection-only" visits. This allows me to monitor incremental response to treatment and pick up any fellow-eye changes as soon as possible. I'm amazed by the number of patients I'm following who develop fellow-eye CNV early in the middle of a series of injections. For me, the goal is to find and treat any new or recurring lesions before symptom manifestation.

"It's my firm opinion that the OCT-guided approach has led to earlier detection and better outcomes."

• **Complete image review.** It's ideal to look at every slice that composes the OCT macular cube scan so that the entire macula is evaluated. Doing so commonly reveals lesions that are out of the central subfield, and which wouldn't have been seen if only one or two cross-sections through the macula were viewed. Being aware of these lesions allows me to treat them before they extend into the fovea and cause vision loss.

In today's era of anti-VEGF therapy, I believe it's substandard to view a printout of just one slice through the macula when evaluating a patient, although resources can sometimes dictate that. Also, OCT elevation maps often don't pick up small changes that should be addressed.

• **Treat until the macula is dry.** In AMD, good visual acuity over time is an end goal. Tactically, complete resolution of fluid in the macula is most important for dictating my treatment plans. The expanding anti-VEGF medication armamentarium is making complete resolution more possible than ever. Some retina specialists may consider some amount of subretinal fluid to be acceptable and not detrimental to a patient's current or future vision, but I only feel comfortable when the macula is dry, which is wholly guided by OCT.

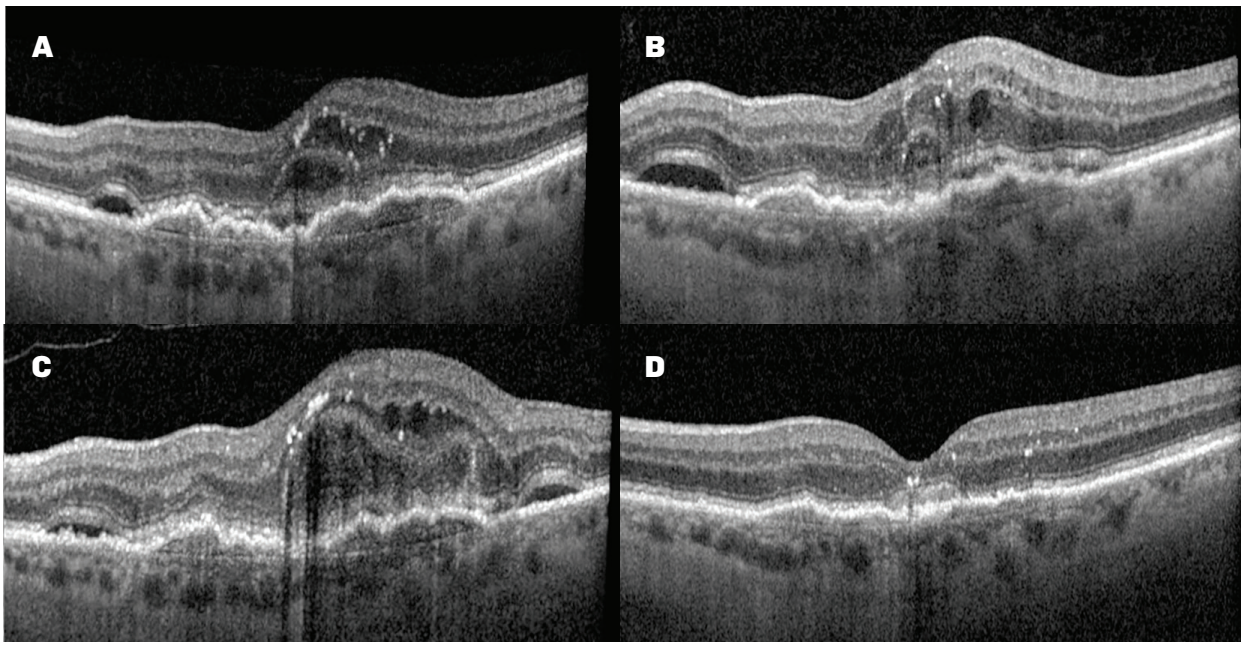


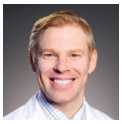
Figure 1. OCT is crucial for evaluating the need to switch treatment. Although vision remained stable in the near term, this monocular patient with wet AMD exhibited a poor response to multiple monthly injections of an anti-VEGF agent, images A-C. One injection of a different anti-VEGF agent yielded significant improvement and macular drying, image D.

• **Use OCT to engage patients in their care.** OCT is an amazing patient education tool. I show my patients images at every visit. It helps them to understand their condition and goes a long way toward convincing them they need treatment when they do. This is increasingly important as we follow the evidence that leads us toward recommending treatment earlier, often before patients are aware of any symptoms. Walking patients through their OCT images illustrates for them improvement over time, which eases their minds and nurtures trust, and usually makes them more amenable to injections.

• **Use image management and analysis tools.** By now the majority of retina specialists are using OCT imaging software to review images, which typically includes the ability to register images from two different timepoints. However, more powerful tools have emerged. For example, the platform from ZEISS includes FORUM, which enables access to exam data from all DICOM-compliant diagnostic instruments in one place. The platform also includes Retina Workplace, which goes well beyond being an image repository to being a retinal data center, providing insights that can be used to improve patient care. Workplace automatically analyzes and overlays imaging data in new ways. For instance, aspects of OCT images, such as central subfield thickness, are graphed over time for at-a-glance trend recognition. Visit history charts allow visualization of the efficacy of different treatments over time. Images can be dragged and dropped to quickly compare OCT raster scans and cubes, fluorescein angiography and fundus images across multiple visits, and injection data can be annotated and integrated with OCT data.

• **Get familiar with OCTA.** As the newest application of OCT technology, OCT angiography (OCTA) has not taken root yet as the standard of care, but its potential importance in AMD diagnosis and management is large. OCTA gives us the ability to visualize and monitor the retina blood vessels directly, watching for changes that could be happening independently of changes in our surrogate markers of disease activity. As such it will add new, valuable information to our decision-making. The more we educate ourselves on a daily basis on the use case for OCTA, the better off we'll be in the future.

In the meantime, by capturing structural OCT data frequently and making use of cutting-edge image management and analytics tools, we can make the most informed and personalized treatment decisions for each of our AMD patients.



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THE INTEGRAL ROLE OF OCT IN MANAGEMENT OF MACULAR HOLE

OCT surpasses clinical exam as the most sensitive way to diagnose FTMH

By Christina Y. Weng, MD, MBA

Optical coherence tomography (OCT) has improved retina specialists' ability to manage full-thickness macular hole (FTMH) in multiple ways. OCT enables definitive diagnosis, aids surgical planning, and provides information that may prognosticate postoperative outcomes.

PREOPERATIVE OCT

OCT has surpassed clinical examination as the most sensitive way to diagnose FTMH. Based on slit lamp examination and indirect ophthalmoscopy alone, FTMH can appear similar to lamellar hole, pseudohole, or vitreomacular traction (VMT). It's crucial to utilize OCT to differentiate between these distinct entities because they are managed with vastly different approaches. As I instruct trainees who work with me in our program, it is also very important—regardless of which OCT machine is used—to review all captured images. When only single-line raster scans are reviewed, small macular holes can be overlooked.

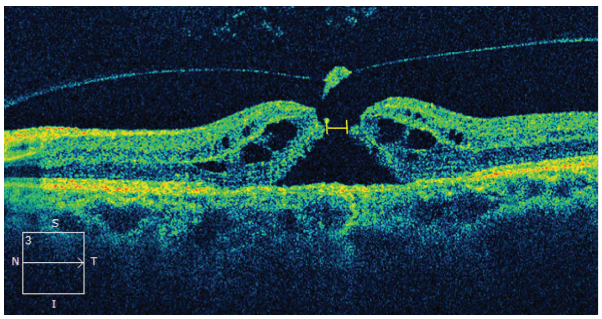

Image courtesy of Christina Y. Weng, MD, MBA

Figure 1. Based on minimum linear dimension, the OCT caliber function (yellow bracket) indicates a medium-size full-thickness macular hole. Overlying posterior vitreous detachment with operculum is also seen. Cystoid macular edema and slight lifting can be observed at the hole edges. These features are thought to predict a greater likelihood of closure following surgical repair.

Once FTMH is diagnosed, OCT enables precise measurement of the hole's size. Size affects treatment decision-making and is one factor that informs visual and anatomic prognosis. [International Vitreomacular Traction Study Group size classification: small (<250 µm), medium (250-400 µm), large (>400 µm).][1]

SURGICAL PLANNING AND EXECUTION

OCT should also be used prior to FTMH surgery to confirm the presence or absence of persistent VMT, a key consideration in surgical planning. Even when there appears to be a complete posterior vitreous detachment on clinical examination, I find that patients with cortical vitreoschisis may still have partial attachment of the hyaloid face to the underlying retinal surface. This presents the risk of the surgeon inadvertently peeling tissue other than the internal limiting membrane (ILM) during FTMH surgery, which detracts from the likelihood of success. (I peel the ILM in every FTMH surgery regardless of the hole's size, but there is some data to suggest that outcomes may not differ with or without ILM peeling for smaller FTMH.[2])

Three-dimensional volume scans are particularly helpful for determining the extent and location of vitreous adhesions to the retina. When OCT reveals VMT, the surgeon knows to elevate the hyaloid before initiating ILM peeling.

OCT can also alert the surgeon to the presence of epiretinal membrane, which can occur concurrently with FTMH and must be removed prior to ILM peeling. OCT may also be helpful in guiding the surgeon to the most efficacious place to begin the peeling process. Intraoperative OCT is a relatively new technology that can be used to guide surgeons through these aspects of the procedure in real-time.

My preferred treatment for FTMH is pars plana vitrectomy with ILM peeling and gas tamponade; however, other options, such as ocriplasmin or pneumatic vitreolysis with air or gas, can be considered. Especially for small holes with persistent VMT, these other options may be effective and spare the patient a surgical procedure.

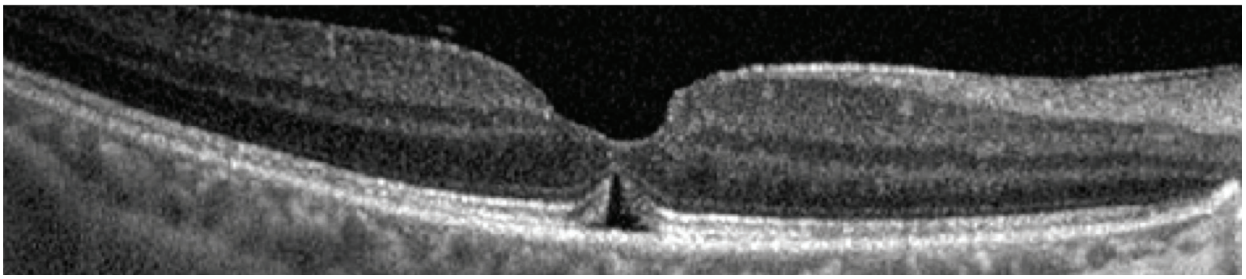

Image courtesy of Nitish Mehta, MD

Figure 2. One month after pars plana vitrectomy, internal limiting membrane peel, air-fluid exchange, and gas tamponade for repair of full-thickness macular hole, OCT confirms anatomic closure of the hole along with a subfoveal lucency that is often seen during the early postoperative period and typically not a concern.

PROGNOSTIC CLUES

While the postoperative closure rate of FTMH in general has been reported to be greater than 90%, visual acuity (VA) outcomes following closure can be more variable. OCT-measured FTMH size is one factor that may affect postoperative visual acuity. Smaller holes tend to have a higher probability of closure postoperatively, and they also seem to have better VA outcomes.[3]

Aside from FTMH size, another preoperative OCT finding that may be associated with the likelihood of a FTMH to close is a slight lifting of the hole edges with the presence of cystoid macular edema (Figure 1).

For reasons not completely understood, patients with these findings tend to have better closure rates. One theory is that these findings indicate a hole of shorter duration.

POSTOPERATIVE OCT

Postoperative OCT findings can also help to explain patients' VA. Loss of integrity of the ellipsoid zone and outer retina layers can be a limiting factor[4,5] and a decrease in inner macular volume has been shown to correlate with a decrease in VA.[6] On the other hand, after hole closure, it is not uncommon for OCT to show a small pocket of subretinal fluid or subfoveal lucency (Figure 2). This generally resolves with time and does not seem to correlate with worse visual outcomes.

Interpretable OCT images can be obtained as early as postoperative day 1, even if gas tamponade is present. While I tend to wait until week 1 or month 1 to order a repeat OCT, day-1 scans can be useful. For example, FTMH may close as soon as the next day after surgery, and some surgeons use postoperative day-1 OCT findings to guide how long to position the patient face-down.[7,8] Surgeons who use ILM or retinal free flaps in repairing FTMH may also find postoperative day-1 OCT beneficial in ensuring proper localization of the adjuvant tissue.

Finally, it is worthwhile to mention that I personally find both preoperative and postoperative OCT images to be invaluable for patient education and motivation. Showing patients their OCT images truly helps them to understand their condition, the need for treatment, and the potential outcomes more fully.

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